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HORSESHOE KIDNEY: CASE PRESENTATION AND LITERATURE REVIEW

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Abstract

The horseshoe kidney (HSK) is the most frequent renal fusion anomaly characterized by malposition, malrotation and/or vascular anomalies of the kidney. It's incidence is 1:400-600 with a male predominance (male: female= 2:1) and it can be associated with other genitourinary, gastrointestinal, cardiovascular or musculoskeletal malformations. Though it has been reported some familial aggregation and it can be found associated with different chromosomal anomalies, the majority of the cases are sporadic. ***The aim*** *of this paper is to present a case of incidentally identified HSK and describe the main characteristics of this anomaly based on literature review.*

Case presentation. *49-year old female patient was admitted to the Emergency Unit with significant abdominal pain in the right hypochondrium and right flank which began >8 hours previously to presentation. The patient's own medical history included cholecystectomy, well treated hypertension, two ischemic right cerebral vascular attacks with left spastic hemiparesis and antiphospholipid syndrome diagnosed in 2013 without chronic anticoagulation therapy. Her vital signs at the presentation were stable; laboratory evaluation revealed leukocytosis with a white blood cell count of 15500 thou/µl, platelets 274000 thou/ µl, normal renal function (serum creatinine 0.79 mg/dl). The abdominal ultrasound was negative for urolithiasis, hydronephrosis or genitally modifications so contrast-enhanced computed tomography (CT) was performed. This revealed the presence of a HSK: the lower poles of the right and left kidney were fused by a parenchymal isthmus located at L3-L4 level anterior to the abdominal aorta and inferior vena cava. The U shaped renal structure was asymmetrical, the right arm being larger than the left. On the CT examination a triangular hypodense lesion was described at the level corresponding to the right lower renal pole visible on both venous and arterial phase suggestive for renal infarction. No vascular anomalies were detected.*

As the patient presented late after the onset of symptoms, revascularization was overdue, and the patient was admitted to the Nephrology Compartment. Pain relievers, antibiotics and anticoagulation therapy was initiated. Considering the antiphospholipid syndrome immunologic markers (antinuclear antibody, anti-double stranded DNA antibodies) were determined; all negative. During hospitalization the renal function was monitored, without serum creatinine elevation or other complications so after 7 days the patient was discharged with referral for immunologic/hematologic evaluation to determine the etiology of the antiphospholipid syndrome. For the HSK nephrologic reavaluation was programmed after 1 month but the patient did not showed for this appointment.

Conclusion. *The renal infarction was most probably due to the antiphospholipid syndrome, the radiologic investigations incidentally identified a HSK. Physicians must be aware of this condition and its clinical implications.*

Keywords: horseshoe kidney, renal fusion anomaly, renal infarction

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Abnormalities of the genitourinary tract are among the most common birth defects. First described in the 16th century by da Carpi as an autopsy finding, the horseshoe kidney (HSK) is the most frequent fusion anomaly (90%) of the kidney.

The aim of this paper is to present the case of a female patient with incidentally identified HSK and to describe the most important anatomic and clinical aspects of this anomaly based on literature review.

Case presentation. 49-year old female patient was admitted to the Emergency Unit with significant abdominal pain in the right hypochondrium and right flank which began >8 hours previously to presentation. The patient's own medical history included cholecystectomy, well treated hypertension, two ischemic right cerebral vascular attacks (2008, 2013) with left spastic hemiparesis and antiphospholipid syndrome diagnosed in 2013 without chronic anticoagulation therapy. Her vital signs at the presentation were stable (TA 140/75 mmHg, SaO_2 95% without O_2 mask); laboratory evaluation revealed leukocytosis with a white blood cell count of 15,500 thou/µl, platelets 274,000 thou/µl, normal renal function (creatinine 0.79 mg/dl). The abdominal ultrasound was negative for urolithiasis or hydronephrosis so contrast-enhanced computed tomography (CT) was performed. This revealed the presence of a HSK (Figure 1): the lower poles of the right and left kidney were fused by a parenchymal isthmus located at L3-L4 level anterior to the abdominal aorta and inferior vena cava. The U shaped renal structure was asymmetrical, the right arm being larger than the left. Due to this unequal form, the left kidney position was abnormal : the upper pole was situated lateral to the L2 vertebra. No supranumeral renal arteries or other vascular anomalies were described.

On the CT examination a triangular hypodense lesion was disclosed at the area corresponding to the right lower renal pole visible on both venous and arterial phase (Figure 2) as well on arterial reconstruction (Figure 3) suggestive for renal infarction. As the patient presented late after the onset of symptoms, revascularization was overdue, and the patient was admitted to the Nephrology Compartment. Pain relievers, antibiotics and anticoagulation therapy (low molecular weight heparin followed by acenocumarol) was initiated. Considering the presence of antiphospholipid syndrome immunologic markers (antinuclear antibody, anti-double stranded DNA antibodies) were determined; all negative. During hospitalization the renal function was monitorized, without serum creatinine elevation or other complications so after 7 days the patient was discharged with referral for immunologic/haematologic evaluation to determine the etiology of the antiphospholipid syndrome. For the HSK nephrologic reavaluation was programmed after 1 month but the patient did not showed for this appointment.

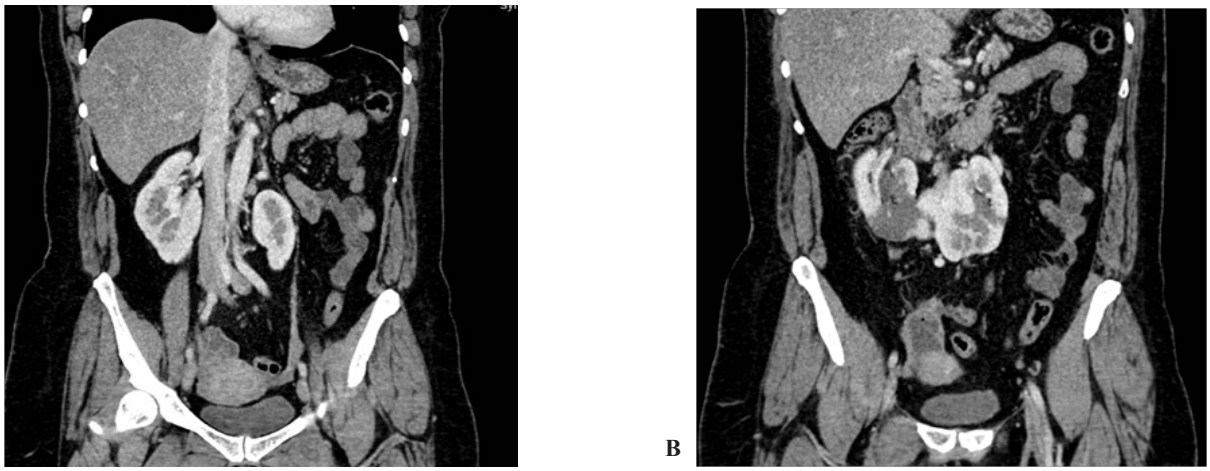
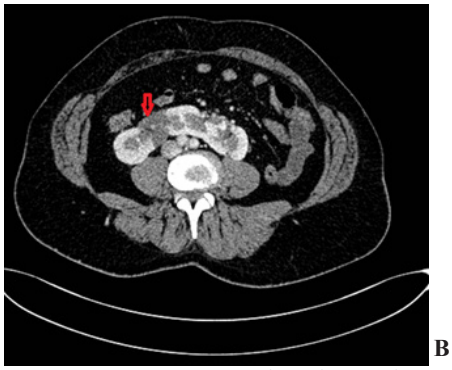


Figure 1. Two coronal CT section. A. low positioned left kidney; B. parenchymal isthmus connecting the two lower renal poles resulting in HSK.



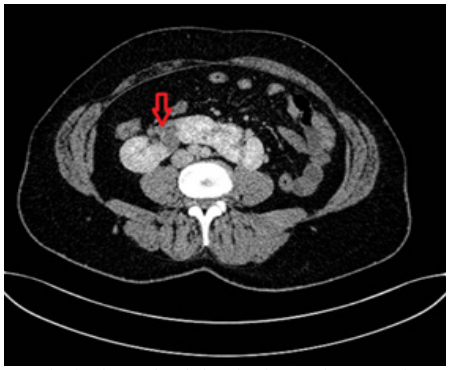


Figure 2. Two transverse CT section. The HSK located anteriorly the main abdominal vessels. Hypodense lesion (red arrow) described on both arterial (A) and venous (B) phase suggestive for renal infarction.

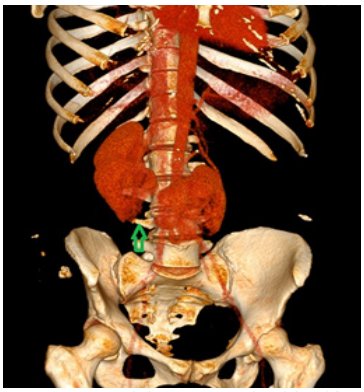


Figure 3. Arterial reconstruction identifies an avascular zone corresponding two the hypodense lesion described previously

Discussion, literature review

The HSK represents approximately 90% of all renal fusion malformation characterized by malposition, malrotation and/or vascular anomalies of the kidney. Most frequently the two lower renal poles are fused by an isthmus formed by functional renal parenchyma or connective tissue. Generally, the HSK is asymptomatic and is identified only during imagistic investigations/ autopsy. However due to the fact that it can be associated with other malformations (genitourinary, gastrointestinal, cardiovascular, musculoskeletal) or it can contribute to complications, physicians should be aware of this condition.

Epidemiology

Initially the incidence of HSK was based on autopsy studies on small patient number conducted sixty-fifty years ago and was reported between 1:400 - 1:600 with a male domination (male: female ratio: 2:1) [1]. Later, the broad availability of imagistic techniques (computed tomography-CT, ultrasound-US, urography) offered information from a larger number of patients (Weizer et al. published an incidence of 1:666 after analyzing 15320 abdominal CT and US, Glodny et al. reported different incidence by the evaluation method- 1:708 for abdominal US and 1:474 for abdominal CT) but the overall incidence does not differ significantly from the autopsy based data [2,3]. Although it has been reported some familial aggregation and it can be found associated with different chromosomal anomalies, the majority of the cases are sporadic [4].

Embriology

The development of the kidney is a complex process; it begins in the 4th gestational week due to the mutual induction between the ureteric bud and the metanephric blastema. During the next weeks (till 8th -9th gestational week) the embryonic kidney undergoes an ascending process to its' final location (the renal fossa) and an axial rotation of 90° so the initially anteriorly positioned renal hilum becomes medial.

The exact mechanism of development of renal fusion anomalies is not fully understood; different theories regarding the formation of the HSK were presented. According to the mechanical theory the two kidney metanephric blastema come in contact during the early embryonal period due to abnormal flexion/ growth of the vertebral column or abnormal position of the ombilical arteries. As the renal capsule is absent at this moment the two osculant metanephric blastema fuse resulting the formation of fibrous isthmus. The inferior mesenteric artery represents a barrier in the ascending process consequently the isthmus is trapped under this artery (at L3-L4 level), arresting further ascent and rotation resulting in a malpositioned kidney and an anteriorly faced renal hilum. The teratogenic theory is based on the migration anomaly of the posterior nephrogenic cells resulting the formation of a parenchymal isthmus. This theory is supported by the fact that the risk of developing renal cancer is greater in the HSK than in normal kidney. The *genetic theory* suggests that different genetic factors may play a role in developing HSK and it is based on the occurrence of this fusion anomaly among siblings or twins. Additionally, HSK is more frequent in different chromosomal anomalies like Down syndrome, Turner syndrome (approximately 7% have HSK), Edward syndrome (20% have HSK) and Patau syndrome. However, further research is needed to unveil the possible genetic mechanisms contributing to the development of urinary system anomalies [1,5-7].

Anatomy-morphology

The HSK can be located anywhere along the ascending path of the developing kidney; however the most frequent position is at level L3-L5 under the origin of inferior mesenteric artery. It is positioned anteriorly to the vertebral column and the major abdominal vessels (inferior vena cava and abdominal aorta).

In 90% of the cases the two lower renal poles are fused forming an U or L shaped structure. The U shaped structure results from the midline fusion of the kidneys located symmetric on the lateral side of the vertebral column. The L shaped HSK results from the fusion of two asymmetric located kidneys (one horizontal, one vertical) resulting in a structure with two unequal arms (the left dominant is more common) and a laterally deviated isthmus. Rarely the upper poles are involved in the fusion process resulting an inverted U shape HSK. The isthmus can be functional parenchima or fibrous tissue [1,4,8].

The lack of rotation is responsible for the abnormal position of the renal hilum (it remains anteriorly not medial), consequently the ureteropelvic junction lies higher than the normal and the ureter usually crosses the anterior surfaces of the isthmus.

There is a great variabily in the arterial vascularization of the HSK, it can be supplied by normal renal arteries (RA) and/or accessory RAs (entering the renal hilum) and/or aberrant arteries originated from different level of abdominal aorta or iliac vessels and entering directly one of the poles or isthmus. The incidence of supranumerary renal arteries is high even in normal kidney (28-30%), but in HSK it is significantly higher: cadaveric or imagistic studies reported incidence between 81-92%, the mean renal arteries being 3.87-3.9/ HSK [9].

Considering that the vascular pattern represents clinical implications during different surgical interventions (abdominal aorta aneurysm reparation, HSK separation surgery) classification systems were elaborated which summarize this diverse system: *Papin et al. (1924)* autopsy study on 139 HSK represents the first classification; later *Graves et al. (1969)* divided each kidney in 3 segments (upper-U, middle-M, lower-L, the isthmus corresponding to the lower poles) and described 6 vascular types based on the origin of renal vessels (Table I) [1,4,9].

Table I. Different classification systems regarding the HSK arterial vascular pattern.

HSK's vascular pattern classification system	
By Papin et al	
Type 1	one renal artery for each kidney
Type 2	three to five renal arteries (most common variant-66%)
Type 3	more than five renal arteries
By Graves et al.	
Type A-normal pattern	The U, M, L segments of each kidney supplied by the "normal" RA
Type B	The U, M segments supplied by the "normal" RA, the L segments supplied by a direct, symmetrical branch from abdominal aorta
Type C	The U, M segments supplied by the "normal" RA, the L segments supplied by a direct branch from abdominal aorta, the two supranumerary arteries arise with a common trunk
Type D	Each segments supplied by a renal artery originated directly from the abdominal aorta
Type E	Type D+ the isthmus is also supplied by arteries originated below the HSK but from abdominal aorta
Type F	Type D+ the isthmus is also supplied by arteries originated below the HSK from iliac vessels

Besides arterial variations, venous anomalies were described in HSK patients. A study elaborated by *Ichikawa T* on 105 patients reported venous modifications in 24 (22.9%) of them consisting of supranumerar (2, 3) or abnormal positioned (circumaortic or retroaortic) renal veins. Moreover in HSK patient inferior vena cava (IVC) anomalies occur more often (3.9-5.7%) than in normal patients and can manifest in various form: double IVC, left positioned IVC or IVC located anterior the isthmus [1,10].

Complications

Although the HSK is generally asymptomatic (30% of cases) and often it is only an incidental finding during imagistic evaluations, due to the abnormal position and malrotation complications, especially urological complications can occur. Multiple factors lead to the development of the urological complications: high insertion of ureter into the renal pelvis, the ureter trajectory which crosses anteriorly the isthmus and possible intersections between the ureter and aberant vessels [11]. In a study elaborated by B-Kyung Je 46.1% of the 380 investigated HSK cases presented renal complications, most frequently ureteropelvic junction obstruction, vesico-ureteral reflux, lithiasis and urinary tract infections developed [12]. A meta-analysis by Pawar et al. reported an estimated incidence of 36% for nephrolithiasis in HSK; calcium based stones being the most common type [13]. The management of nephrolithiasis in HSK patients due to the abnormal anatomy can be challenging, however multiple urological techniques (extracorporeal shockwave lithotripsy, percutaneous nephrolitothomy and ureteroscopy) were applied with good result but with slightly higher complication rate or need for secondary procedures compared with normal kidney [14-16].

Beside urological complications there is also a greater risk for renal lesion during trauma (the protective effect of ribcage is missing) and certain renal malignancies have a higher incidence [11]. Though the renal cell carcinoma is the most common malignancy in HSK (45%) its incidence doesn't differ from normal kidney. Transitional cell carcinoma occurs in 28% of the malignancies in HSK, and has a 3-4 fold higher incidence than in normal kidney. This can be explained by the hydronephrosis, infections and nephrolithiasis associated with HSK. Wilm's tumor develops twice as frequently in HSK than in normal kidney, and it is located predominantly to the isthmus; this can be explained by the teratogenic event that proceeds during kidney development. Carcinoid tumor is rare, but the relative risk is 62 times higher than in normal kidney; similar to Wilm's tumor is affect predominantly the isthmus because the presence of neuroendocrine cells within the metanephric blastema [6,11].

Conclusion

The HSK represents the most frequent fusion anomaly of the kidney. In general it is an incidental finding during imagistic evaluations. However due to the possible complications and the higher risk for malignancies, it requires medical follow up.

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A RARE CASE OF TOTAL DIVERTICULAR HEMORRHAGE SHOCK

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***Mihart Bianca, Mitre Andrei Otto, Bartoș Dana Monica, Bartoș Adrian and Mitre Călin Iosif have contributed equally to this case report; in consequence they are all principal authors.**

Abstract

Colonic Diverticulosis (CD) is a disease caused by the presence of multiple diverticula in the colon. Because various colonic arterioles penetrate the diverticulum and also irrigate the dome of the diverticulum, they can suffer structural changes leading to vessel disruption and further to hemorrhage. Diverticular hemorrhage represents a complication of CD, which in rare cases might lead to total diverticular hemorrhage and hemorrhagic shock.

A 62 years man presented to the emergency service with melena and hematochezia. He was known with duodenal ulcer and gastritis. A colonoscopy was performed and various diverticulum were discovered but, no precise source of bleeding was found.

The melena ceased and the patient was prepared for another colonoscopy by ingesting Fortans. After 1L of Fortrans the patient had a hemorrhagic shock and an emergency surgery was performed. During the surgery it was discovered that the hemorrhage was pancolonic and all the diverticulum were bleeding. Accordingly, he suffered a total colectomy with right flank ileostomy. After surgery the recovery was complete, with no complications.

CD is a disease caused by the presence of multiple diverticula in the colonic wall. CD can be treated and also prevented with a high fiber diet.

Increased pressure in the weakened walls is involved in development of diverticula. With age, the myenteric plexus is degraded leading to uncoordinated contractions, resulting in an increased pressure level. Genetics also play an important role in the development of diverticulitis due to a specific gene TNFSF15 SNP rs7848647 which was linked to the development of diverticula. Other factors that have been suggested to lead to diverticulitis are red meat diets, sedentary lifestyles, smoking and nonsteroidal anti-inflammatory medication. It is usually a harmless disease, but it's complications can lead to serious problems like diverticulitis and diverticular hemorrhage.

This rare case, shows that total diverticular hemorrhage should also be taken into consideration because this complication could easily lead to fulminant death.

Keywords: colonic diverticulosis, hemorrhagic shock, total colectomy

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Introduction

Colonic diverticulosis (CD) is a disease caused by the presence of multiple diverticula in the colon wall [1]. Diverticula are formed by several diverticulum, which are small pouches protruding from the colon's wall. There are two types of diverticula: true diverticula (TD) and false diverticula or pseudodiverticula (FD). FD are formed only by the mucosa and submucosa and are protruding through the muscular layer, being covered only by serosa, whereas TD are composed by all the layers of the intestinal wall [2,3]. In the case of CD it is possible for both forms of diverticula to exist. TD are specific for the right colon's diverticulosis while FD are specific for the left colon's diverticulosis [4].

Although it was believed that CD is caused only by lack of fibers in the diet, which creates high pressure in the colonic wall, there were also other factors discovered that may cause CD, such as colonic motility and its structure, microbiota and genetic factors [5].

In many cases the patients are unaware of their condition until it is discovered by accident during other medical investigations such as colonoscopy, so it is usually an asymptomatic disease. However, there are also some patients who suffer from CD and may have signs of cramping, bloating, flatulence or constipation [6]. Because CD's symptoms are similar to other diseases like appendicitis, ovarian cyst, ectopic pregnancy, Crohn's disease or colon cancer, it is important to make further investigations like: barium enema (BE), computer tomography colonography (CTC), computer tomography (CT), but the gold standard for diagnosing CD is colonoscopy [7]. By using these methods we can give a positive diagnostic for CD [3,8,9].

CD can be treated and also prevented with a high fiber diet. CD is a harmless disease, but its complications can lead to serious problems like diverticulitis and diverticular hemorrhage [3,10].

Case presentation

A male patient, age 62 was sent from another hospital to our emergency service with the diagnosis of hemorrhagic shock, duodenal ulcer, erosive gastritis, erosive bulbitis after non-steroidal anti-inflammatory drugs (NSAID) intake. The symptomatology consisted of melena and hematochezia, which started 3 days before the patient's arrival to the hospital.

Clinical examination revealed altered general state, pale mucosa and teguments, rectal exam presented no pathological lesions of the rectal ampulla, melena with no clots on the examining glove.

Biochemical tests revealed severe anemia, pronounced thrombocytopenia, hypocalcemia, hypomagnesemia, low protein levels with hypoalbuminemia.

Emergency colonoscopy was performed, which showed multiple diverticula, but without identifying the precise bleeding outbreak, at the point of examination there were no active bleeding. Because the melenic stools have stopped, surgery was postponed in favor of blood transfusion, hydroelectrically rebalancing, gastric antisecretory and hemostatic drugs as well as antibiotics. For a precise and oriented surgical approach, Fortrans preparation of the patient was initiated. After one liter of Fortrans, the patient's general state rapidly degraded and melena reappeared and evolved with hemorrhagic shock. From 9.5 hemoglobin in 5 minutes his hemoglobin was 3; the patient lost his consciousness and he was rushed into emergency surgery room.

Management and Outcome

Emergency surgery was performed with total colectomy and terminal ileostomy on the right flank (Figure 1).

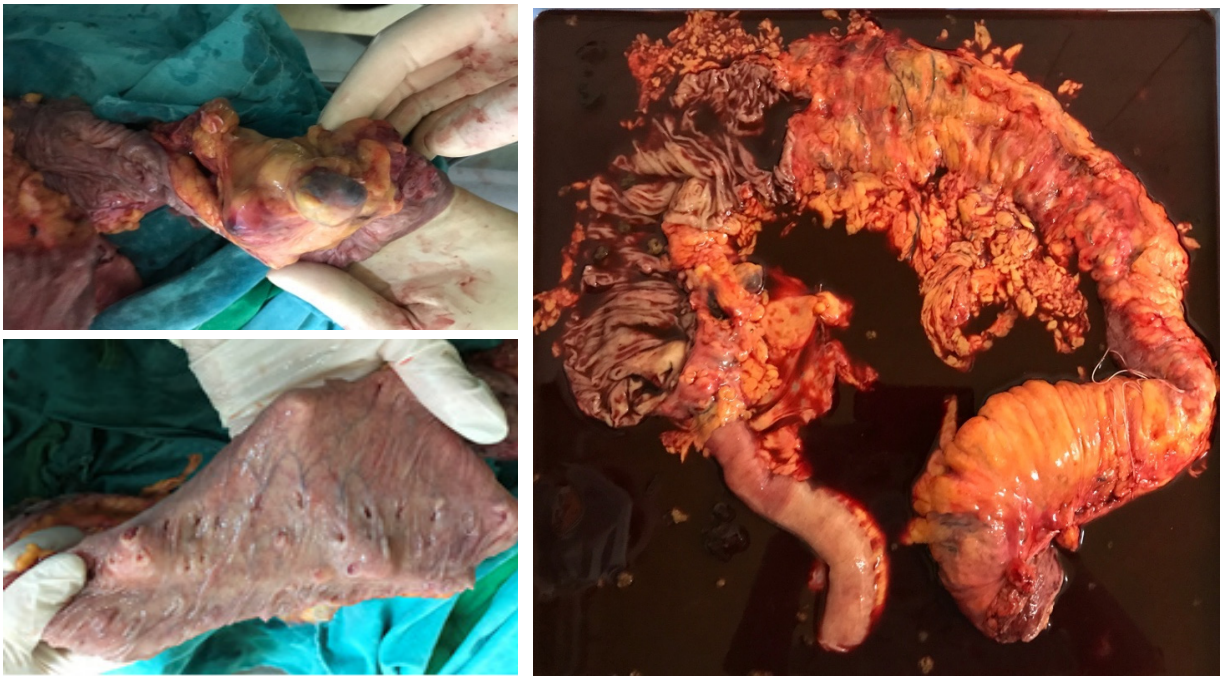

Figure 1. Postoperatory pictures taken of the resection piese. The diverticula can be observed on the entire colonic surface.

The total colectomy was necessary because the bleeding was pancolonic.

Post operatory evolution was favorable, with blood transfusions, hydroelectrically rebalancing, painkillers, antisecretory, anticoagulant drugs and antibiotics. In the second day after surgery, intestinal transit and oral feeding was resumed.

Discussion

The formation of diverticula, pouches in the colonic wall caused by an increased pressure applied on weakened intestinal walls, is leading to CD. This rise in pressure can be caused by ageing, the nervous plexuses degrading and leading to uncoordinated contraction, or a diet with a low fiber intake [9,11]. Genetics have been found to be a part of CD, as the expression of the TNFSF15 SNP rs7848647 gene was linked with the formation of diverticula. Other factors that have been suggested are red meat diets, a sedentary lifestyle, smoking and NSAID [5].

In our case, the patient had followed a NSAID which caused him gastritis and this might have been linked to the development of the disease.

The diverticular pouches are usually harmless and the patient can never develop any symptoms or even know of the existence of his disease [10]. If the pressure in the diverticula increases it will affect the arteries surrounding the dome, causing them to bleed; this causes diverticular hemorrhage and melenas [12]. In this case it is presented a rare complication of the CD, the hemorrhagic shock [13]. If is not urgently treated it can lead to fulminant death caused by blood loss. In this situation, urgent surgery to remove the bleeding segment should be performed.

Conclusions

CD is a normally harmless disease, that can be prevented by a high fiber diet and a healthy lifestyle [4,14].

A physician should always be prepared and aware that a patient presenting CD can have internal bleeding from the diverticula and even, in rare cases, present total or heavy diverticular hemorrhage and go into hemorrhagic shock.

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ORTHODONTIC TREATMENT OF GUMMY SMILE USING REVERSE CURVE OF SPEE ARCH WIRES: CASE REPORT

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Abstract

Objective. *The aim of this paper is to present the case of a 24-year-old female patient with deep overbite and excessive gingival display on smiling (5 mm) caused by supra-eruption of the upper anterior teeth treated using only reverse curve of Spee arch wires during orthodontic therapy.*

Material and method. *The orthodontic treatment sequence and biomechanical plan included bonding maxillary arch along with molars with brackets using the straight-wire technique. After 6 months of treatment, the lower arch was bonded along with molars and the same arch wire sequence was used. When enough intrusion was obtained and the gingival exposure was in the aesthetic limits (less than 1mm), leveling continued using .017x.025¨ Nickel-Titanium arch wire. To correct the lower dental midline shift, 5/16¨ inter-maxillary elastics were used for about 2 months.*

Results. *The final result achieved after the orthodontic treatment consisted of correcting the excessive overbite, aligning the teeth, coincidental dental midlines and less than 1 mm gingival exposure. After 23 months of orthodontic therapy, the patient is satisfied with her smile and follows the retention check-up.*

Conclusions. *There are several therapeutic means of correcting excessive gingival exposure, but the most efficient and easiest therapy without relapse is the one that considers the etiology.*

Keywords: gingival smile, orthodontic treatment

Introduction

Nowadays, the aesthetic requirements of the patients who address the orthodontist have considerably risen, thus determining physicians to offer particular importance not only to aligning teeth, but also to gingival morphology concerning the degree of gum exposure, gingival contour, zenith position and the presence of gingival papillae. Even though the adult patients who address an orthodontist are very compliant, they are always a challenge due to the fact that they have absent teeth or tooth wear, uneven gingival margins, atrophy of the bone and gingival papillae, satin-like and friable mucosa, gingival losses stippling aspect, thinner epithelial tissues, a reduced number of capillaries, diminished keratinization, reduced number of cells in connective tissue, increased quantity of intercellular substances, reduced blood supply, decreased oxygen consumption, which can alter the aesthetics of the result at the end of the orthodontic treatment. Thus, a complex, interdisciplinary treatment and the use of various treatment methods in children and adolescents with dental-maxillary anomalies is justified in order to improve the index of life quality. The increase of the index of life quality implies an improvement of the self-esteem, social self-esteem, performances and the global self-related current thoughts [1,2,3,4].

Excessive gingival display can be caused by a large number of factors or even a combination of these, such as: upper lip morphology, altered passive eruption, excessive vertical maxillary growth by excessive growth of the lower third of the face or lip incompetence, hereditary, congenital

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and acquired factors by altering the gingival morphology as a result of drug consumption (most frequently incriminated: antihypertensive, antiepileptic and immunosuppressant drugs), systemic causes (hormonal imbalances occurring in puberty or pregnancy), pathologic causes (leukemia), orthodontic appliances or bacterial plaque [5,6]. However, Peck et al. (1992) emphasizes that the upper lip length and the incisors crown height cannot be associated factors [7].

Variations of the upper lip morphology that can cause the gingival smile are related to upper lip length (short philtrum compared to oral intercommissural distance, average upper lip length in males is 22±2 mm and in females 20±2 mm) and hypermobile upper lip due to the hyperfunction of the elevator muscles (an apical movement of the upper lip from rest to a maximum smile of more than 9-10 mm compared to the average upper lip movement of 7-8 mm) [8].

The aim of this paper is to present the case of a 24-year-old female patient with deep overbite, excessive gingival display on smiling (5 mm) caused by supraeruption of the upper anterior teeth and treated using only reverse curve of Spee arch wires without altering the dimensions of the clinical crowns.

Patient information

A 24-year-old female patient came to our private office claiming deep overbite and excessive gingival display on smiling. The patient had no previously undergoing orthodontic treatment, medical and dental histories were noncontributory and findings from a temporomandibular joint (TMJ) examination were normal with adequate range of jaw movements.

Clinical findings

Pretreatment included extra-oral analysis, smile analysis, cephalometric analysis, radiographic examination, intra-oral analysis and functional analysis. Extra-oral analysis revealed a mezoprosopic facial form, without facial asymmetries, coincidental chin point with facial midline, straight facial profile, a normal proportion between upper facial height and lower facial height, respectively between lower facial height and throat depth, competent lips normally positioned, normal naso-labial angle and mento-labial sulcus (Figure 1). Smile analysis included incisor display at rest of 7 mm, 5 mm of gingival display, lateral tooth display from the second bicuspid to the second bicuspid, normal buccal corridors, gingival margins of the maxillary central incisors slightly more incisal in relation to the lateral incisors, present papillae, normal tooth size, proportion, shape (Figure 2), maxillary teeth retro-inclined, coincidental dental midline with facial midline, lower dental midline shifted 2 mm to the right. Cephalometric analysis (Figure 3) showed a decreased IMPA angle (77° compared to the normal value between 88°±3°) and a decreased IF angle (98° compared to the normal value of 107°), an increased proportion between posterior facial height and anterior facial height (0.77 compared to the normal value of 0.69), increased Z angle (84° compared to the normal value of 78°). Radiographic examination (Figure 4) noted missing both maxillary and mandibular third molars and several cavities treated. Intra-oral analysis revealed that the patient had a complete permanent dentition both maxillary and mandibular with absent third molars, molar and canine class I relation bilaterally, 0 mm over-jet, total overbite, M shaped and symmetric maxillary arch with slight anterior crowding and steep curve of Spee, trapeze shaped mandibular arch with moderate anterior crowding and steep curve of Spee, a good oral hygiene, a satisfactory periodontal condition (Figure 5). Regarding functional analysis, swallowing follows a normal adult pattern and the temporo-mandibular joint has an adequate range of jaw movements.

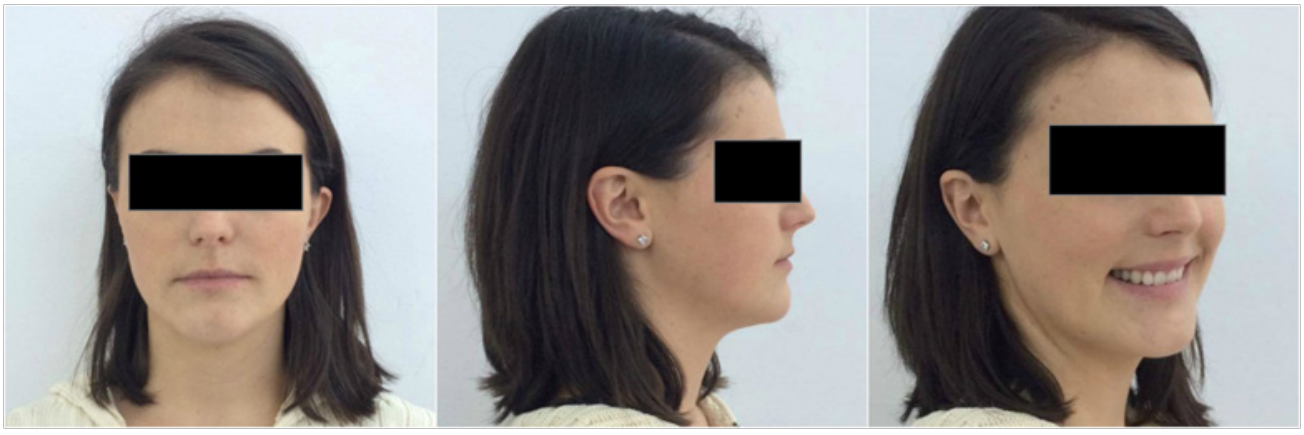

Figure 1. Initial extra-oral pictures from frontal view, lateral view and semi-profile.

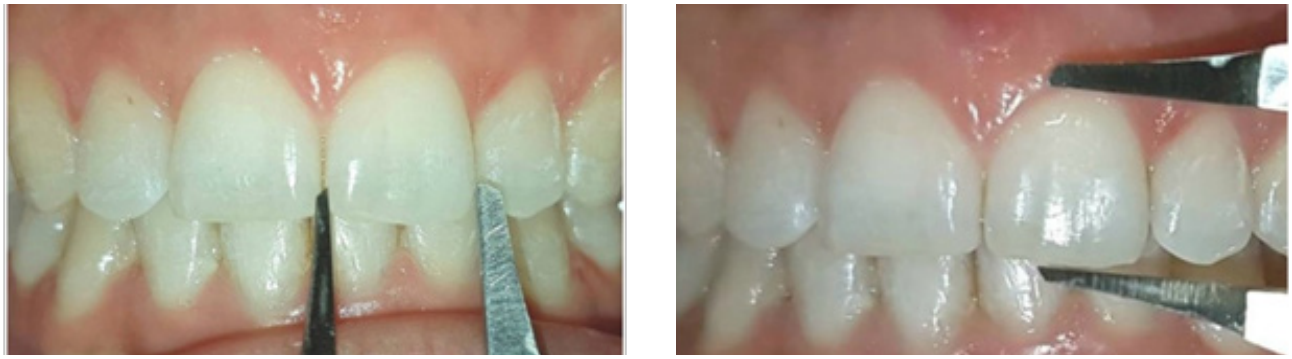

Figure 2. The golden ratio between the height and the width of the upper central incisors.

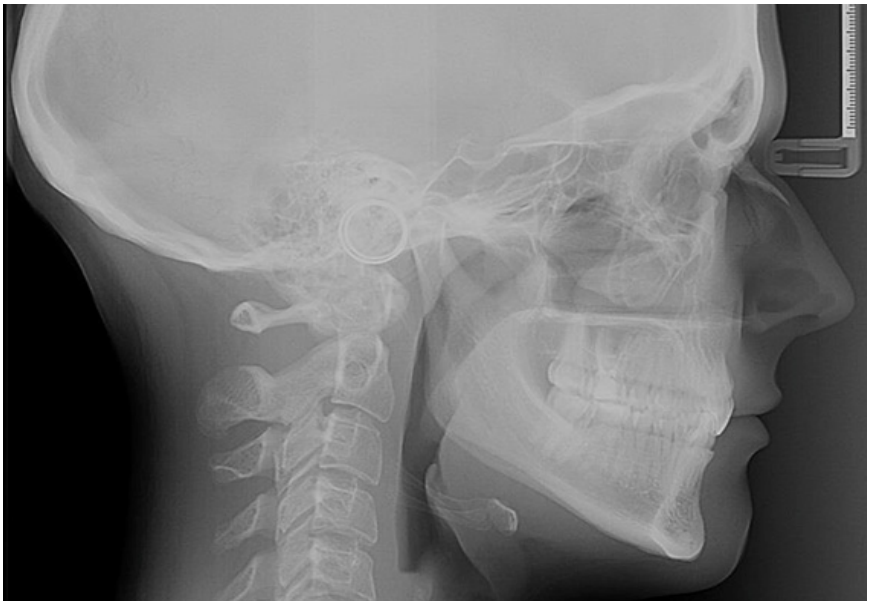

Figure 3. The cephalometric analysis.

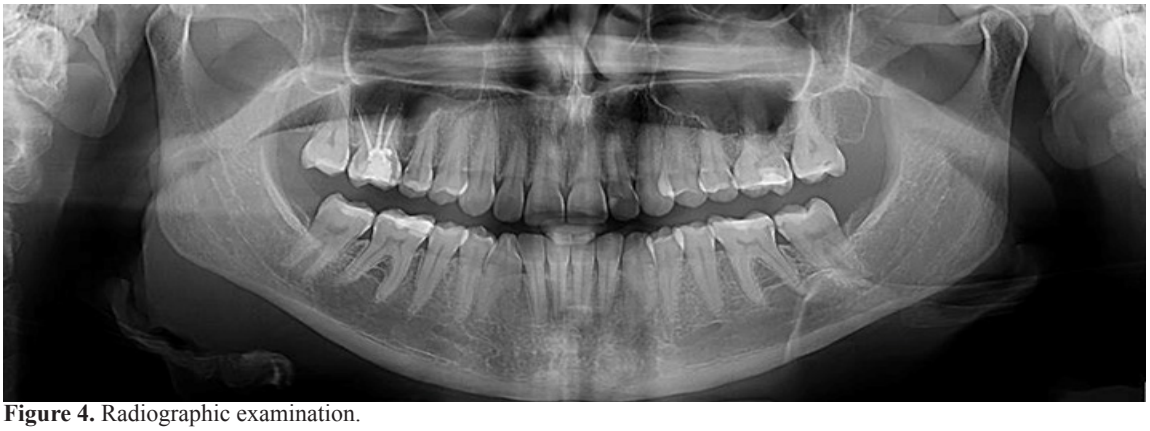

Figure 4. Radiographic examination.

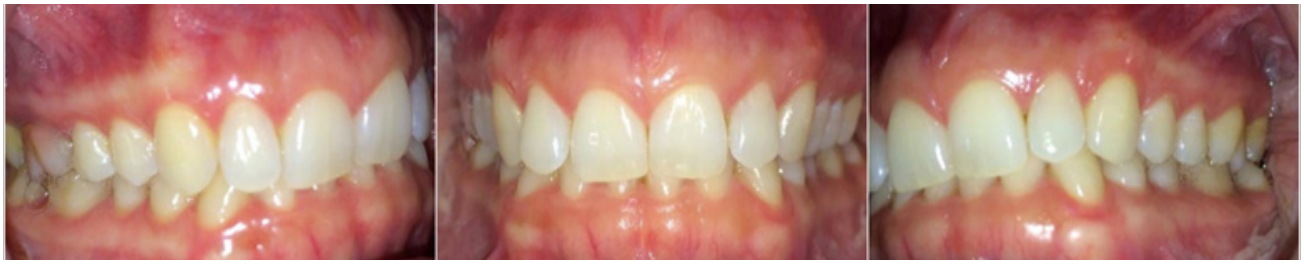

Figure 5. Intra-oral pictures from right lateral view, frontal view and left lateral view.

Diagnostic assessment

Diagnosis: a 24-year-old female patient with straight soft tissue profile, a class I malocclusion, increased gingival display on smiling (5 mm), 100% deep bite due to supra-erupted maxillary anterior teeth, mild to moderate dental crowding, mandibular midline shifted 2 mm to the right.

Therapeutic intervention

Based on the clinical characteristics showed above, the main treatment objective is to reduce the complete overbite and the gingival display, without altering the size of the anterior teeth. Other treatment objectives are aligning maxillary and mandibular teeth, intruding maxillary anterior teeth to correct overbite and reduce maxillary incisor display at rest and on smile, reducing gingival display by intrusion and/without crown lengthening, coincidental lower midline to facial midline.

The treatment sequence and biomechanical plan included bonding maxillary arch along with molars with brackets of Roth .022¨ prescription using Straight-wire technique, aligning the upper teeth using .012¨, .014¨, .016¨, .16x.016¨ and .016x.022¨ Nickel-Titanium arch wires, intruding anterior teeth using .016x.022¨ intrusion (reverse curve of Spee) arch wires. We used about three intrusion arch wires (Figure 6), for three months each. During the first intrusion arch wire, the mandibular arch was bonded along with molars and the same arch wire sequence for aligning teeth was used. When enough intrusion was obtained and the gingival exposure was in the aesthetic limits (less than 1mm), leveling continued using .017x.025¨ Nickel-Titanium arch wire. Before changing for the last arch wire, a panoramic radiograph was performed for a proper positioning of the teeth roots. The last arch wire was a .017x.025¨ stainless steel one. In order to correct the lower dental midline shift, 5/16¨ inter-maxillary elastics between the lower right canine and the upper left canine were used for about 2 months at night (Figure 7, Figure 8). After 23 months of treatment, the brackets were debonded, a lower fixed canine-canine retainer and an upper wrap around retainer were used for retention. The patient was recalled after 6 months for retention check.

Based on the clinical data obtained at the end of the orthodontic treatment, a correction of the excessive overbite, crowding, lower dental midline shift and gingival smile was achieved, giving the patient the smile that she dreamt of (Figure 9).

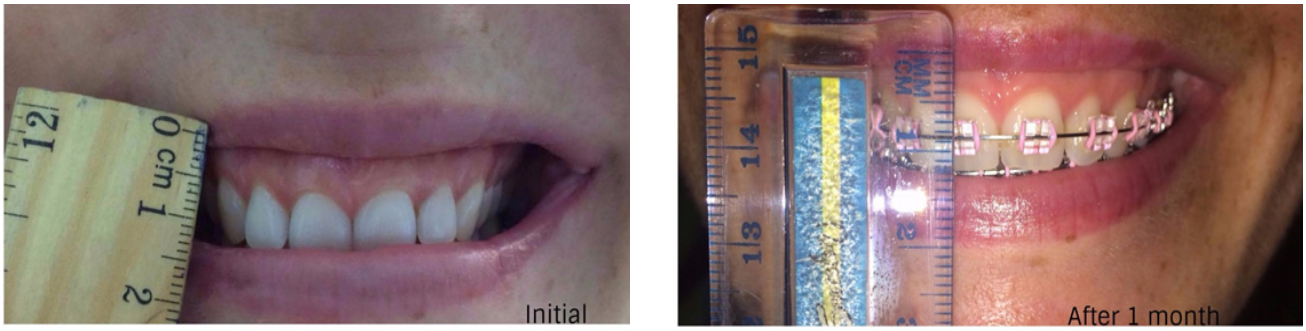

Figure 6. Gummy smile correction after 1 month of the first reverse curve of Spee arch wire.

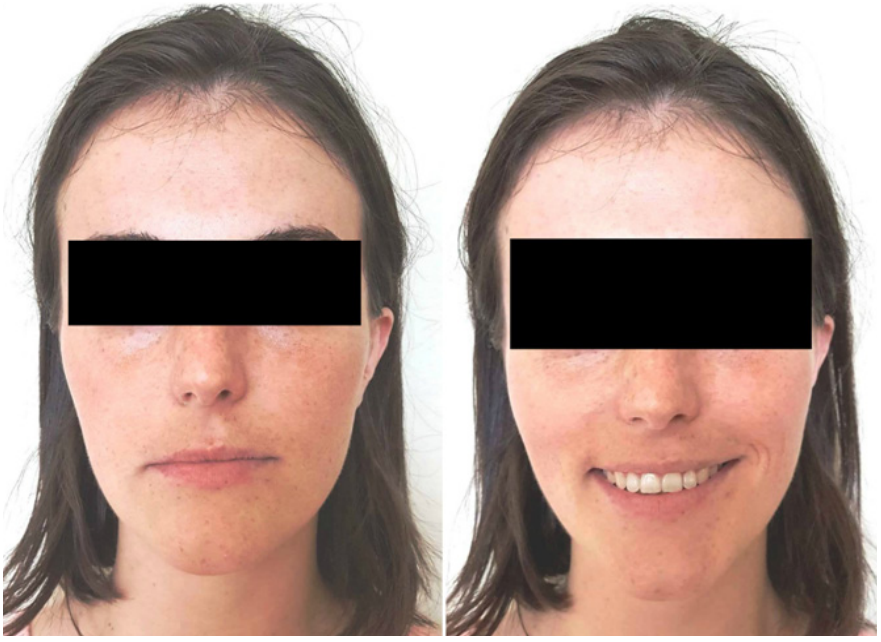

Figure 7. Final extra-oral frontal view at rest and smiling.

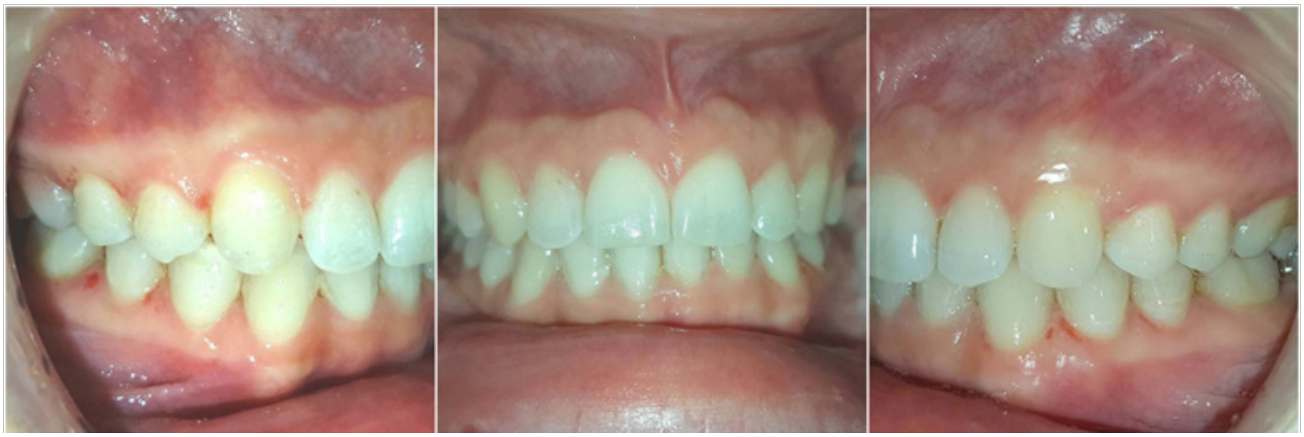

Figure 8. Final intra-oral view from right lateral side, frontal side and left lateral side.

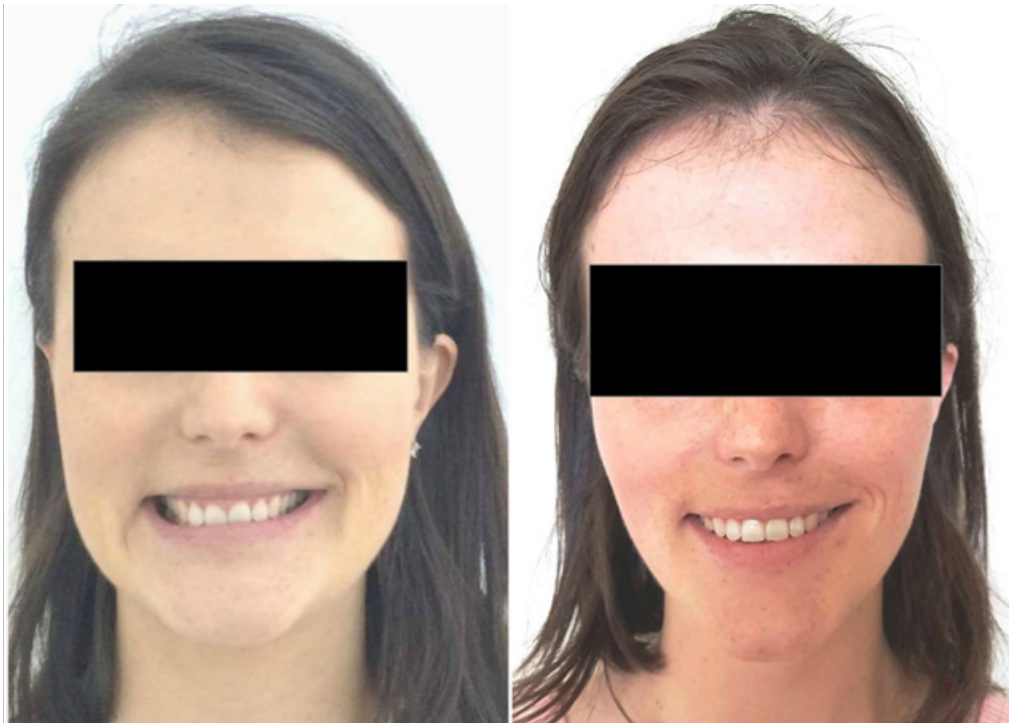

Figure 9. A comparison between the initial and the final aspect of the face.

Discussion

Treatment alternatives for gummy smiles include various combinations of orthodontic, periodontal and surgical therapies. The differential diagnosis must take into consideration the amount of maxillary incisor display at rest, position of the lips and the amount of gingivae shown on smiling [9].

Excessive overbite can be treated using the following mechanics options: extrusion of posterior teeth, incisors intrusion, a maxilla clockwise rotation, increasing the lower anterior facial height, flattening the curve of Spee [10].

If the maxillary incisor show at rest is optimal, active upper incisor intrusion should not be initiated. Instead, local gingivectomies or surgical crown lengthening with removal of crestal alveolar bone should be done. Such procedures are indicated in cases with altered passive eruption, excessive marginal gingivae and short clinical crowns, since they will expose more the anatomic crowns. When crestal alveolar bone is removed during surgical crown lengthening, the gingival margin will stabilize within 6 months at about 3mm from the new bone level [9].

The curve of Spee can be leveled using an intrusion arch wire or a continuous arch wire with an incorporated reverse curve of Spee. The choice depends on the treatment objectives regarding the correction of the deep bite. Pure intrusion can be obtained using an intrusion arch, while both leveling the arch and extrusion of the posterior teeth can be obtained using reverse curve of Spee arch wires [9].

The amount of intrusion of the incisors in response to an intrusion arch wire is 2 mm when measured on the

center of resistance. This could lead to a 4mm overbite correction if the incisal edge is displaced labially with the intrusion. When associated with excessive gingival display, incisor intrusion using an intrusion arch wire can be combined with gingivectomy to obtain a greater correction when needed [9].

In this case, the patient had an excessive gingival display of 5mm, complete overbite and the tooth size was within the limits of the golden ratio (H:W = 1.618). The dimensions of the anterior teeth were determined at the beginning of the treatment. However, the patient was told that using reverse curve of Spee arch wires in order to correct the gummy smile and the complete overbite may be followed at the end by some surgical procedures of crown lengthening in order to increase the clinical crowns which can become smaller. After changing three reverse curve of Spee arch wires, it can be observed that the gummy smile has been reduced completely, the overbite is now reduced ½ and that the ratio height: width of the central incisors continues to follow the golden ratio. This shows that even though the patient is an adult, the mechanism of intruding the anterior teeth has been done together with the alveolar process, maintaining the golden ratio height: width of the central incisor and without requiring any gingivectomy. If our adult patient had pure intrusion of the anterior teeth like we were expecting, the clinical crown would have shrunk and therefore she needed some surgical procedures of crown lengthening to obtain a proportional smile. If an adult patient has a greater height of the central incisors, pure intrusion of the anterior teeth without the alveolar process is required in order to obtain the correct height of the central incisors.

Correcting the deep bite in a patient with brachyfacial pattern can be done using anterior bite stops placed on the lingual surface of the maxillary anterior teeth. Anterior bite stops disocclude the dentition and allow the eruption of the posterior teeth into the interocclusal space [9].

When the excessive gingival display is caused by hyperfunctional upper lip elevator muscles, the most minimally-invasive treatment consists of injecting botulinum toxin for neuromuscular correction, but the effect has been reported to be transitory, for a maximum of 6 months. [nanda, esthetics and biomechanics in orthodontic, cap 3, pag. 70] These cosmetic procedures are available and began to be studied in patients with facial paralysis since 1973. The techniques that have favorable aesthetic results includes beside injecting botulinum toxin A, silicon implants on the bottom of the vestibule at the base of the anterior nasal spine and the resective procedures in the muscles that are responsible for the upper lip mobility [11,12]. More recently, a lip repositioning surgery technique has been used to treat the excessive gingival display. It includes removing a strip of outlined mucosa by a superficial split thickness dissection and leaving the connective tissue exposed. This procedure obtained 80% average reduction in gingival display considering only 6 months of follow-up [13].

Treatment of the most severe gummy smile may require maxillary superior repositioning surgery (Le Fort I osteotomy), along with reduction of the associated vertical maxillary excess [9].

Conclusions

The type of orthodontic mechanic must be chosen only after a good treatment planning following the pretreatment phase which settles the patient`s clinical and cephalometric characteristics. Using anti curve of Spee arch wires and inter-maxillary elastics is a simple and conservative orthodontic treatment, which needs a good cooperation with the patient in order to obtain effective and favorable results.

The patient gave the informed consent.

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SEVERE OLIGOHYDRAMNIOS DURING THE SECOND TRIMESTER OF PREGNANCY

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Abstract

Introduction. *The amniotic fluid forms in the amniotic cavity and it is essential for the fetus development. The amniotic fluid index (AFI) is an estimated quantity of the amniotic fluid expressed in centimeters and it is considered normal when it varies between 8 and 24 cm. An index less than 5 results in oligohydramnios.*

Study objective. *The following article presents the evolution of a pregnancy diagnosed with severe oligohydramnios, which occurred in the second trimester. The case we present was not submitted to any treatment because the patient refused to do so. The patient was under clinical observation throughout the pregnancy and the final outcome was totally different than the results expected.*

Material and methods. *The patient M. S., 22 years old, had the second doctor's appointment when the pregnancy was in the 19th week. She was diagnosed with oligohydramnios, caused by the fetus's left kidney dysfunction. M. S was referred to different specialists. The different diagnoses were consistent with the first finding that it was a severe oligohydramnios caused by a polycystic kidney disease of the fetus. Later on, M. S was admitted to the hospital through the emergency department due to a severe pelvic abdominal pain. A team of specialists diagnosed the pregnancy as severe oligohydramnios, multi-malformation syndrome, without stomach and bladder, with pulmonary hypoplasia and polycystic ovary syndrome. The doctor in charge advised M. S. to terminate the pregnancy. M.S. refused to have an abortion and she was discharged from the hospital at her request.*

Results. *In the thirty-first week of pregnancy, M.S had an induced labour and she gave birth to a female child weighting only 1400 grams with an Apgar score of 4/5. The child was initially in a very poor health condition. After only 6 weeks and 2 days, M. S and her child were discharged from the hospital. The last screenings showed that the baby was in general good health without presenting any malformation.*

Conclusion. *According to doctors, scans and procedures performed throughout the pregnancy, the fetus had multi-malformations. Postnatal, all the results showed no signs of malformation and the baby was in good health.*

Keywords: oligohydramnios, kidney, amniotic fluid

Backgorund and aims

The amniotic fluid is a liquid that fills the amniotic cavity. There are several factors underlying its formation. The first one is the fetus's urine. Another one is the maternal plasma that due to a higher tonicity, compared to the fetus's urine, passes through the fetal circulation from the placenta to the fetus. Another factor that regulates the development of the amniotic fluid is the respiratory tract. Towards the end of the pregnancy, about 350 ml of amniotic fluid is produced, and half of which is swallowed. Another mechanism of synthetizing amniotic fluid is the diffusion of the extracellular fluid through the fetus's skin [1]. The volume of the amniotic fluid increases progressively throughout the pregnancy with approximately 10 ml per

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week, starting from the eighth week of gestation. During the tenth week, there are about 30 ml and during the third semester, it reaches about 800 ml [1]. The Amniotic Fluid Index (AFI) is the most commonly used method to evaluate the amniotic fluid. The uterus is divided into four quadrants for measurement. The transducer of the ultrasound is placed perpendicularly on the spine. Thus, the longest vertical diameter of each pocket is identified and measured in each quadrant. These amounts are added up and the sum represents the amniotic fluid index [2]. In order to avoid including the umbilical cord in the measurement, Color Doppler Ultrasound is used [1]. AFI is quantified in centimeters and it varies between 8 and 24 centimeters. If it is lower than 5, a pregnancy anomaly called "oligohydramnios" occurs. When the quantity of the liquid cannot be measured, we are dealing with anhydramnios.

This study analyzes the evolution of a pregnancy with severe oligohydramnios developed during the second trimester of pregnancy. The following case was not subject to any treatment as the patient refused it. Therefore, the case was observed by different doctors, some of them advocating the idea of developing malformations that are incompatible with life because of the oligohydramnios. Despite this, the results were different from what those specialists expected.

Material and method

Patient M. S., aged 22, had her first doctor's appointment during the fourth week of pregnancy and he concluded that the gestation had evolved within the normal parameters. The patient's blood type was 0 negative. During the nineteenth week, she went for a check-up. Meanwhile, the patient had lost 10 kg. The doctor noticed that the pregnancy had developed an oligohydramnios. The cause of this anomaly was identified to be a dysfunction of the left kidney. The patient was redirected to a practitioner specialized in fetal morphology imaging. He concluded that the left kidney was enlarged, approximately 24/18/15 mm, hyperechoic, with no distinction between the sinus and the parenchyma (polycystic disease). In addition to this, the bladder was barely visible, with a minimum quantity of urine inside. The doctor concluded that the patient was dealing with anhydramnios, minimum ventriculomegaly, the diameter of the lateral ventricles being minimally increased – about 10-11 mm at the level of the atrium – and left renal polycystic disease. He recommended the termination of the pregnancy according to therapeutic standards. Following the refusal of the patient, the gynecologist set up a check-up schedule every other day in order to monitor the state of pregnancy and prevent complications that could appear in the case of intrauterine fetal decease. This took place regularly for five weeks during which the fetus had survived. After this period of time, the patient was sent again to be seen by other doctors, in order to obtain the opinion of several specialists. Each of them suggested the termination of the pregnancy. After another two weeks, using an ultrasound, a board made up of five doctors decided that they were dealing with severe oligohydramnios, severe fetal hypotrophy, a multi-malformed fetus without stomach and urinary bladder, and with a polycystic ovary, dysfunctional kidneys and pulmonary hypoplasia. During the 24th week, the patient addressed a doctor that, according to tests, observed that the fetus was underdeveloped, weighing about 200 grams less than the standard (412 g) [1].

Table 1.

Weeks/ Diameter (cm)	24	27
BPD (Hadlock)	4.84	5.55
OFD (HC)	6.91	8.91
HC (Hadlock)	18.78	23.34
HC* (Hadlock)	18.63	23.03
AC (Hadlock)	16.16	20.44
FL (Hadlock)	3.6	4.30
HL (Jeanty)	3.75	3,49

The initial diagnosis was also confirmed – severe oligohydramnios – with renal polycystic disease. During the 27th week, the same practitioner determined that the fetus was weighing 714 grams. In addition to this, he measured the biparietal diameter, the circumference of the head, the abdominal circumference, the length of the femur and the length of the humerus in order to assess the development of the fetus (Table 1). The diameters were not in the normal parameters [3,4,5,6]. After 28 weeks, M. S. was urgently admitted into the hospital because of pelvic and abdominal pain. Fetal morphology ultrasound was recommended, a procedure that the patient has declined, saying that the previous tests had already proved that the fetus did not have chances to survive. In addition to this, labor induction and therefore, the cessation of the pregnancy, was suggested in order to follow the therapeutic conduct. The woman refused and was discharged upon her request.

Results

After 31 weeks of gestation and labor induction, the patient gave birth to a female newborn with severely-altered general state, weighing 1400 grams, 4/5 Apgar score, mechanically ventilated with 100% O2. Postnatally, the newborn's general state was critical with extended bruising of the limbs, superficial breathing, generalized retraction, xiphoid retraction, ventricular rate 140 bpm, hypotonia and hyporeflexia. For approximately two months, she was provided thermic comfort, CPAP respiratory system (subsequently, SIMV), hydroelectrolytic and metabolic rebalancing perfusions, AB IV plasma, MER 01 surfactant, antibiotherapy, human albumin and immunoglobulin. Starting with the second month of life, prevention of rickets and prophylaxis of premature infants' anemia were initiated

with D3 vitamin and Ferrous Hausmann. After six weeks and two days, the patient was released, and the newborn was in a good general state, without presenting any malformations.

Discussion

It is considered that severe oligohydramnios developed during the second trimester of the pregnancy is associated with a high rate of mortality, with different postnatal malformations that are incompatible with life because, in order to develop normally and to be able to move, the fetus depends on the volume of the amniotic fluid. There are recent studies that have evaluated cases of oligohydramnios during the second trimester of gestation and the results have been positive, all fetuses surviving [7,8,9]. However, these studies have not taken into consideration the cases of high-risk pregnancies or those in which the fetuses had congenital anomalies (renal chronic diseases, hypertension, preeclampsia). They have concluded that the pregnancy should not be ceased since this gestation anomaly only causes complications such as a low Apgar score, a higher rate of Cesarean births, hypocalcemia, hypoglycemia, and reduced dimensions for the gestational age, which also occur in other types of pregnancies [7,8,9].

The conducted studies have pursued cases that did not present fetal diseases or anomalies connected to amniotic fluid variations. In the analyzed case, a severe oligohydramnios was developed during the second trimester of pregnancy generated by a left renal polycystic disease. Thus, previous studies have not taken into consideration such cases, which indicates that the conclusion of these studies is not necessarily valid for this case as well. Initially, the left kidney was polycystic, and this is the reason why the risk of postnatal malformations was high. However, the result of the presented case contradicts this idea because after analyzing the state of the newborn child, the new screenings showed that there no longer was a dysfunction of the left kidney, nor renal cysts.

Conclusion

According to the tests performed during pregnancy, it was concluded that the fetus was multi-malformed and that there were minimum chances of normal development and normally-functioning kidneys after birth. However, the child was in good state at discharge from the hospital. Currently, all the recommended tests have been performed and they all have proved that the child does not present any kind of malformations or anomalies.

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A RARE CASE OF HIRSCHSPRUNG'S DISEASE ASSOCIATED WITH SIGMOID VOLVULUS IN AN ADULT PATIENT

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***Mitre Andrei Otto, Mihart Bianca, Bartoș Dana Monica, Adrian Bartoș and Mitre Calin Iosif have contributed equally to this case report; in consequence they are all principal authors.**

Abstract

Hirschsprung's disease (HD) is a congenital disorder characterized by the lack of enteric plexuses. It is usually diagnosed right after birth, which makes adult HD cases very rare [1]. This pathology association must be known, because the devolvulation without resection will result in great medical errors.

A 70 years old woman came to the emergency department presenting altered general state, pale teguments and mucosa, nausea, intense abdominal pain, absence of hydroaeric sounds, no intestinal transit for 7-8 days and a largely distended abdomen.

An abdominal XR was performed. The examination revealed pronounced air levels in the entire colic area and multiple hydroaeric levels in the hypogastric, right iliac fossa and right flank, all this indicating an intestinal occlusion.

Emergency surgery was performed for the intestinal occlusion. At the intraabdominal exploration a SV was observed, with the specification that the bowels did not have peristaltic movements; at that point a HD was thought to be the diagnostic, for that reason a sigmoidectomy was performed with terminal colostomy and rectal biopsies. Dissection piece and rectal biopsies were sent to histological examination where absence of enteric ganglions was observed.

At the postoperative control the patient recovered completely with no contingency issues or other complications.

SV is not often seen in adult patients and it is rarely associated with HD. A history of lifelong recurrent constipation should raise the suspicion of HD and a rectal biopsy should be performed to certify the diagnosis. Surgeons must be aware of this rare pathology in adult patients. If resection of the aganglionic segment is not performed the sigmoid colon will volvulate again or even without volvulation dynamic occlusion will occur.

Keywords: Adult Hirschsprung's Disease, Sigmoid Volvulus, Intestinal Occlusion, Surgery

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Introduction

Hirschsprung's disease (HD), also known as congenital megacolon, is a congenital neurocristiopathy, caused by aganglionosis of a certain gut region [2–5]. This leads to the lack of peristaltic movements and so, difficulty or impossibility in passing stool, causing a large dilation of the affected segment of the intestine. Usually it is diagnosed in newborns by the lack of meconium in the first 48 hours of life [4]. In rare cases of ultra-short HD the diagnosis can be delayed until adulthood, the patient experiencing lifelong constipation [6]. This case report present a case of a 70 years old woman with sigmoid volvulus (SV) that also suffers of HD.

Case Report

A 70-years-old female was admitted in the emergency unit of IRGH "Prof. Dr. O. Fodor" presenting nausea, intense abdominal pain, absence of hydroaeric sounds and no intestinal transit for feces and gases for 7-8 days. She reported mild chronic constipation since childhood. Before diagnosis, she suffered severe constipation, which was treated several times with enemas. Objectively, her general state was altered, with pale teguments and mucosa and a largely distended abdomen that participated at the respiratory movements. Palpation of the abdomen revealed sensibility, more pronounced on the right flank and iliac fossa area. Diuresis was present, the Giordano sign was negative bilaterally, osteotendinous reflexes present bilaterally. Blood tests showed no major unbalances, with slightly increased creatinine and urea levels and slightly decreased calcium and magnesium.

An abdominal XR, performed in another medical center, showed massive air levels in the entire colic area and multiple hydroaeric levels in the hypogastric, right iliac fossa and right flank area. After the complete examination of the patient the intestinal occlusion diagnosis was given and emergency surgical procedure was decided to be the treatment of choice.

The surgical procedure was performed under general anaesthesia with oro-tracheal intubation. At the opening of the peritoneal cavity, a large, dilated sigmoid colon (SC) was observed, with a diameter of approximate 25 cm.

Ascites of moderate quantity was noticed and evacuated. A probe was sent for bacteriological examination, where no bacterial growth has been found. The SC was volvulated at the right flank level and pulled in the subhepatic space. It lacked peristaltic movements and presented an ischemic aspect. The devolvulation of the sigmoid colon was performed, the bowel recovered in concern with the ischemic aspect but no peristaltic movements were detected, not even after tactile stimulation. At that point, HD was suspected, rectal biopsies and colonic resection was performed with closure of the rectal stump and terminal left flank colostomy. The resected piece together with a rectal biopsy was sent to histological examination, where a lack of ganglionic cells was found. Thus the diagnosis of sigmoid aganglionosis.

Post operatory outcome was favorable. Treatment with hydroelectrolitic agents, pain killers, anticoagulant and antibiotic drugs was administered. The intestinal transit was reestablished on the 3rd post operatory day.

The patient was discharged with good overall state, with intestinal transit present at the stoma level, actively orally intake, no suture leaks, suture wires on place.

Check up at 30 days was performed, with favorable outcome. Three months after surgery, the colostomy was removed and the bowel reconstruction was done by colo-rectal anastomosis. The 6 months and 1 year follow-up of the patient revealed complete recovery, with no contingency issues.

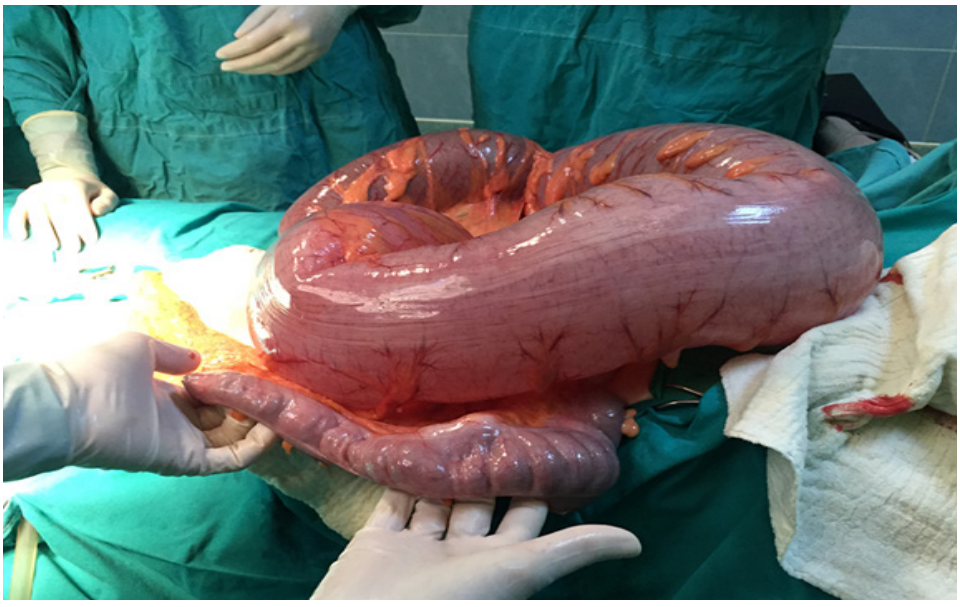

Figure 1. Sigmoid colon. Picture taken during surgery, before resection.

Discussion

Hirschsprung's disease is a congenital pathology characterized by lack of ganglion cells in a certain segment of the bowel. This causes lack in movement of the aganglionic segment, which in turn generates constipation, accumulation of feces and dilation, causing megacolon in undiagnosed patients.

Genetics play a key role, with an incidence of 1:5000 patients, more predominant in males (4:1 ratio), with a complicated inheritance pattern and a high sibling recurrence risk [2,3]. It is caused by a lack of enteric neurons in a certain gut area, usually the distal segment of the large intestine, but the aganglionosis can affect the entire colon or intestine [7].

Between the 5th and 12th week of pregnancy, embryonic neural cells migrate from the migratory vagal neural crest to the gut region to form what will later become the enteric nervous system (ENS). In this process more than 12 genes have been found to be involved, out of which *RET* is of considerable importance [2,8,9].

It is uncommon to be diagnosed in elderly patients because it is usually observed right after birth or in some cases at adolescence or adulthood. Mild HD cases, also called ultra-short segment HD, can pass unnoticed and be misdiagnosed as refractory constipation [10,11].

Diagnostic methods include contrast enemas and anorectal manometry, but the gold standard is rectal biopsy [4,12], where an absence of ganglionic cells accompanied by hypertrophic nerves in the submucosa can be noticed [13]. The gold standard treatment for these patients is surgery and consists in removing the aganglionic intestinal segment.

In the surgical theatre, a volvulated SC was observed. SV incidence increases with age, but it is uncommon to be associated with HD [14–16]. SV is a frequent cause of intestinal obstruction in elderly patients and its best treatment with surgery [17]. Because of the comorbidity usually associated with age, SV has a high mortality rate in patients older than 70 [16].

Chronic constipation and fecal overload causes elongation and dilation of the SC, which paired with a narrow mesentery, also called a dolichosigmoid, is believed to be responsible for the twist. This can cause ischemia through venous and arterial obstruction, thus leading to necrosis of a certain gut segment [16,18].

The surgical procedure included the resection of the volvulated SC, which was send for histopathological evaluation. Results showed a lack of ganglionic cells in the resected piece.

The aganglionosis can also be associated with dilation of the bowel segment. It might be that due to the dilation and ischemia, ganglia cells suffer a "drop out" phenomenon in which the myenteric plexus loses ganglion cells [19]. So, a rectal biopsy, the gold standard for diagnosing HD, was also collected and histologically examined. Result showed aganglionosis, leading to a clear diagnosis of congenital megacolon.

In this case, the genetic factor can also be observed, since at a further consultation she reported that her niece also presented chronic constipation for 2 years. Since the transmission of HD is non-Mendelian with complicated inheritance patterns, we can presume it is also a case of HD [2,7].

SV associated with HD is a rare condition. Several reports in the literature were found, most of them presenting patients with recurrent constipation. Some have treated the blockage with enemas, but when intestinal occlusion occurred, surgery was performed [6,10,11,20].

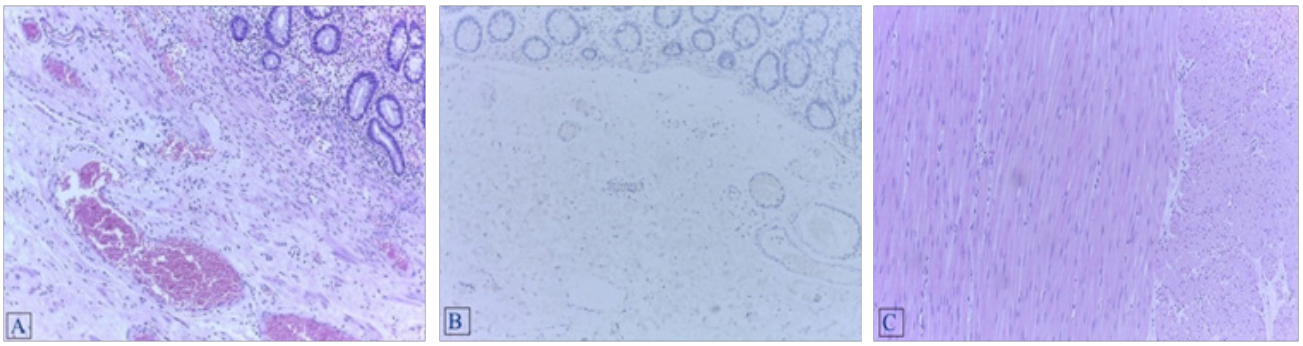

Figure 2. A. Hematoxylin Eosin staining -magnification 200x. Submucosa with lack of ganglion cells; B. Calretinin immunohistochemical stain shows lack of staining in the lamina propria, muscularis mucosae or submucosa. Original magnification-200X; C. Hematoxylin Eosin staining-magnification 200x. Lack of ganglion cells in muscularis propria.

Conclusions

Congenital megacolon is a disease usually diagnosed right after birth, when meconium fails to pass. If left unnoticed or in case of a very short segment aganglionosis it can lead to refractory or chronic constipation. This can be tried to be treated with the use of enemas, but it can also lead to infections or serious complication caused by the dilation of the distal colon.

Volvulus of the sigmoid is usually caused by a long or dilated sigmoid, which causes its twisting with the development of ischemia due to lack of vascularization of a certain segment.

Medical professionals should take into account that, even though HD is rarely found in elderly patients or associated with SV, when the patient reports chronic constipation HD should be suspected for the differential diagnosis and rectal biopsy, the gold standard in diagnosis, should be performed [6,17]. Delaying the surgical treatment can lead to intestinal ischemia or bowel necrosis [10,21].

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MOVEMENT DISORDERS AT THE TIP OF GUILLAIN AND MOLLARET'S TRIANGLE: A CASE REPORT

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Abstract

Introduction. *The nature of a neurologist is that of a detective, each sign being filtered through semiological and topographical principles. The lesions in the brainstem have a special output, given the complexity of its anatomy and high density of functional structures, one such being the triangle of Guillain and Molaret.*

Case presentation. *We present the case of a 65 year old male who is admitted for gait disturbances, inability to coordinate his right limbs, decreased muscle strength at the same level and speech disturbances.*

The neurological examination revealed a right neocerebellar syndrome. The initial native cerebral CT did not reveal any pathological modifications. The follow-up cerebral MRI revealed a hemorrhage in the right AICA/SCA territory on the T2 sequence.*

Three years later, the patient presents for a routine check-up, where a palatal myoclonus is noted, along with a static and intentional tremor with predominant distal localization on the right upper limb. The cerebral MRI showed the resorbtion of the hematoma with porencephalic remnants in the right superior cerebellar peduncle and bilateral hypertophic olives.

Discussion. *The triangle of Guillain and Molaret consists of the red nucleus and inferior olivary nucleus on the same side and the contralateral dentate nucleus in the cerebellum, along the fibers in between. Fibers come from the dentate nucleus, ascend through the superior cerebellar peduncle and decussate in the brachium conjunctivum inferior towards the red nucleus, descending afterwards to the inferior olivary nucleus via the central tegmental tract. The bundle of fibers that goes through the inferior cerebellar peduncle from the inferior olivary nucleus to the dentate nucleus completes the triangle.*

Any lesion that appears in these structures decreases the inhibitory output of the dentate nucleus on the inferior olivary nucleus, henceforth increasing signal firing rate on the ambiguous nucleus. This gives rise to involuntary, rhythmic contractions of the levator veli palatine muscles, translating into palatal myoclonus.

Given that the lesion occurred in the right AICA/SCA territory, a static and intentional tremor localized predominantly distally in the right upper limb was facilitated. This is due to the interruption of the dento-rubro-thalamo-cortical pathway, in which coordination of limb movements is severely affected.

Conclusions. *Posterior fossa pathology is of equal beauty and complexity. Lesions occurring in the triangle of Guillain and Molaret have a high localization value if neuroanatomy, neurology and neuroimaging are sound and up to date.*

Keywords: intention tremor, static tremor, palatal myoclonus, movement disorders

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Introduction

The nature of a neurologist is that of a detective, each sign being filtered through semiological and topographical principles. The lesions in the brainstem have a special output, given the complexity of its anatomy and high density of functional structures.

A step by step approach to topographical diagnosis in this region draws attention to the triangle of Guillain and Mollaret, an anatomical and functional structure involved in motor control. The triangle was described by the two neurologists in 1931, after studying hypertrophic olivary degeneration.

It ensures that fine movements are precisely executed by way of a more complex cortico-ponto-cerebellar loop. Disturbances at this level, rare in their nature, would manifest as movement disorders.

In our case, the lesion that appeared in the aforementioned triangle has given rise to two particular hyperkinetic movement disorders, namely palatal myoclonus and dento-rubral tremor.

Palatal myoclonus was first described by Politzer in 1878 [1]. The consistent rhythmicity of the palatal myoclonus was the main reason for modifying the terminology to palatal tremor (PT) at the First International Congress of Movement Disorders in 1990. PT is a rare involuntary movement described as upward or lateral deviation of the soft palate. The frequency usually ranges from 0.5 to 3 Hz. It is commonly described after lesions in the triangle of Guillain and Mollaret, due to deafferentation of the inferior olivary nucleus [2].

Dento-rubral tremor (or Holmes tremor) was first described by Holmes in 1904. The current definition of Holmes tremor (Consensus Statement of the Movement Disorder Society on Tremor – 1998) is of a rest, postural and intention tremor with a large amplitude, irregular character, mostly unilateral, which appears long after the initial lesion took place. The cerebello-thalamo-cortical, dentato-rubro-olivary pathways and nigrostriatal system are mainly affected [2,3].

A special note is made to their manifestation at different points in time, suggesting a more elusive pathophysiological underlying mechanism.

Case Presentation

We present the case of a 65 year old male of left hemispheric dominance, with prior history of hypertension, atrial fibrillation, diabetes mellitus type 2, stenosis of the vertebral arteries, who is admitted for gait disturbances, inability to coordinate his right limbs, decreased muscle strength at the same level and speech disturbances.

The disease debuted abruptly five years ago. The neurological examination revealed:

- intentional tremor at the right upper limb, low frequency, permanent character
- right lateropulsion
- gait and stance possible with one sided support
- titubating gait
- astazo-abasia of ataxic type
- dysmetria at index-nose maneuver, Holmes - Stewart and heel-shin
- dysdiadochokinesia
- scanning speech.

The neurological examination revealed a right neocerebellar syndrome.

The initial native cerebral CT did not reveal any pathological modifications. The follow-up cerebral MRI performed after two weeks revealed a hemorrhage (validated on the T2* sequence) in the right cerebellar hemisphere, which extended into the superior cerebellar peduncle. We concluded that the patient most likely had an ischemic stroke with hemorrhagic transformation (there is no oncological or genetic history). Eco-doppler of the vertebral arteries showed bilateral hypoperfusion, predominantly on the right side.

Three years later, the patient presents for a routine check-up, where a palatal tremor is noted (of low amplitude and moderate frequency), along with a static and intentional tremor with predominant distal localization on the right upper limb, with increasing amplitude, low frequency and permanent character. The cerebral MRI showed the resorbtion of the hematoma, leaving instead a CSF-filled cavity in the right cerebellar hemisphere and right superior cerebellar peduncle, alongside bilateral hypertophic olives.

Discussion

Lesions in the triangle of Guillain and Mollaret and the dento-rubro-thalamo-cortical pathway are the cause of the palatal myoclonus/tremor and the Holmes tremor. Both entities are secondary to cerebrovascular insults. The hemorrhage extended from the right cerebellar hemisphere into the superior cerebellar peduncle, before the decussation of the cerebello-dento-rubro-thalamo-cortical pathway.

The triangle of Guillain and Mollaret consists of the ipsilateral red nucleus and inferior olivary nucleus and the contralateral dentate nucleus in the cerebellum.

Fibers from the dentate nucleus ascend via the dento-rubral tract through the superior cerebellar peduncle, decussate in its inferior part and continue towards the contralateral red nucleus, in the parvocellular part. Fibers from the red nucleus descend ipsilaterally via the central tegmental tract to the inferior olivary nucleus. Efferents from the inferior olivary nucleus are sent towards the contralateral cerebellar cortex via climbing fibers. The contralateral dentate nucleus receives both direct fibers from the ION and indirect fibers from the cerebellar cortex [4,5,6].

The afferents of the inferior olive are the crossed inhibitory nucleo-olivary projection and the excitatory projections from somatosensory, vestibular, optokinetic nuclei and the nuclei at the meso-diencephalic junction (nuclei of Darkschewitsch, Bechterew and the parvocellular

red nucleus). The main descending fibers come from the latter nuclei and they reach the olive by way of the medial and central tegmental tracts [7].

One notable afferent of the olivary complex, although not as exhaustively described as others, is the spino-olivary tract. The tract forms from axons of neurons that are found in the deeper laminae of spinal grey matter, collecting proprioceptive and cutaneous sensory information and sending it towards the dorsal and medial accessory olivary nuclei. Its influence on the olivary complex cannot be denied, given that postmortem studies after cordotomies in humans show degenerated axonal terminals at the aforementioned level [8].

The central tegumental tract takes its origin from the parvocellular part of the red nucleus. Its fibers traverse the capsule of the brachium conjunctivum in a dorsolateral direction. At its origin from the red nucleus the central and medial tegmental tracts constitute a single area in the mesencephalic tegumentum. Caudally it can be traced into the amiculum [7,9]. The inferior olive presents a slow, rhythmic, spontaneous activity [6].

The descending tracts that control and influence segmental spinal cord motor activity include the corticospinal, rubrospinal, vestibulospinal, medial and lateral reticulospinal, olivospinal and the tectospinal tracts [10].

The olivary complex is an important station for gathering sensory and motor information, supplying it to the cerebellum. Studies have shown that removal of the olive in animals produces contralateral increase in tone and rigidity in the extremities, alongside the impairment of movement coordination [11].

Correcting errors in the diagram and execution of movement is a complex process, requiring two feedback circuits: the dentato-rubro-olivary circuit, which is part of the larger cortico-ponto-cerebellar circuit. The inferior olivary complex receives a copy of the motor schematic from collaterals of the corticospinal tract, which is compared with the cerebellar diagram that is sent towards the parvocellular red nucleus via the superior cerebellar peduncle and projected afterwards to the inferior olive [8,12].

By receiving collaterals from all the afferent pathways that involve the cerebellum, the olivary nucleus can follow how the precise execution of planned movements is carried on and relay information by way of the climbing fibers [12].

Given their multitude of cerebral, spinal and cerebellar afferents and efferents, olivary nuclei have been proved to display somatotopy, particularly in their cerebellar connections [8].

Palatal tremor is of two types: essential (in which the causative lesion is not identified) and symptomatic (where the lesion is located in the brainstem/superior cerebellar peduncle) [2]. The patient has a symptomatic palatal tremor, given the lesion's location and the existence of other neurological manifestations suggestive of the affected area.

The development of symptomatic PT after disruption of the dento-rubro-olivary tract is thought to result from a reduction in inhibitory GABAergic input from the dentate nucleus. The successive increase in synchronization of the olivary neurons leads to an autonomously working olivary oscillator. The abnormal rhythm of the olivary oscillator is carried through the inferior cerebellar peduncle to the contralateral cerebellar hemisphere and subsequently interferes with the cerebello-reticular systems. This leads to the rhythmic activity of brainstem muscles [2], henceforth increasing signal firing rate of the ambiguus nucleus, which gives rise to involuntary, rhythmic contractions of the levator veli palatine muscles, translating into PT [5].

Symptomatic PT and hypertrophic olivary degeneration are secondary to lesions involving the dento-rubral and central tegmental tracts, since it is olivary deafferentation that triggers the hypertrophic degenerative changes with consecutive functional consequences [13].

Normally, a hypertrophic olivary degeneration ensues and can be revealed by imaging as soon as 6 months after the initial event and can remain for up to 4 years, after which it regresses and does not leave traces behind [13,14]. In our case, both olivary complexes were increased in size, but were isointense to surrounding parenchyma.

The red nucleus facilitates both proximal and distal muscle activation and is, henceforth, involved in controlling movements that require coordination of proximal and distal joints of the limbs. The disruption of its activity increases the cerebellar outflow through the dento-rubro-thalamo-cortical pathway, generating a tremor that affects the proximal and distal joints [15].

Conclusions

Posterior fossa pathology is of equal beauty and complexity. The olive is a mysterious, gyrus-shaped structure that closely resembles the telencephalon. Combined with its high number of sensory afferents and involvement in the motor loop, one could consider the olive a form of archaic cortex.

The morphology (gyrus-shaped form) and function (high number of afferents from the entire length of the neuraxis and efferents, which greatly influence movement coordination) of the olivary complex entices one to think of its close resemblance to the telencephalon, only that they are found at different moments in time on the evolutionary axis.

A unilateral lesion of the myoclonic triangle can lead to bilateral hypertrophy of the olivary complex.

Lesions occurring in the triangle of Guillain and Mollaret have a high localization value if neuroanatomy, neurology and neuroimaging are sound and up to date.

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A CASE OF SYSTEMIC SCLERODERMA WITH MYOCARDIAL INVOLVEMENT

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Abstract

Aim of the study. *Systemic scleroderma is an autoimmune disease of the connective tissue, featuring thickened skin, blood vessel issues and articular pain. However, cardiac involvement is not an unusual finding in these patients. Give this fact, our purpose is to present a case with certain particularities, investigated by morphologic and rhythmologic methods.*

Patient and methods. *We present the case of a 47 years old diabetic female diagnosed with systemic scleroderma intricated with rheumatoid polyarthritis, who accuses non-specific cardiac symptoms. Considering the underlying disease, the patient was investigated exhaustively by ECG, cardiac ultrasound, cardiac MRI and 24-hour Holter monitoring.*

Results. *The ECG showed no ischemic changes of the myocardium. The 24-hour Holter examination captured 12 supraventricular events and 1 ventricular event, which was insignificant for diagnosis. However, heart rate variability parameters were decreased, which is consistent with an early onset of diabetic neuropathy. Cardiac ultrasound revealed normal kinetic features. However, the MRI revealed an intense contrast enhanced 2,3 cm subepicardial lesion, localized in the inferior and median wall of the left ventricle, towards the interventricular septum and inferior wall of the right ventricle. The lesion had a thickness of 7 mm. Taking into account the morphologic and enhancing characteristics, the lesions was classified as focal myocarditis with fibrotic changes, without ischemic features. The MRI measures of left ventricle function were in normal limits.*

Conclusions. *The case highlights the multi-organ tropism of systemic scleroderma, particularly a rare and unspecific cardiac involvement in the form of a focal myocarditis lesion, diagnosed by contrast enhanced cardiac MRI. The case emphases the importance of a complex evaluation by morphologic and functional methods in patients with systemic scleroderma, revealing the underlying changes that express through unspecific and apparently benign symptoms.*

Keywords: systemic scleroderma, myocarditis, cardiac MRI

Introduction

Systemic sclerosis is an autoimmune, diffuse disease of the connective tissue, featuring thickened skin, blood vessel issues and articular pain, with unknown etiology (Meduri, 2017; Saito, 2017; Soukup, 2018). Clinical manifestation of this disease is classed based on the preponderant pathogenetic process; the manifestation of systemic inflammation is also accentuated by pleurisy, pericarditis, synovitis or arthritis (Soukup, 2018). Nevertheless, pulmonary arterial hypertension is also a major complication of systemic connective tissue disease (Schwartz EI, 2018). However, cardiac involvement is not an unusual finding in these patients (Meduri, 2017).

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Aim of the study

Given this fact, our purpose is to present a case with certain cardiac particularities, investigated by morphologic and rhythmologic methods.

Patient and methods

We present the case of a 47 years old diabetic female diagnosed with systemic scleroderma intricated with rheumatoid polyarthritis. Biologically, the patient presented ANA positive (nucleolar), anti-Scl70 positive. Rheumatoid factor was in normal limits. From a clinical point a view, the patient accused Reynaud syndrome, arterial hypertension, muscle pain and insulin-dependent type II diabetes. The patient also accused non-specific cardiac symptoms. Considering the underlying disease, the patient was investigated exhaustively by ECG, cardiac ultrasound, cardiac MRI and 24-hour Holter monitoring.

Results

The ECG showed no ischemic changes of the myocardium. The 24-hour Holter examination captured 12 supraventricular events and 1 ventricular event, which was insignificant for diagnosis (Figure 1). The dominant rhythm was sinus rhythm. However, heart rate variability parameters were decreased, which is consistent with an early onset of diabetic neuropathy. NN50 and pNN50 parameters were decreased; SDNN as also decreased, compared to general population (Kudat, 2006).

Cardiac ultrasound revealed normal kinetic features. However, the MRI revealed an intense contrast enhanced 2,3 cm subepicardial lesion, localized in the inferior and median wall of the left ventricle, towards the interventricular septum and inferior wall of the right ventricle (Figure 2).

The lesion had a thickness of 7 mm. Taking into account the morphologic and enhancing characteristics, the lesions was classified as focal myocarditis with fibrotic changes, without ischemic features. The MRI measures of left ventricle function were in normal limits. Also, no perfusion defects were found, which is consistent with the literature (Hachulla, 2009; Mavrogeni, 2017).

According to literature, cardiac MRI is strongly recommended in patients with systemic sclerosis; also, cardiac evaluation has to be thoroughly conducted in preoperatory management of patients. (Meduri, 2017; Hasan, 2018; Hachulla, 2009; Mavrogeni, 2017). Cardiac MRI also evaluates left and right ventricular function, which are also affected in sclerodema (Saito, 2017).

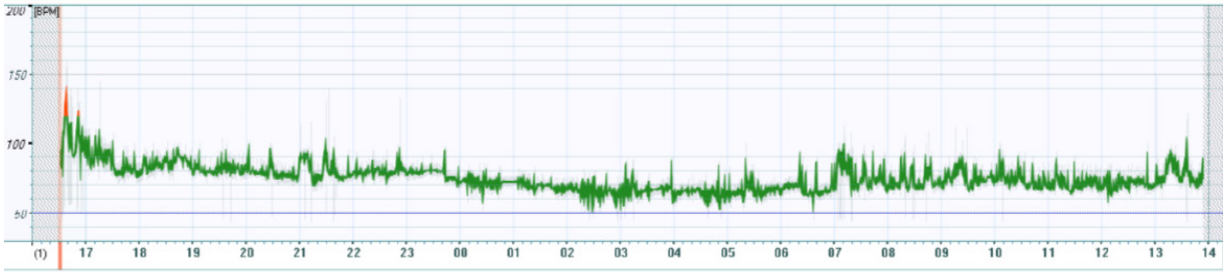

Figure 1. 24-hour Holter trace showing normal cardiac heart rate, without supraventricular events.

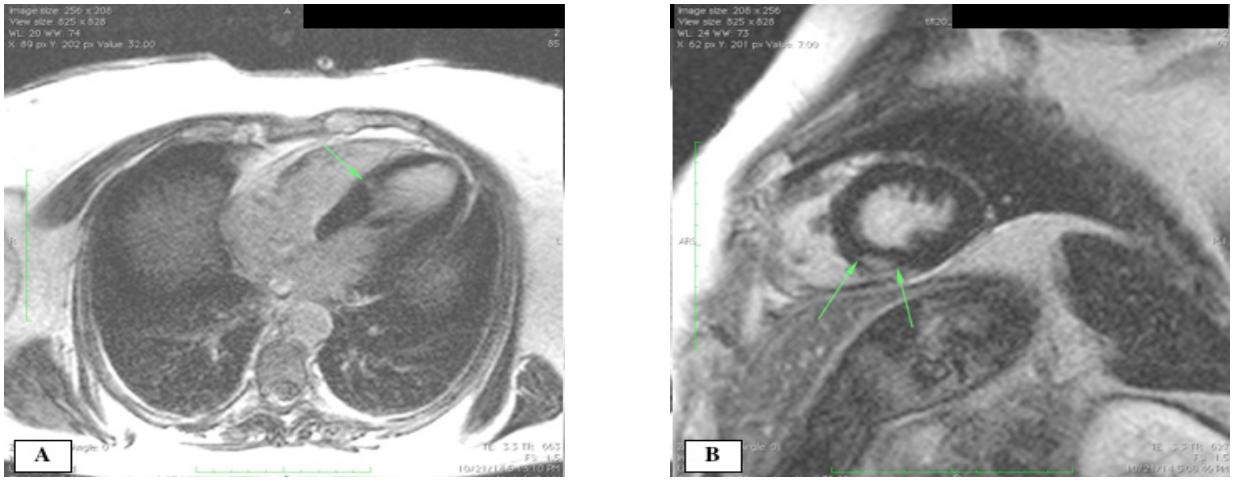

Figure 2. Late enhancement phase shows basal hypercaptating areas, extending in the interventricular septum.

Conclusions

The case highlights the multi-organ tropism of systemic scleroderma, particularly a rare and unspecific cardiac involvement in the form of a focal myocarditis lesion, diagnosed by contrast enhanced cardiac MRI. The case emphases the importance of a complex evaluation by morphologic and functional methods in patients with systemic scleroderma, revealing the underlying changes that express through unspecific and apparently benign symptoms.

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IMPORTANCE OF BREAST DEVELOPMENT IN THE DIAGNOSIS OF BREAST PATHOLOGIES IN CHILDREN AND TEENAGERS. CASE PRESENTATION

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Abstract

Introduction. *Experience of medical professionals regarding the diagnosis and management of breast pathologies in children is limited, as the incidence of these pathologies is low, and there is scarce information available in literature. Being familiar with the developmental stages of the breast has a significant contribution to making the correct therapeutic choice.*

Material and method. *We performed breast ultrasound of two patients aged 7.5 years, and 16 years, respectively, who had unilateral, mobile, and mildly tender breast lump.*

Results. *In case of the 7.5 years old patient bilateral retroareolar breast tissue was identified in different stages of development. In case of the 16 years old patient a large (>5 cm), macronodular, hypoechoic, inhomogeneous, well circumscribed, vascularized structure was identified, which had an elastography score of 2 (non-rigid), macrolobular contours and showed an accelerated growth pattern. Histopathological diagnosis of the biopsy sample confirmed juvenile fibroadenoma, and surgical excision was recommended.*

Conclusions. *Malignant breast lesions are very rare in children. The most frequent benign lesions are asymmetric development of the breasts and fibroadenomas. Diagnostic and therapeutic management of these lesions should be conservative, in order to avoid secondary lesions in the developing breast.*

Keywords: breast development, thelarche, fibroadenoma

Introduction

Certain signs and anomalies of the breast in children raise concerns of the parents, considering the high incidence of breast cancer in adults. Nevertheless, malignant lesions of the breast are very rare in children (0.1/100000 individuals) [1,2]. Pathology of the breast in children and teenagers is different from that of adults, and usually develops on a background of congenital disorders, genetic factors, changes of hormone status or unknown reasons [2]. In order to provide adequate diagnostic and therapeutic management of these lesions, medical professionals should be thoroughly familiar with the development of the breast. Development of the breast occurs in two phases: prenatal and during puberty.

The breast primordium appears during week 5 of intrauterine life as an ectodermal proliferation, extending from the axilla to the groin, and called mammary band [2,3,4]. By week 8 of intrauterine life the mammary crest is reduced to a round shaped ectodermal proliferation in the axillary region. Between weeks 8 to 19 the nipple develops from this ectodermal primordium and its surrounding mesenchyme. The lactiferous ducts of the breast start to develop at week 19 of gestation [5].

Early morphogenesis of the breast is regulated by a mechanism of signaling between the epithelium and the

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underlying mesenchyme [6], and in the third trimester by maternal estrogens [2,3,4]. After the first 2 weeks of extrauterine life ductal ramifications undergo regression and the breast primordium will be inactive until thelarche [2,3,5].

The development of the female breast during puberty is called thelarche. Estrogens stimulate ramification of the ducts, and progesterone stimulates alveolar, lobular differentiation, and contributes to formation of terminal duct lobular units. In Caucasian women thelarche generally begins at the age of 8 to 10 years, and ends around the age of 13 years [1,2,4,7].

Developmental stages of the breast during puberty are described by the 5 Tanner stages, which can also be correlated with ultrasonographic changes [1,2] (Table I).

We present two cases to demonstrate the current diagnostic and therapeutic management of the most frequent breast anomalies in children and teenagers.

CASE 1

Female patient aged 7.5 years presented for breast ultrasound. Physical examination identified a retroareolar, nodular, palpable structure in the left breast, which was tender, mobile and of intermediate consistency. There was no personal or family history of breast cancer, there were no inflammatory signs and no nipple secretions were present. No signs of puberty were observed.

Ultrasound examination was performed using a linear transducer (Mindray DC-70) at Dora Medicals, Târgu Mureș. Ultrasound scan of the left breast showed a retroareolar hyperechoic area with a stellated central hypoechoic zone and no vascular signals (Tanner stage 3) (Table I). In case of the right breast there was a smaller hyperechoic area with central, oval shaped hypoechoic zone and no vascular signal (Tanner stage 2) (Table I) (Figures 1, 2). If no cystic or solid benign/malign lesion is identified, the final diagnosis is asymmetrical development of the breasts. The recommendation is ultrasound follow-up within 6 months.

Table I. Tanner stages [1,2,4,8].

Tanner stage	Ultrasonographic findings	Clinical findings
1	Mildly heterogeneous retroareolar tissue	Elevation of the breast papilla
2	Nodular, hyperechoic retroareolar tissue with a linear or stellated hypoechoic central area (breast bud), which corresponds to the primordium of the ducts.	Elevation of the entire breast. The subareolar bud is palpable, the areola is slightly pinker.
3	Expansion of the hyperechoic fibroglandular structures, ramification of the retroareolar hypoechoic area	Volume of the breast and of the areola increases, without a separation between the breast and areola contour.
4	Retroareolar hyperechoic glandular area with hypoechoic central nodule. Subcutaneous adipose tissue appears.	The areola and the papilla begin to enlarge and project above the contour level of the breast.
5	Aspect similar to that of mature breast tissue; stellated, nodular, hypoechoic retroareolar area missing; subcutaneous adipose tissue layer becomes wider.	Only the papilla projects, due to recession of the areola of the general contour of the breast.

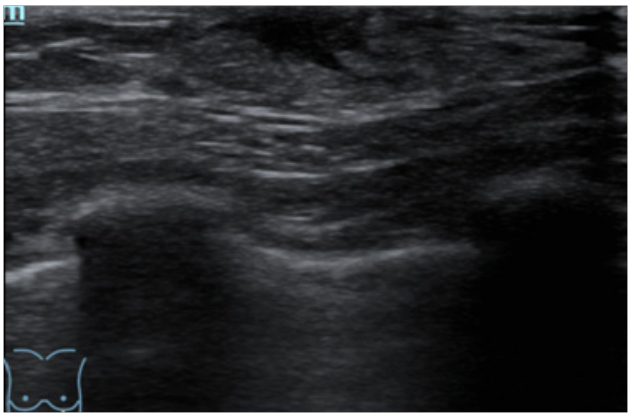

Figure 1. Patient aged 7.5 years. The left breast contains a retroareolar hyperechoic area with a ramified central hypoechoic zone (Tanner stage 3).

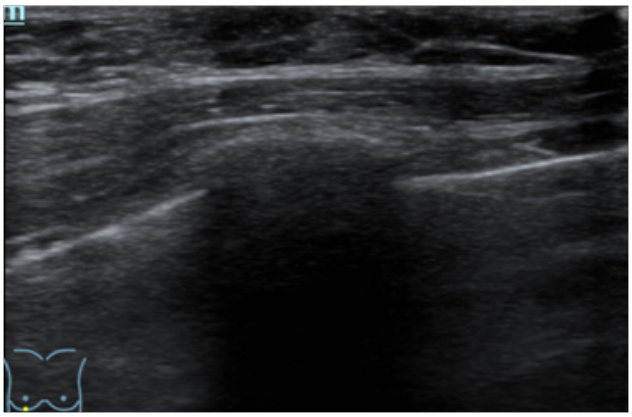

Figure 2. The right breast contains a retroareolar hyperechoic area with an oval shaped central hypoechoic zone (Tanner stage 2).

CASE 2

Female patient aged 16, without clinically relevant personal or family history presented at our department due to an increase in size of the right breast, with a palpable nodule that showed accelerated growth in the last 6 months. Physical examination identified a larger right breast, containing a mobile, macronodular structure in the central quadrant, which was tender to palpation and was associated with nipple retraction. There were no inflammatory signs.

Breast ultrasound was performed using the linear transducer of the Hitachi Aloka equipment at the Radiology Clinic of the County Clinical Emergency Hospital Târgu Mureş. Ultrasound finding: the central quadrant contains a hypoechoic, diffusely inhomogeneous, relatively well circumscribed macronodular structure of 58/62 mm, with Doppler vascular signal, elastography score 2 (non-rigid), macrolobular contours, which compresses the surrounding breast tissue, but no architectural distortions are present. The right axilla contains a few oval shaped lymph nodes with ecogenic center and measuring up to 12/6 mm - these properties are suggestive for reactive lymph nodes. BIRADS score of the lesion was 4a (Figure 3).

Histopathological diagnosis of the biopsy sample was juvenile breast fibroadenoma without atypical cells and surgical excision was recommended.

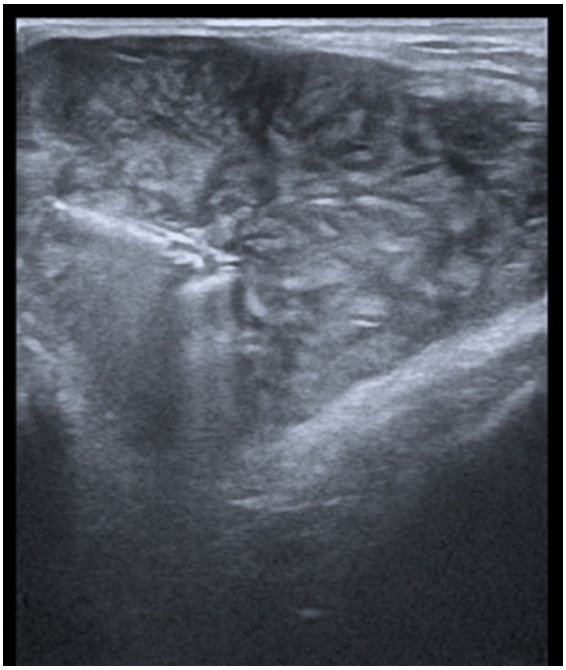

Figure 3. Patient aged 16 years. Macronodular, hypoechoic, relatively well circumscribed, inhomogeneous structure with macrolobular contours.

Discussions

Considering the effects of iatrogenic injury to the developing breast and very low incidence of malignant lesions of the breast in children, we have to observe the "first do no harm" algorithm in management of pediatric breast lesions. Thorough physical examination and disease history contribute to correct diagnosis of breast lesions [1]. Most frequent clinical signs in children are the palpable lump, inflammatory signs, nipple discharge and mastodynia [7,9,10].

All palpable lesions have to undergo ultrasound examination [4,9]. Ultrasound is essential for a correct diagnosis and identification of non-neoplastic benign lesions, hematomas, inflammatory lesions, and asymmetrical development of the breasts. Presumably benign lesions (oval shaped structures of up to 3-4 cm, circumscribed, and parallel to the underlying muscle plane) are mostly fibroadenomas, and ultrasound follow-up is recommended in such cases. Core needle biopsy is indicated in case of lesions with suspicious clinical and imaging properties (over 5 cm) and rapid growth [1,4].

In the first case discussed here, physical examination and ultrasound aspect excludes any non-neoplastic benign lesion and any cystic or solid structure. Being familiar with both clinical and imaging aspects of Tanner stages, guides us to the correct diagnosis: asymmetrical development of the breast.

According to published reports, asymmetrical development of the breasts is considered normal in case of up to 2 years difference between the developmental stages, and it is the most frequent cause of retroareolar and unilateral masses in children [1,11].

Age of the patient prompted for differential diagnosis with early thelarche and precocious puberty. Early thelarche may have unilateral or bilateral onset by approximately 1 to 3 years earlier, before the age of 7.5-8 years, compared to thelarche [1,8,11]. Early thelarche may also be associated with increased body mass index, or precocious puberty in approximately 20% of the cases. In case of the latter, other signs of sexual maturation are present besides thelarche, and additional imaging studies and laboratory tests are recommended [1,2,12]. Premature thelarche is benign and sometimes undergoes spontaneous involution [1].

Benign breast lesions in children are 100 times more frequent than malignant ones. Fibroadenomas are the most frequent causes of mammary solid masses in teenagers aged 15 to 17 years [1,10]. These are hormone-dependent fibroepithelial tumors, with the following clinical properties: non-tender lump, mobile, firm, diameter generally 2-3 cm, and slow growth rate. Ultrasound characteristics include the following: circumscribed hypoechoic structure delimited by its own walls, oval shaped, parallel to the underlying muscle plane, and possibly macrolobular contours. If there are no suspicious signs, and no rapid growth pattern, short time ultrasound follow-up is recommended [1,4,9]. Surgical removal is recommended if size gain is 50% over a period of 6 months or if tenderness and pain are present [9].

Juvenile fibroadenoma is a rare histological variant of fibroadenoma (4%), where stroma proliferation is more enhanced compared to intraductal epithelial hyperplasia. It has a rapid growth rate, and over 5 cm it is considered gigantic juvenile fibroadenoma. Based on the imaging and biopsy findings, differential diagnosis with phyllodes tumors is impossible. Consequently, total surgical removal is recommended. Ultrasound properties are similar to those of fibroadenoma and phyllodes tumors [1,4,11].

Fibroadenoma should be differentiated from non-neoplastic benign lesions (cysts, hematomas, mastitis, abscesses), other benign (hamartoma, intraductal papilloma, juvenile papillomatosis) and malignant (metastases, phyllodes tumors, carcinoma) masses [1,2,4,11].

Phyllodes tumors are the most frequent primary malignant lesions in children and teenagers. It has a very high rate of recurrence and no lymphatic metastases. Clinical and imaging findings are very similar to fibroadenomas. Heterogeneous ultrasound structure differentiates them from benign fibroadenomas, but not from gigantic fibroadenomas. Surgical removal with extended safety margins is recommended. Young patients with malignant phyllodes tumors require strict monitoring [1,2,4,9].

Experience of medical professionals regarding diagnosis and management of breast pathologies in children is limited, as the incidence of these pathologies is low, and there is scarce information available in the literature. Clinical and imaging findings in malignant and benign lesions are many times similar. Diagnostic and therapeutic management of these lesions should be conservative, in order to avoid development of secondary lesions in the developing breast. Breast ultrasound findings in children have to be correlated with age, personal and family disease history, and racial background [2,4].

We **conclude** that of all imaging modalities, ultrasound examination contributes most frequently to the study of breast development, and aids in early and non-invasive differential diagnosis of breast lesions in children and teenagers.

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FIRST METACARPAL LENGTHENING AND LITTLE FINGER DEFORMITY CORRECTION IN A COMPLEX HAND TRAUMA, SECONDARY TO SUCCESSFUL RECONSTRUCTION IN EMERGENCY BY A FREE ALT FLAP– CASE PRESENTATION – PRELIMINARY REPORT

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Abstract

We report a case of an 18 year-old male patient which suffered a complex injury of the right hand that initially managed successfully in emergency by a free vascularized ALT flap two years ago. The ALT flap has been fitted with great precision at the lesion margins, ensuring a good quality and esthetic skin coverage to the patient's hand.

Two years after the accident, while the management with microsurgical reconstructions has been completed, the patient was admitted in our clinic for first metacarpal lengthening.

We remark that the patient had already excluded any other surgical solution for improving his hand, including tow transfer.

***Operative Procedure. Step I.** A flap division at the level of the first ray of the right hand and first interdigital web space reconstruction have been performed, aiming a better functional result. **Step II.** Following a first right metacarpal osteotomy by an electrical saw, an external mini rail fixator-distractor has been applied. **Step III.** After the flap division, all the donor site areas defects of the new formed thumb has been grafted by free split thickness skin. **Step IV.** A Corrective osteotomy of the distal phalanx of the little finger of the right hand and DIP(Distal Interphalangeal joint) arthrodesis using percutaneous Kirschner wires have been done.*

The first metacarpal bone lengthening was initiated the 7th postop day.

Keywords: metacarpal lengthening, ALT flap, surgery, metacarpal osteotomy, external fixator

Introduction

Metacarpal lengthening based on the distraction osteogenesis or "calotasis" principle (G.Ilizarov technique which initially was applied to the big long bones) is a reliable technique fully indicated for the correction of the brachydactyly, congenitally short metacarpals, traumatic amputations or complex trauma of the hand. Mansoor and Matev [1,2] were he first to introduce a technique that allows for metacarpal lengthening. The most frequently used techniques to lengthen the metacarpal bones are one-stage lengthening with a bone graft interposition or

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gradual lengthening by callus distraction [3,4,5]. We report the case of an 18 years old male patient which suffered a complex right hand trauma initially reconstructed with ALT flap two years ago. The patient underwent the following surgery: Division of the ALT free flap at the level of the first ray of the right hand and first interdigital web space reconstruction. First right metacarpal osteotomy and metacarpal lengthening using an external mini rail fixator according to "Distraction osteogenesis technique for small long bones". Free skin grafting of the donor site thumb area defects has been performed. A corrective osteotomy of the distal interphalangeal (DIP) joint of the little finger of the right hand and DIP arthrodesis using two percutaneous Kirschner wires was done.

Case presentation

We present a case of an 18 year-old male patient who suffered a complex right hand injury caused by corn harvester device (Figure 1), which had been initially managed successfully by multiple (three) surgical interventions, ensuring to the patient an esthetic and resistant hand coverage.

Subsequently, the patient was admitted in our clinic, where after clinical and paraclinical examinations (right hand radiography and computer tomography) has been operated. The case has been registered as complex right hand trauma reconstructed/covered in emergency by a salvage and coverage free vascularized ALT flap (Figure 2).

On admission, the patient signed the informed consent form and the consent form for using his medical data in scientific purposes. The operation was done under general anesthesia and a pneumatic tourniquet was applied to the arm. During the above reported surgery we have performed the following interventions: 1.Division of the coverage flap at the level of the first ray of the right hand and 2.first interdigital web space reconstruction. 3.First right metacarpal osteotomy and 3.An external mini-rail device fixation destined for diaphysis lengthening. Free skin grafting of the donor site thumb area defects. 4. Corrective osteotomy of the distal joint of the little finger of the right hand and arthrodesis using percutaneous Kirschner wires.

The Metacarpal initiation lengthening was scheduled the 7th postop day.

Intraoperatively we used the Orthofix MiniRail external fixator.

The postoperative evolution was successful (Figure 3) and the patient has been discharged from the clinic three days after the operation. The 1st metacarpal lengthening was initiated 7 days post-operatively. The patient has been instructed on the lengthening procedure and the first rotations of the distractor by Allen key have been done under supervision. Distraction was completed 51 days post-operatively, after we gained the scheduled 2.5 cm metacarpal length. Adequate union of the bone has been achieved in 118 postoperative days, then the distractor has been removed. The patient was advised to perform a 90 degrees rotation of the distractor twice per day (every 12 hours), using an Allen key; this daily rotation corresponding to a lengthening rate of 0.5 mm per day. Postoperatively both clinical and radiological follow-up of the right thumb and little finger (Figures 4, 5, 6), showed full bone healing and functional rehabilitation 4.2 month postoperatively.

The Kirschner wires from the little finger have been removed 56 days after surgery, while the external fixator from the first metacarpal had been removed 4.2 months after surgery. Daily efficient sessions of hand therapy had been started 15 days postoperatively and have been intensified when the lengthening was finished (50 days postop).

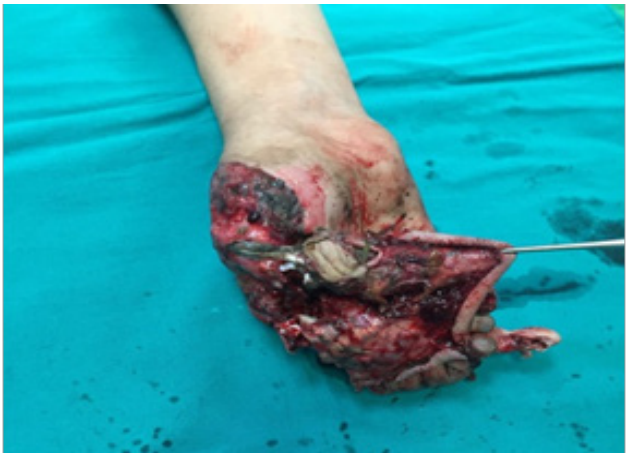

Figure 1. right hand after the traumatic accident.

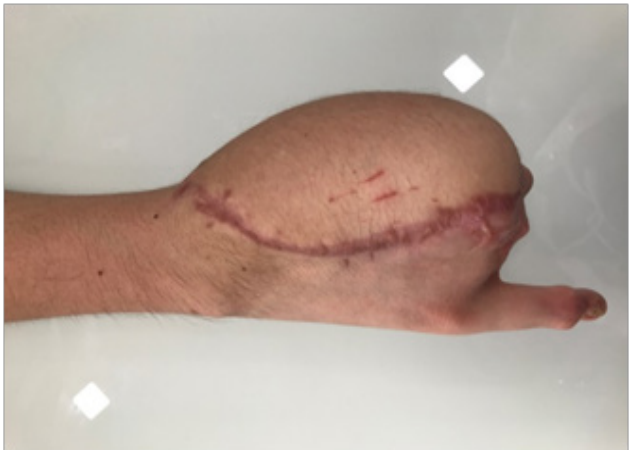

Figure 2. Right hand – two years after a fully successful coverage by an ALT free flap.

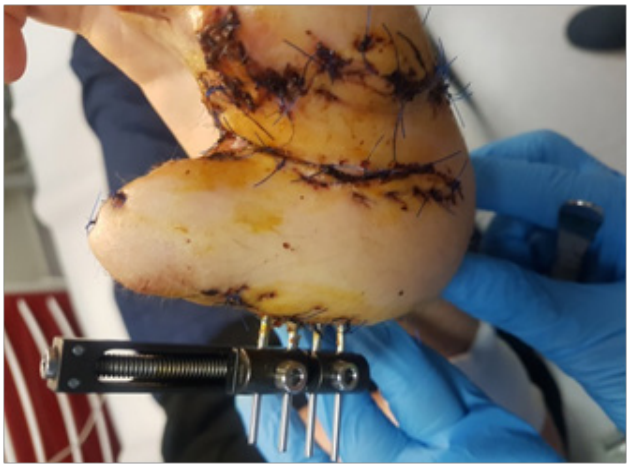

Figure 3. Ten days postoperative - Satisfactory evolution of the free skin grafting of the right thumb defects.

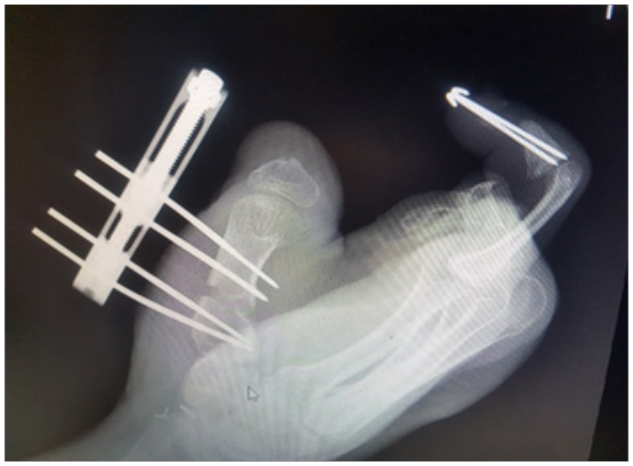

Figure 4. 12 days postoperative radiography -5 mm lengthening of the first right metacarpal bone.

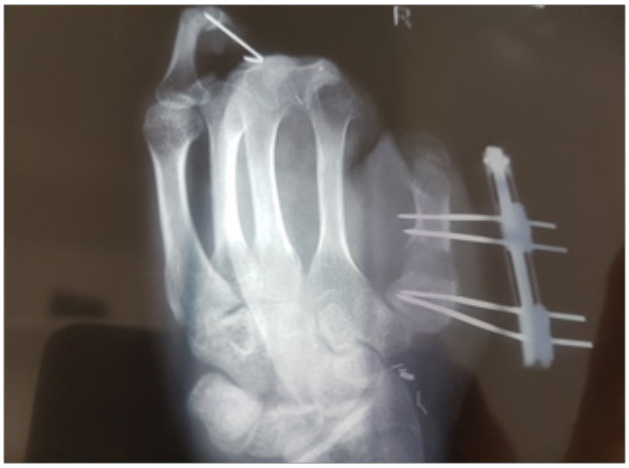

Figure 5. 37 days postoperative radiography – 18 mm lengthening of the first right metacarpal bone.

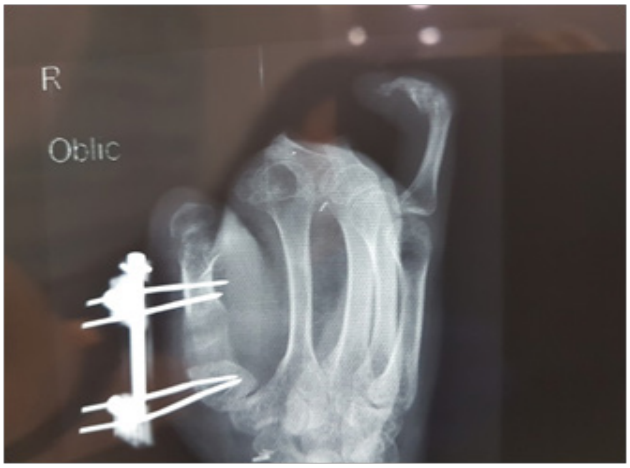

Figure 6. 51 days postoperative radiography - 25 mm lengthening of the first right metacarpal bone.

Discussion

The patient who underwent the 25 mm 1st metacarpal lengthening confirmed to us that he is fully satisfied of both functional and esthetic improvement of the hand and he is able to perform his basic daily living activities (Figures 7, 8, 9). The right first metacarpal lengthening was 25 mm, which corresponded to other studies results that showed lengthening parameters situated between 13–26 mm [6,7,8]. The metacarpal lengthening corresponded to 37% of the initial bone length. The mini-rail device remained fixed totally 4.2 months, time which agrees with the mean recommended interval from other reliable studies (2.2–4.0 months) for the metacarpal lengthening procedures [6,7,8]. A desirable length of 2.5 cm was gained in 51 days from the surgery and a complete bone healing has been achieved in 67 days.

The most frequently used techniques to lengthen the metacarpal bones are one-stage lengthening with an intercalary bone graft or the gradual lengthening by callus destruction. [3,4,5]. We used the distraction osteogenesis or callotasis, which is currently more popular for metacarpal lengthening. The advantages of this method are: greater final bone length, no morbidity at the donor site, a lower incidence of neurovascular damage because of the graduality of the distraction of both bonny and soft tissue anatomical components of the hand [6,7,8,9,10,11,12]. In our case, bone graft was not used at all. The external fixator was kept until the fracture has been fully healed [6,7,8,9,10,11,12].

Most authors recommend lengthening between 0.5 mm to 1.0 mm per day[13.14,15,16] In our case, two daily lengthenings of 0.25 mm each, giving 0.5 mm per day, was appropriate to us as no complications were noted. Some of the factors that can induce a longer consolidation period after distraction osteogenesis are: damage to the periostal tissue and a distraction rhythm greater than 2×0.25 mm/

day [10,11,12]. Most authors recommend lengthening should not be more than 40% or 20 mm of the pre-operative bone length. If the metacarpal lengthening is larger than 33%-40% of the preoperative bone length, possible complications can be observed: late fracture, angulation, stiffness of the metacarpophalangeal joint , subluxation, delayed union, non-union, premature consolidation, neurovascular injury. In our case the lenghtening obtained was 25 mm, but these postoperative complications were not observed. Preoperatively, we did not know if the thenar region muscles and the carpo-metacarpal joint mobility were preserved.

Contrary to other mammals, basic hand function of the human requires opposition of the thumb, therefore in our case opposition recover was very important, especially because the trauma involved the right hand of the patient. The guide lines from the "Orthofix" company for big long bones distraction (Femur, Tibia, Humerus etc) is to gain 1 mm per day (each 6 hours 0.25 mm or 4 times per day), while practically for small long bones (metacarpals, phalanges) a distraction of 0.5 mm per day is more safe, avoiding bone non-unions. We perform 2 sessions of the distractor rotations per day (each of 0.25 mm) because is much more easy and practical for the patient to turn the key twice per day instead of turning it every 6 hours and by the other hand the efficacy of the technique was not affected at all.

After a period of time the patient was able to use the thumb for the basic hand functions such as abduction, adduction and opposition. We did not choose toe transfer in this case because we considered better functional results and cosmetic appearance by performing first metacarpal lengthening. Any way a toe transfer could be very risky because of the kind of injury (mangled hand), where the vascular and lymphatic supply of the hand have been quite compromised and by the other hand the patient has not agreed for such a demanding surgery. The particularity of this case is represented by performing the metacarpal lengthening two years after the free ALT flap [17], and the possibility that the tendons of the thenar muscles, and the nerves involved in opposition movement could be destroyed. For cosmetic reasons we consider the possibility of future second and third rays metacarpal lengthening.

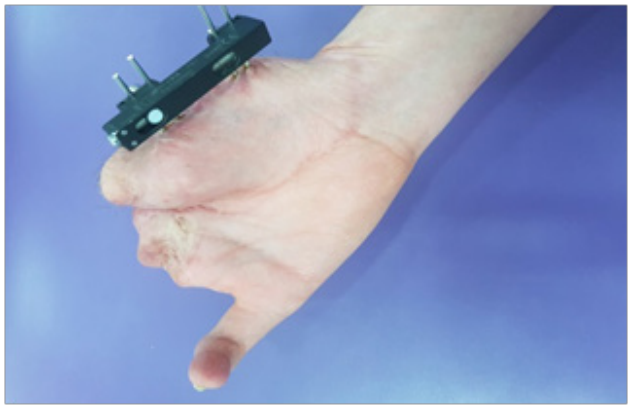

Figure 7. Postoperative functional improvement - adduction of the thumb

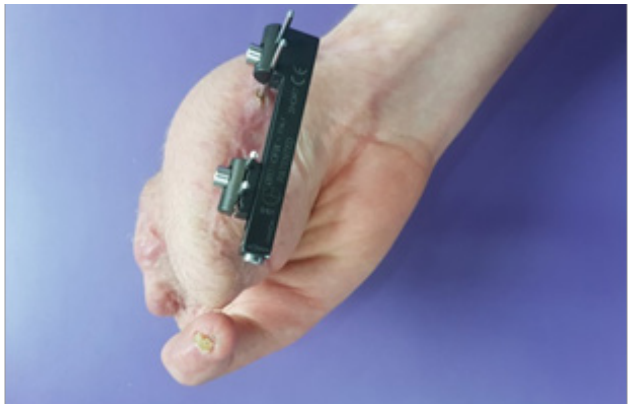

Figure 8. Postoperative functional and esthetic improvement-opposition of the thumb

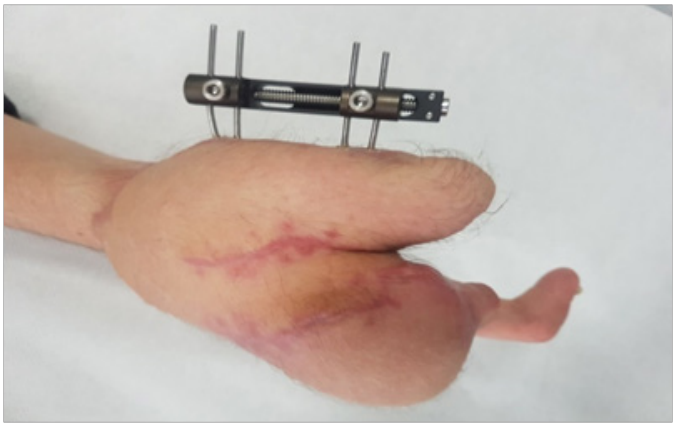

Figure 9. 51 days postoperative – 25 mm lengthening of the first right metacarpal bone and first interdigital web space reconstruction

Conclusions

The distraction osteogenesis procedure is a successful and reliable technique for the lengthening of the metacarpal bones. Complications such as stiffness, angulation, subluxation of the MCP joint and delayed union or non-union are associated with these procedure if distraction rate is more than 2×0.25 mm/day and lengthening a bone by more than 33% ,or more than 20 mm of the preoperative bone length. In our case the lengthening obtained was 25 mm and almost at 37% of the initial bone length, but postoperative complications were not observed. The particularity of this case consists in the fact that preoperatively, we did not know if the thenar musculature, thenar motor innervation and the carpo-metacarpal joint mobility were preserved two years after ALT flap reconstruction, but the patient was able to perform the basic daily activities after a postoperative period of time.

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MODIFIED ANATOMICAL LANDMARKS IN RHINOSINUSAL SURGERY

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Abstract

The thorough knowledge of anatomical landmarks is mandatory in rhinosinusal surgery, only through this is possible to realize a modern surgical intervention. This is characterized by a direct visual control approach and it must be as functional as possible (Functional Endoscopic Sinus Surgery - FESS). Both developed and iatrogenic conditions can modify this indispensable landmarks.

The authors present the importance of the endoscopic anatomy and the modified landmarks through two cases. A case of a symptomatic concha bullosa, which is a pneumatisation of the nasal turbinates and another case of septo-turbinal adherential condition, occurring after septal deviation surgery.

Keywords: functional nasal surgery, concha bullosa, septo-turbinal adherentia, nasal turbinate

Introduction

Functional nasal and sinusal surgery represents the obligation of the surgeon to preserve and restore the normal and functional nasal status. This is possible only through the accurate acquaintance of the nasal anatomy and physiology. Some conditions can modify this essential landmarks, making the surgical intervention more difficult and obliging the surgeon to solve it too. These conditions can simply be developed (like concha bullosa), or can appear as a consequence of naso-sinusal surgery.

The term of concha bullosa it refers to a pneumatized (air-filled) cavity within a nasal turbinate, it can appear in any turbinate, but we mostly find it in the middle one Concha bullosa can be identified in approximately 35% of patients, its clinical importance lies in the caused dysfunction in the ostio-meatal complex [1]. The possible symptoms includes: nasal obstruction, pain, hyposmia, facial tension, retro-orbital pressure, rhinorrhea and sinonasal pathologies [2,3].

Depending on the patient's heeling tendency, even after well done surgical intervention, can appear complications, some of them resulting in modified landmarks, anatomical structures, causing dysfunctions. In the nasal cavity, after surgery, patients may develop adherences, pathological attachments between different structures (septum, inferior-, middle turbinates etc.) with consequential alteration of one or more nasal functions (sinus drainage, respiration, smell etc.) [3].

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Methods

The authors present the importance both of the endoscopic anatomy and the modified landmarks through two cases. A case of a symptomatic concha bullosa, and another case of multiple septo-turbinal adherential condition.

Case reports

Case 1

A 24 years old female patient with repeated upper respiratory infections in her history, is complaining of chronic nasal obstruction, hyposmia, rinoree, symptoms persisting despite of the medical treatment. Clinical examination, including nasal endoscopy reveals a left side septum deviation, an enlarged pneumatized middle turbinate and the hypertrophy of the inferior turbinates (Figure 1). After an imagistic examination (CT scan) the following diagnosis were set up: Nasal septum deviation, chronic hypertrophic rhinitis, right middle turbinate concha bullosa. The indication of a surgical intervention was established.

In general anesthesia we performed a septoplasty, resection of the lateral wall of the right middle concha (Figure 2) and radiofrequency reduction of the hypertrophic inferior turbinates. Nasal packing removed after 24 hours, postoperative care was performed by removing of the scars and cleaning of the nasal cavity with normotonic saline solution.

Nasal respiration normalized after 10 days. The 3 month follow-up shows a normal nasal cavity with midline septum and functional middle meatus due to the normal size middle turbinate (Figures 3 and 4).

Case 2

A 31 years old male patient with nasal septum resection in his history, complaining of persisting nasal obstruction and posterior nasal discharge, 1 year after the surgical intervention.

Clinical examination, including nasal endoscopy identify multiple concrescences between the left inferior turbinate and the septal mucosa, such as a polypoid degeneration of it (Figure 5).

Under local anesthesia (infiltration with Xyline 1%) we performed a radiofrequency cauterization of the involved area, followed by the sectioning of the adherentia (Figure 6). In order to avoid recurrence a resorbable nasal tampon has been inserted.

Postoperative care was performed by removing of the scars and cleaning of the nasal cavity with normotonic saline solution

The 1 month follow up shows a normalizing nasal fossa with recognizable anatomic landmarks.

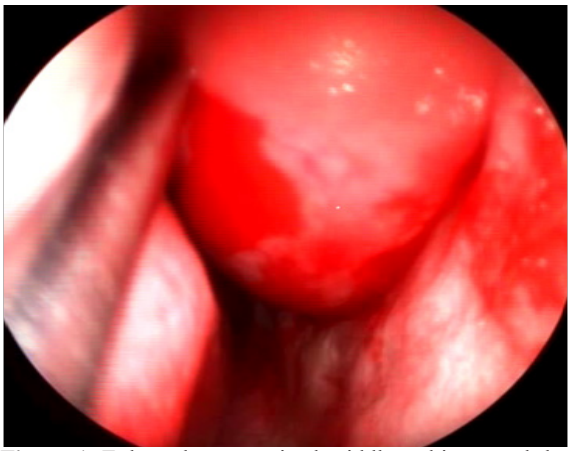

Figure 1. Enlarged pneumatized middle turbinate and the hypertrophy of the inferior turbinates.

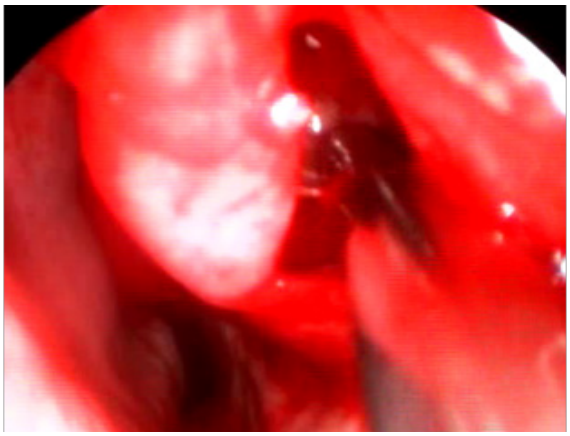

Figure 2. Resection of the lateral wall of the right middle concha.

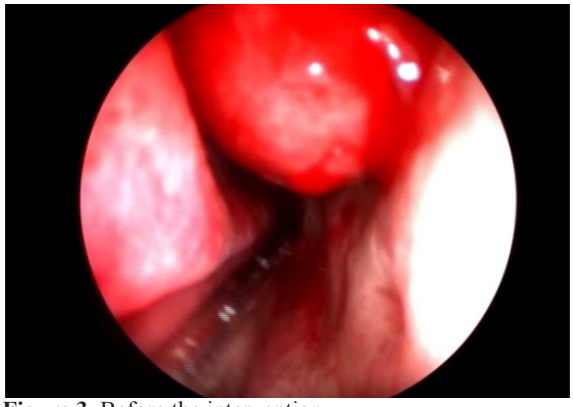

Figure 3. Before the intervention.

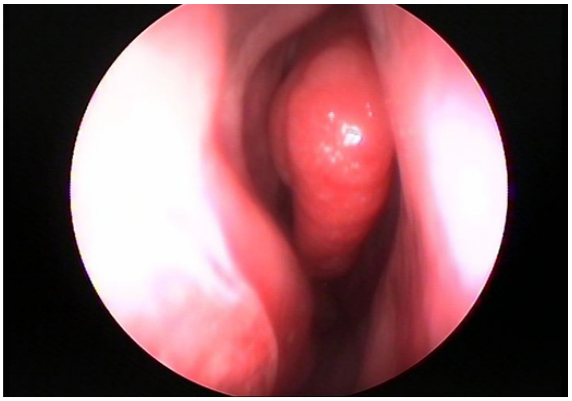

Figure 4. Normal nasal cavity with midline septum and functional middle meatus due to the normal size middle turbinate.

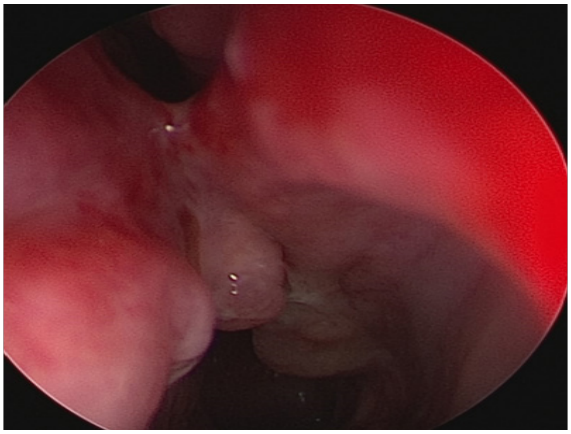

Figure 5. Multiple adherentia between the left inferior turbinate and the septal mucosa, such as a polypoid degeneration.

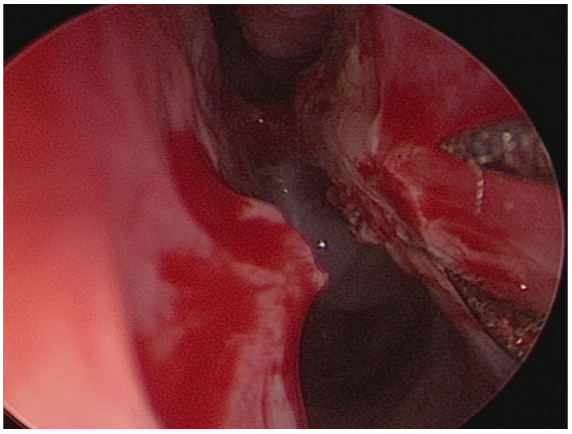

Figure 6. Sectioned adherentia.

Discussion

Modern surgical interventions must be as functional as possible, it must conserve and rebuilt (if necessary) the physiological structures. In order to re-establish the normal nasal condition it is mandatory to recognize and describe during the examination the functional areas of the nasal fossa and through this the potential pathologic modifications too.

Conclusion

Both Concha bullosa and iatrogenic nasal conditions can alter the good function of the nasal physiology causing complaint to the patient.

Performing a functional nasal surgery it is mandatory to recognize and solve all of the pathogen conditions.

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THE LONGEVITY OF THE FIRST PERMANENT RIGHT SUPERIOR MOLAR

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Abstract

The teeth develop due to a complex physiological phenomenon called dental eruption. On the first molar there are early carious lesions, initially on occlusal face, 2 years after the eruption, after this period we detect lesions on the medial face, and after 6 years from the eruption, distal caries lesions are common. The sample consisted of 23 patients aged 22-50 years, with an average age of 31.82 years, who were clinically and radiologically examined in the private dentistry in Oradea. We present the cases of 2 patients who have the second degree of kinship, the first 31-year-old, female, in the urban environment with higher education, presented to the cabinet for the cleaning of the teeth and the treatment of carious processes. After a clinical consultation, radiographic examination of the orthopantomography type was recommended to assess the patient's initial status and to develop a treatment plan. From our study we can see that the first right superior molar has a higher viability, this has been followed from the family point of view.

Keywords: dentistry, mollar teeth, dental therapy

Introduction

In the human body, the highest degree of mineralization is attributed to the tooth by 96-97% [1]. The teeth develop due to a complex physiological phenomenon called dental eruption. This eruption of the permanent teeth begins at the age of 6 with the first molar lower and ends with the rash of the third molar (M3).

Rarely, the first molar is extracted to create space in dental fillings, but they are often extracted due to carious pathology [2]. The first molar occupies the most space on the arch, being the most voluminous.

On the first molar there are early carious lesions, initially on occlusal face, 2 years after the eruption, after this period we detect lesions on the medial face, and after 6 years from the eruption, distal caries lesions are common [3].

The 6-year old molar intervenes in a second degree occlusion, Angle considering it a reference point of normal occlusion, naming Angle's key to position the first lower molar relative to the first molar [4].

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Material and method

The sample consisted of 23 patients aged 22-50 years, with an average age of 31.82 years, who were clinically and radiologically examined in the private dentistry in Oradea. 12 female (52, 17%) and 11 male (47, 83%), 19 urban (82.6%) and 4 rural (17.4%). From an economic point of view, 65% of patients have a low income and 55% of patients have average education.

Results and discussions

In 78.261% of cases, 18 patients respectively, the upper right molar 1 (1.6) is present on the arch, of which 8 female patients and 10 male patients; the presence of the carious processes was not taken into account, only the presence on the arcade and the viability of the tooth.

The upper left molar (2.6) was present on the arcade at 47.826%, in 11 of 23 patients, of whom 6 were female and 5 were male.

The left lower left molar (3.6) was present in 26.087%, of which 3 were female and 3 were male.

The lower right one molar (4.6) was present in 30.435% of the cases, 2 were female, 5 male (Figure 1).

We present the cases of 2 patients who have the second degree of kinship, the first 31-year-old, female, in the urban environment with higher education, presented to the cabinet for the cleaning of the teeth and the treatment of carious processes. After a clinical consultation, radiographic examination of the orthopantomography type (Figure 2) was recommended to assess the patient's initial status and to develop a treatment plan. From a prosthetic point of view, I put Kennedy's third-grade editorial, upper and lower. As an odontal diagnosis, we have multiple treated caries lesions, and at level 3.5 there is a complicated carious process treated with periapical process with cystic transformation of 1.8 / 1.5 / 0.5 cm.

From the clinical and radiological examination we can see that the only 6-year old molar present is 1.6 (upper 1 molar), from the anamnesis it appears that the other six-year-old molars were extracted due to complicated carious processes.

The 2-year-old, 29-year-old, high-school, urban environment presented himself at the 4.4-degree pain management clinic, following treatment of the carious lesion with symptom relief. A radiographic examination of the orthopantomography type (Figure 3) was recommended to create an overview of the dental status. From a prosthetic point of view, I put Kennedy 3rd, upper and lower grade, one-sided right. As an odontal diagnosis we have multiple caries lesions treated and untreated.

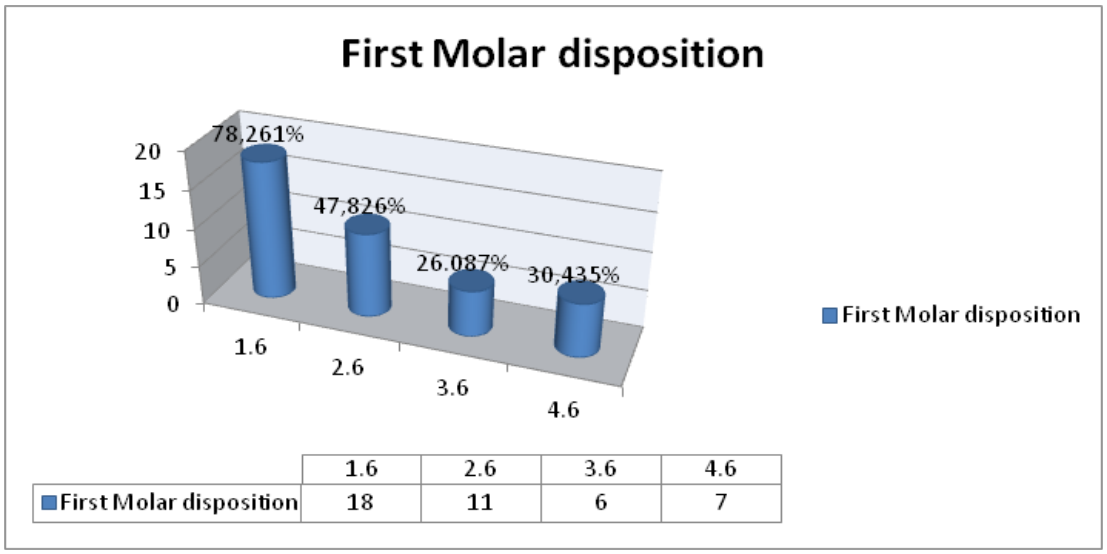

Figure 1. First molar disposition.

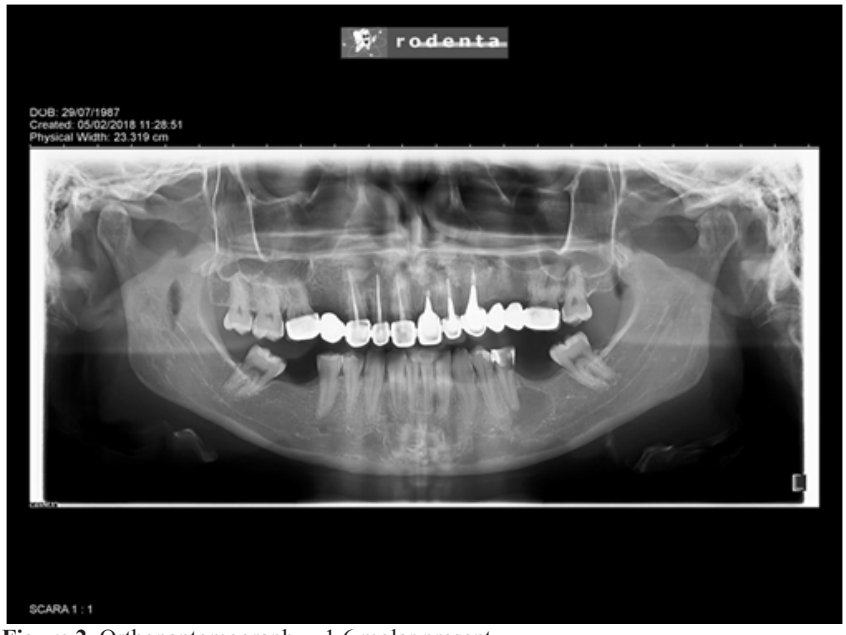

Figure 2. Orthopantomography –1.6 molar present.

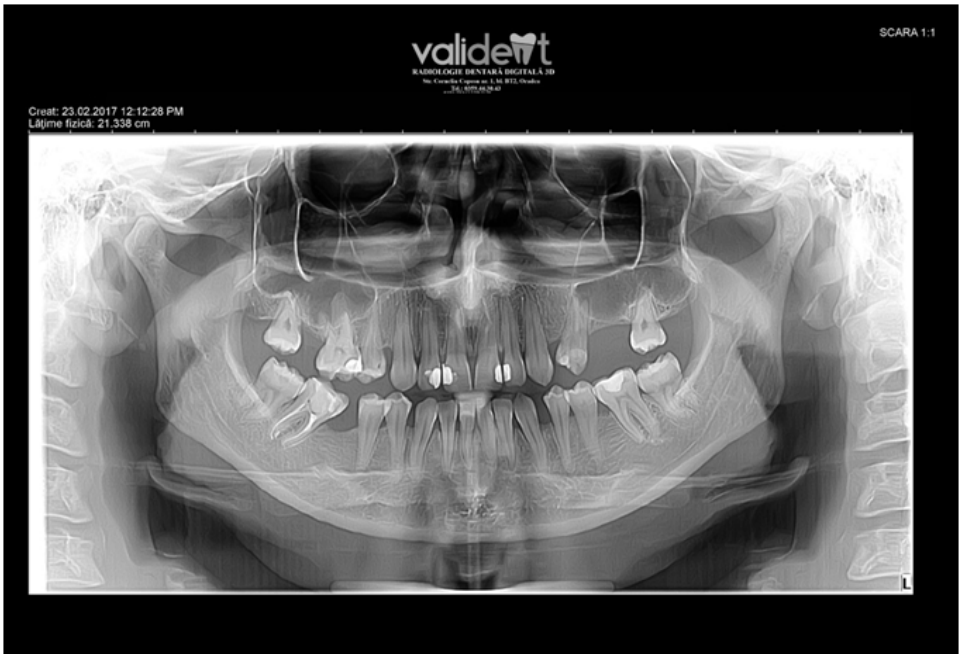

Figure 3. Orthopantomography, 1.6 present on arcade.

From the clinical and radiological examination it appears that among the 6-year old molars, the only one present on the arcade is the upper right molar (1.6).

Higher Molar I has the following clinical implications:

* is the first tooth that erupts on the upper arcade around the age of 6, distal to the temporary second molar with which it resembles a lot;

* is affected prematurely and frequently by carious lesions due to its calcification at birth and lack of interest in oral hygiene manifested at the age of its eruption;

* sealing of ditches and beaks is indicated;

* the complete formation of the apex (closing the root) around the age of 10 years makes difficult endodontic therapy in the case of difficult pulping complications;

* wear is more intense at the level of palatal cusps;

* extraction can be accompanied by complications due to the root gauge, the divergence of roots and proximity to the maxillary sinus [5,6].

Conclusions

From our study we can see that higher right molar 1 has a higher viability, this has been followed from the family point of view.

Data from the literature on the presence of the first upper right molar are few and our study is made up of a small number of patients, which excites our interest in continuing this observational study to publish more data in the future about M1 right superior longevity.

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DETECTION OF LYMPH NODE MICROMETASTASES IN COLORECTAL CANCER USING THE SENTINEL LYMPH NODE

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Abstract

Objectives. *The aim of the study was to identify lymph node micrometastases using the sentinel lymph node method (in vivo and in vitro) in order to improve the staging and prognosis of colorectal cancer patients undergoing curative surgery.*

Method. *We conducted a prospective study on a total of 44 patients with stage I-III colorectal cancer, undergoing radical surgery at the Fifth Department of Surgery of Cluj-Napoca Municipal Clinical Hospital between September 2012 and January 2015. For the identification of micrometastases we used the sentinel lymph node mapping by two techniques, in vivo and ex vivo, using methylene blue. In N0 patients we conducted an immunohistochemical study to identify micrometastases for both sentinel nodes and the other excised lymph nodes.*

Results*. Of the 44 patients, ten patients (12.8%) had stage I cancer, 12 patients (27.3%) had stage IIA cancer, two (4.5) had stage IIIA cancer, 18 patients (40.9%) had stage IIIB cancer and two (4.5%) had stage IIIC cancer. Sentinel lymph node detection rate was 72.7% for the in vivo technique and 81.8% for the ex vivo technique. For the ex vivo technique, accuracy was 88.8% and sensitivity was 83.3%. For the in vivo technique, accuracy was 75% and sensitivity was 75%. The percentage for the detection of micrometastases was 25% in vivo and 33.3% ex vivo.*

Conclusions. *The use of the sentinel lymph node method for the detection of lymph node micrometastases in patients with colorectal cancer is a feasible and safe method.*

Keywords: micrometastases, colorectal cancer, sentinel lymph node, prognosis

Introduction

Treatment for colorectal cancer first consists in the en bloc surgical removal of the tumor-bearing segment of the bowel, together with the adjacent lymph drainage area, as far as the cancer has spread. After the histopathological examination of the surgical sample and the lymph nodes, the stage of the tumor is determined by the identification of T and N stage. These are the most important prognostic factors [1].

N0 stage in which the histopathological examination with hematoxylin and eosin stain did not identify any regional lymph node metastasis requires no adjuvant treatment. N+ with positive lymph nodes requires chemotherapy and/or adjuvant radiotherapy.

However, it has been found that cancer recurrence occurs in approximately 20-30% of NO cases [2]. One reason could be the presence of lymph node micrometastases at the time of surgery. Ideally, all excised lymph nodes should be evaluated for the presence of micrometastases. This objective is achieved by immunohistochemistry and chain-growth polymerization, but these techniques are extremely costly and time-consuming, therefore, they are not part of the current practice. By definition, the sentinel lymph node is the first lymph node receiving drainage from the primary tumor, and once identified, it may be more easily subjected to tests to identify macro or micro metastases. If micrometastases

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are detected, overstaging may occur, which means that a patient that was initially identified with N0 stage becomes N+, with the possibility of being at a more advanced stage and receiving adjuvant treatment [3].

Micrometastases are metastases sized between 0.2 and 2 mm and defined for colorectal cancer by the Union for International Cancer Control (UICC) in 2002. Only a limited number of studies have analyzed the implications of metastases according to this definition and the clinical significance of lymph nodes carrying micrometastases is still an intensely debated issue [4,5].

In colorectal cancer, the method for the detection of the sentinel lymph node has the role of determining lymphatic staging more precisely in order to identify patients at high risk of developing tumor progression or tumor recurrence [6].

The aim of our study is to identify lymph node micrometastases using the sentinel lymph node (in vivo and in vitro) in order to improve the staging and prognosis of colorectal cancer patients undergoing curative surgery.

Material and method

In order to achieve the proposed objectives, we conducted a prospective study consisting of 44 patients with stage I-III colorectal cancer, admitted and undergoing radical surgery at the Fifth Department of Surgery of the Municipal Clinical Hospital in Cluj-Napoca between September 2012 and January 2015. Exclusion criteria in the study were the presence of distant metastases, synchronous primary tumors, locally advanced tumors (T4a, T4b), patients undergoing emergency surgery, patients undergoing palliative surgery, patients with preoperative chemotherapy, patients with tumors located in the medial and lower part of the rectum, patients with BMI >30, patients preoperatively tested positive as allergic to methylene blue, patients with incomplete data and those who did not sign the informed consent form. The study was approved by the Ethics Committee of Cluj-Napoca Municipal Clinical Hospital.

To identify the sentinel lymph node we used two different techniques - *in vivo* and *ex vivo* -using 1% methylene blue vital stain.

The in vivo technique for the detection of the sentinel lymph node was performed as described by Saha et al. [7]. After the peritoneal cavity was opened, loco-regional exploration was performed to identify the tumor, to check tumor topography, features, mobility, penetration in neighboring organs, general examination regarding the presence of synchronous tumors and remote metastases. The tumor mass moved to gain access to the tumor site without interrupting the lymphatic drainage pathways. The injection of 1-5 ml dye was made at circumferential peritumoral level using a 26-28 gauge needle. The injected area was gently massaged for about 5 minutes. The first colored lymph nodes (between 1 and 4) within the first 10 minutes after injection were considered the sentinel lymph nodes and they were stained intraoperatively. Surgery continued in the proposed standard manner. After surgery, the stained sentinel lymph nodes were excised and separately sent to the Department of Pathological Anatomy together with the resection piece.

The ex vivo technique for the detection of the sentinel lymph node was performed as described by Wong et al. [8]. Within 30 minutes after colorectal resection, the specimen was longitudinally incised on the anti-mesostenic edge. Submucosal injection of 0.5-1 ml methylene blue dye was performed into each of the four quadrants around the tumor. The injection sites were gently massaged for 2 to 5 minutes. The lymph nodes stained with blue dye in the first 10 minutes are considered the sentinel lymph nodes and are dissected and presented separately for pathological analysis.

Sentinel lymph nodes and resections were examined morphopathologically using the standard method. N0 was the case of patients with negative sentinel lymph nodes or other types of lymph nodes, performed together with immunohistochemistry in order to identify micrometastases for both sentinel lymph nodes and other lymph node biopsies.

For the immunohistochemical examination, 4-micron sections were cut from each paraffin block where sentinel lymph nodes and other types of lymph node biopsies were embedded, further being dewaxed and rehydrated. The sections were then incubated with anti-cytokeratin 20 antibodies (CK20; K20.8 clone, 1: 400 dilution, DAKO, Carpinteria, CA) for 30 minutes. The Streptavidin-biotin complex method was used for detection of antigen-antibody reaction. The presence of staining of cell nuclei of any intensity was considered positive and assessed by the anatomo-pathologist [9].

The aim was to study the detection rate, defined as the number of successful procedures of the total number of procedures performed; accuracy, defined as the number of correct predictions of sentinel lymph nodes in relation to the number of patients with sentinel lymph nodes identified; sensitivity, defined as the number of patients with positive sentinel lymph nodes for the hematoxylin-eosin examination in relation to the number of patients with positive lymph nodes; false negative rate, defined as the number of cases with negative sentinel lymph nodes, but with other positive lymph nodes; overstaging, defined as the number of patients with micrometastasis in sentinel lymph nodes in relation to the number of patients staged N0 during routine histopathological examination. Moreover, our intention was to compare the two methods, in vivo and ex vivo, in sentinel lymph node detection and the identification of micrometastases in patients with colorectal cancer undergoing surgery in order to identify the recurrence rate (local or remote) in overstaged patients and to compare it with the recurrence rate of N0 stage patients.

Results

A total of 44 patients were enrolled in the study after applying inclusion and exclusion criteria. The in vivo technique for the detection of the sentinel lymph node was

performed in 22 patients and the ex vivo technique in the other 22 patients. Mean age in the study group was 63 years ranging between 46 and 84 years. Of these, 24 (54.5%) were men and 20 (45.5%) women. In terms of tumor location, the tumor was located in the cecum in 6 (13.6%) patients, in the ascending colon in 6 (13.6%) patients, in the transverse colon in 6 (13.6%) patients, in the left colic flexure in two patients, in the descending colon in two patients, in the sigmoid colon in 16 (36.6%) patients, and in the rectum in 6 (13.6%) patients.

Of the 44 patients, two were classified as stage T1, 10 were stage T2 and the other 32 were stage T3. In 17 cases, the tumor was moderately differentiated. Ten patients were classified as stage I according to the TNM staging system, 12 patients as stage IIA, two patients as stage IIIA, 18 patients as stage IIIB and two patients as stage IIIC. There were 72.3% patients with more than 12 resected lymph nodes in the study group. The main clinical and morphopathological characteristics of the patients in the study group, subdivided according to the applied technique, are presented in Table I.

Table I. The main clinical and morphopathological characteristics of the patients in the study group.

Clinical and morphopathological characteristics	*Ex vivo (no. /%)*	*In vivo (no. /%)*
Men	14(63.6)	10 (45.5)
Women	8 (36.4)	12 (54.5)
Right colon	6 (27.3)	6 (27.3)
Transverse colon	4 (9.1)	8 (18.2)
Left colon	14 (63.3)	6 (27.3)
Rectum	-	6 (27.3)
T1	-	2 (9.1)
T2	4 (18.2)	6 (27.3)
T3	18 (81.8)	14 (63.6)
N0	10 (45.5)	12 (54.5)
N1a	4 (18.2)	2 (9.1)
N1b	4 (18.2)	6 (27.3)
N2a	2 (9.1)	2 (9.1)
N2b	2 (9.1)	-
I	4 (18.2)	6 (27.3)
IIA	6 (27.3)	6 (27.3)
IIB	-	-
IIIA	-	2 (9.1)
IIIB	10 (45.5)	8 (36.3)
IIIC	2 (9.1)	-
Number of excised lymph nodes		
>12	18 (81.2)	16 (72.7)

Sentinel lymph node detection was performed in 16 out of 22 patients (72.7%) using the in vivo technique and in 18 out of 22 patients (81.8%) using the ex vivo technique. In all cases where the sentinel lymph node could not be detected, the failure was due to technical mistakes.

The ex vivo technique was characterized by 88.8% accuracy, 83.3% sensitivity and a false negative rate of 16.7%. The in vivo technique was characterized by 75% accuracy, 75% sensitivity and a false negative rate of 25%. There were no statistically significant differences between the two techniques regarding the detection rate, accuracy, sensitivity, false negative rate and overstaging (Table II).

Table II. The main characteristics of the sentinel lymph node technique in the study group.

Variable	*In vivo*	*Ex vivo*
No. of lymph nodes	1,63±0,6	1,71 ±0,9
Detection rate	16/22 (72.7%)	18/22(81.8%)
Accuracy	12/16 (75%)	16/18(88.8%)
Sensitivity	6/8 (75%)	10/12 (83.3%)
False negative rate	2/8 (25%)	2/12 (16.7%)
Overstaging	2/8(25%)	2/6 (33.3%)

In patients where standard examination of lymph nodes using hematoxylin and eosin staining did not detect any invasion (N0), immunohistochemical examination was performed to highlight possible micrometastasis, using cytokeratin, in both sentinel lymph nodes and the other lymph node biopsies. As part of the *in vivo* technique, two cases of micrometastases in sentinel lymph nodes were identified in a number of 8 N0 cases, while for the *ex vivo* technique, two cases of micrometastases in sentinel lymph nodes were identified out of 6 N0 cases. In the two cases, the other resected lymph nodes were negative. The resulting overstaging phenomenon was 25% in *in vivo* and 33.3% in *ex vivo*, which increased sensitivity in both cases. From a total of 44 patients in the present study, we identified 14 cases of N0 where we were able to apply the immunohistochemical method and the result was 4 positive cases. Overstaging occurred in 28.6% of N0 patients and in 9% of the entire study group. Overstaging was superior when using the *ex vivo* technique compared to the *in vivo* technique, but there were no statistically significant differences. This shows that the identification of micrometastases using the sentinel lymph node in both techniques is feasible, cheap and shows promising results. Of the two patients overstaged using the *ex vivo* technique, one was stage I and the other stage IIA, and both patients overstaged using the *in vivo* technique were stage IIA. The four patients were followed for 3 years postoperatively and none followed adjuvant therapy. In the postoperative follow-up period, a single patient, stage IIA and overstaged using the ex vivo technique, showed relapse, respectively secondary hepatic tumors. The result was a recurrence rate of 25% in overstaged patients.

Discussion

In our study, sentinel lymph node detection rate was 72.7% when using the *in vivo* technique and 88.8% for the *ex vivo* technique. The results are related to data in the literature,

where the detection rate ranges from 58 to 100% [10].

The sensitivity of sentinel lymph node detection varies in the literature [10,12] between 33.3 and 100%, in our study the *ex vivo* technique was characterized by 83.3% sensitivity and the *in vivo* technique by 75% sensitivity. In locally advanced cancers (T3/T4), sensitivity decreases and false negative rate increases, while in T1/T2 cancers sensitivity increases and false negative rate decreases. The explanation lies in the fact that advanced tumors either obstruct or interrupt lymphatic drainage.

In our study, the number of locally advanced tumors (T3) accounted for 72.7% of all cases. This explains the reduced sensitivity rate and the increased false negative rate.

In our study, as in other studies in the literature [11], there were no statistically significant differences between the two techniques in terms of detection rate, accuracy, sensitivity, false negative rate and overstaging.

Overstaging, one of the reasons for the detection of the sentinel lymph node, was 33.3% for the *ex vivo* technique and 25% for the *in vivo* technique, using immunohistochemistry to identify micrometastases in sentinel lymph nodes, while the rest of the lymph nodes remained negative. These values correlated with data in the literature, ranging between 0 and 50%. Overstaging was 28.6% in N0 patients and 9% in the entire study group, results slightly lower than other data in the literature [12] due to the fact that almost half of the patients in the study group were diagnosed in stage III (N+).

Recurrence rate was 25% in overstaged patients, compared with N0 patients, which was a statistically significant difference. Data on recurrence and survival in overstaged patients are contradictory in the literature, some studies showing similar results [4,13], while others do not confirm the results [14], therefore further studies on larger and more homogeneous groups of patients with colorectal cancer are necessary, in which the technique used for the detection of the sentinel lymph node and of micrometastases should have higher detection rate and specificity.

Conclusions

The sentinel lymph node detection techniques using methylene blue for the identification of lymphatic micrometastases in colorectal cancer patients is a feasible, safe and inexpensive method both *in vivo* and *ex vivo*. The recurrence rate in overstaged patients is significantly higher when using this technique and the presence of micrometastases should be considered in N0 patients with colorectal cancer.

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DIAGNOSIS AND STAGING OF HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Abstract

Head and neck squamous cell carcinoma is a tumor that arises from specific cells called squamous cells, which are found in the outer layer of skin and in the mucous membranes. It develops in the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, thyroid, and salivary glands.

Aim. *In this single institution study, we aimed to establish the head and neck squamous cell carcinoma patient's demographics and the individual incidence of this malignancies, regarding their anatomical localization, risk factors and main histopathological type.*

Methods. *We investigated 135 patients of the ENT Clinic of Targu Mures between 2012 and 2016. In a retrospective study we followed the incidence of the head and neck squamous cell carcinoma and the histological types based on anatomical localization. All the 135 patients had a rigorous anamnesis, clinical examination and imagistic evaluation. Tissue samples were taken from every tumor followed by pathological examination.*

Results. *In our study 95% of the patients were males. The total number of female patients has been doubled over the examined period. The average age was 62 years, the diagnostic peak of the squamous cell carcinoma was between 60 and 69 years age group. Tobacco use was present at 73% of the patients. Daily alcohol consumption was admitted by 34% of all patients. Most of the tumors were arising from larynx and were diagnosed in stage T4.*

Conclusions. *In this case study, most cases of head and neck squamous cell carcinoma developed at the larynx and the hypopharynx. The incidence of these lesions showed a continuous increase in female sex during the study period, the most frequent risk factor being smoking. Most cases have been diagnosed in advanced stages and have a moderate or poorly differentiated histological appearance.*

Keywords: head and neck, squamous cell carcinoma, risk factors, anatomical localization, histopathology

Introduction

Squamous cell carcinoma (SCC) is a cancer that arises from particular cells called squamous cells, which are found in the outer layer of skin and in the mucous membranes. Head and neck squamous cell carcinoma (HNSCC) develops in the mucous membranes of the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, thyroid, and salivary glands [1].

Epidemiology and risk factors. The incidence and primary site of head and neck cancers presents a large geographic difference. These likely reflect the prevalence of risk factors, such as tobacco and alcohol consumption, as well as ethnic and genetic variety among populations. The most important known risk factor for the seems to be the tobacco (smoked and smokeless). In addition, tobacco and

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alcohol consumption appear to have a synergistic effect [2]. The repeated exposure of the mucosa to the carcinogenic effects of tobacco, alcohol, or both cause multiple primary and secondary tumors in the upper aerodigestive tract, this phenomenon described as "field cancerization" [3]. The highest rates of HNSCC are in older males, but the incidence has been increasing in females due to the fact that more and more women smoke cigarettes. Also, in young non-smokers human papillomavirus (HPV) plays an increasingly prominent role as an etiologic factor in the development of oropharyngeal cancer [4]. Other risk factors include radiation exposure, vitamin deficiencies, periodontal disease, immunosuppression, environmental and occupational exposures, betel nut chewing [5].

Anatomic subsites. HNSCC is classified by its location, arising from a variety of sites.

• The oral cavity includes the lips, buccal mucosa, anterior tongue, floor of the mouth, hard palate, and upper and lower gingiva.

• The pharynx, which is divided into three anatomic regions: nasopharynx, oropharynx, and hypopharynx.

• The larynx is divided into the supraglottic region, the glottic larynx (true vocal cords, anterior and posterior commissures), and the subglottic region, which extends to the inferior border of the cricoid cartilage.

• The nasal cavity and the paranasal sinuses (maxillary, ethmoid, frontal and sphenoid).

• The major (parotid, submandibular, and sublingual) and minor salivary glands [6].

Clinical presentation. The clinical presentation of head and neck cancer varies widely depending upon the primary site.

• Nasopharyngeal carcinoma – Affected patients may present with nasal obstruction and pain, hearing loss (associated with serous otitis media), tinnitus.

• Oral cavity tumors – Symptoms due to the primary tumor may include mouth pain or nonhealing mouth ulcers, loosening of teeth, dysphagia, odynophagia, weight loss, bleeding, referred otalgia.

• Oropharyngeal tumors – Patients may complain dysphagia, odynophagia, otalgia, bleeding, or a neck mass.

• Hypopharyngeal tumors – Common presenting symptoms are dysphagia, odynophagia, otalgia, weight loss, hemoptysis, dyspnea, and neck mass. Patients with these types of tumors often remain asymptomatic for a longer period and are more likely diagnosed in the later stages of the disease.

• Laryngeal cancer – Persistent hoarseness may be the first complaint in glottic cancers; symptoms may include dysphagia, referred otalgia, hemoptysis, stridor. Supraglottic cancers may present with airway obstruction are often discovered later. Patients with a subglottic tumor present with stridor or dyspnea [7] (Figure 1).

Pathology. Squamous cell carcinomas represent 90-95% of the lesions in the oral cavity and larynx. They can be categorized by their differentiation: well, moderately and poorly differentiated tumors. Basaloid, acantholytic, sarcomatoid (spindle cell), verrucous carcinoma are different variants of SCC with distinct pathologic characteristics [8].

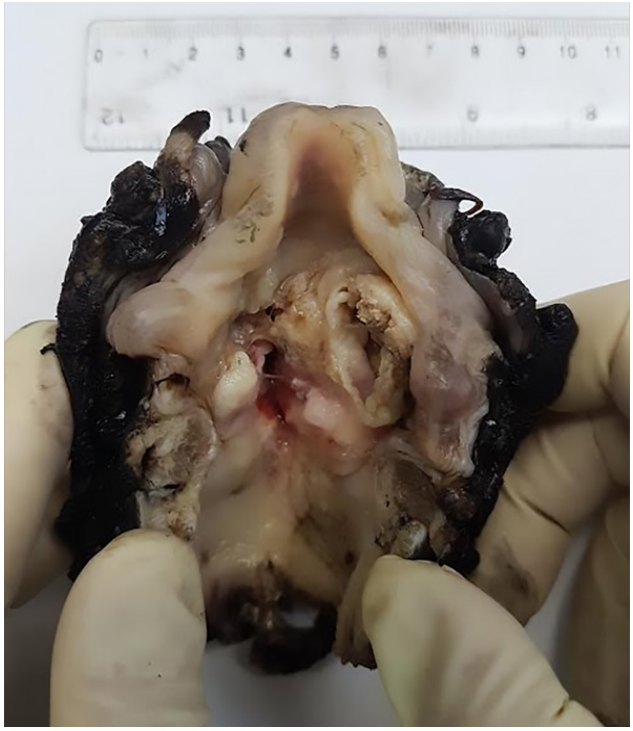

Figure 1. Macroscopic appearance of laryngeal cancer.

TNM staging system. The tumor node metastases (TNM) staging system of the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC) is used to classify cancers of the head and neck. The T classifications shows the extension of the primary tumor and are highly site specific. The cervical node (N) classifications has significant overlap in different anatomical locations and describes regional lymph nodes that are involved. M describes distant metastasis, which means spread of cancer from one part of the body to another. TNM staging varies depending upon the primary tumor site [9].

Diagnosis and staging evaluation. Initial evaluation of the primary tumor is based on a thorough anamnesis and combination of accurate otolaryngology examination (Figure 2). Physical investigation should include inspection, palpation, indirect mirror examination, or direct flexible laryngoscopy. Imaging evaluation (computed tomography, magnetic resonance imaging, PET/CT) is important for assessing the degree of local infiltration, involvement of regional lymph nodes, presence of distant metastases and in planning the surgery (Figure 3). The most important part in the process of determining the presence or extent of a disease is the biopsy. Sampling can be performed by different techniques like ultrasound guided fine needle aspiration, excisional or incisional surgical biopsy [10].

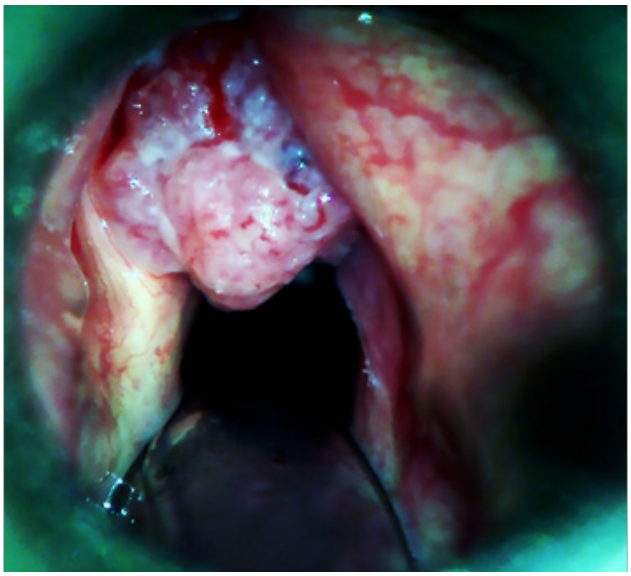

Figure 2. Endoscopic image of a laryngeal squamous cell carcinoma.

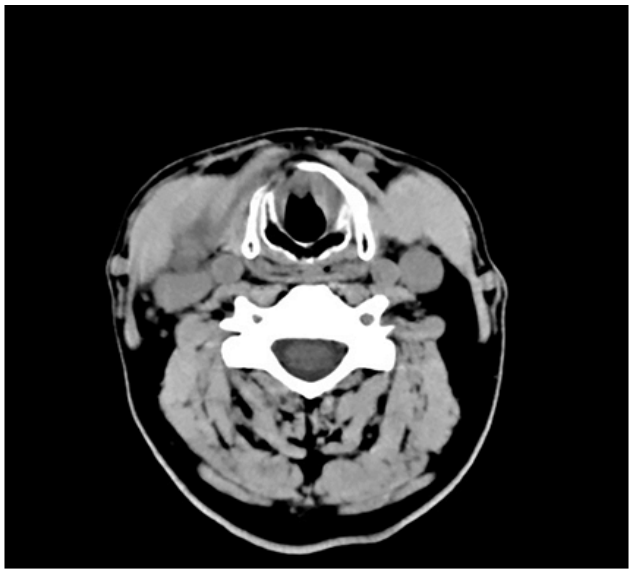

Figure 3. CT image of a laryngeal tumor.

Aim

In this single institution study, we aimed to establish the head and neck squamous cell carcinoma patient's demographics and the individual incidence of this malignancies, regarding their anatomical localization, risk factors and main histopathological type.

Methods

In this retrospective study we examined the patients of the ENT Clinic of Targu Mures. We followed the incidence of the head and neck squamous cell carcinoma and the histological types based on anatomical localization. Data sampling period was between 2012 and 2016. All the 135 patients had a rigorous anamnesis, clinical examination and imagistic evaluation. We had taken biopsies from every tumor, performed by the same surgeon. In addition, our cases were grouped by age group and gender, risk factors as tobacco and alcohol consumption. When was indicated some of the patients after the biopsy had a complete tumor removal surgery followed by pathological examination. Removing the entire primary tumor allowed for a detailed postsurgical pathologic TNM classification (pTNM).

Results

In the examined patient population, we found 128 males and 7 females diagnosed with HNSCC during this 5-year period. In the first year (2012) there were 22 cases diagnosed, only 5% of it were females. By 2016 the total number of patients has been doubled comparing to the first year (Figure 4).

The youngest patient was 39 years old and the oldest had 85 years, the average age was 62 years. Investigating the incidence of HNSCC by age groups we found that most of the patients developed the disease between 50 and 70 years. The proportion of people aged between 50 - 59 years was 39% and between 60 – 69 years was 41% (Figure 5).

Tobacco use was extremely high in the examined patient population. 73% of the patients said that they are smoking cigarettes on daily basis. In addition, another 13% of the patients declared that they are former smokers. Daily alcohol consumption was admitted by 34% of all patients.

Surveying the different anatomical locations, we found tumors arising from a variety of sites. 75 cases (56%) had an initial origin from the larynx. There were 32 patients (24%) with oropharyngeal tumor and 28 cases (20%) had hypopharyngeal presentation (Figure 6).

67% of the patients had the indication for the complete tumor removal surgery. The postsurgical histopathologic TNM classification (pTNM) revealed that 42% of these patients had their tumor diagnosed in T4 stage, and just 6% of them presented in an early T1 stage, which definitely has a better prognostic chance. 37 patients already had involved regional lymph nodes in different stages. We had no data about distant metastases. Categorizing by their histological differentiation only 2% of the cases were well differentiated, the rest of the patients had moderately or poorly differentiated tumors.

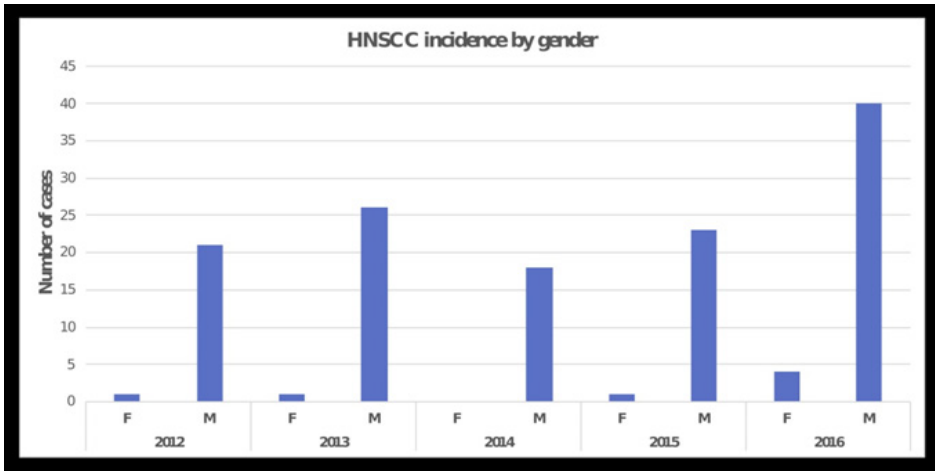

Figure 4. HNSCC incidence by gender.

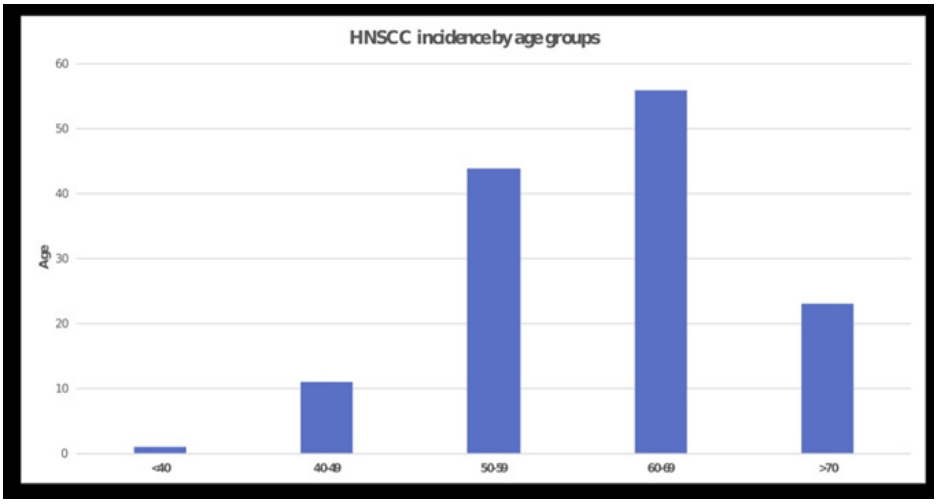

Figure 5. HNSCC incidence by age groups.

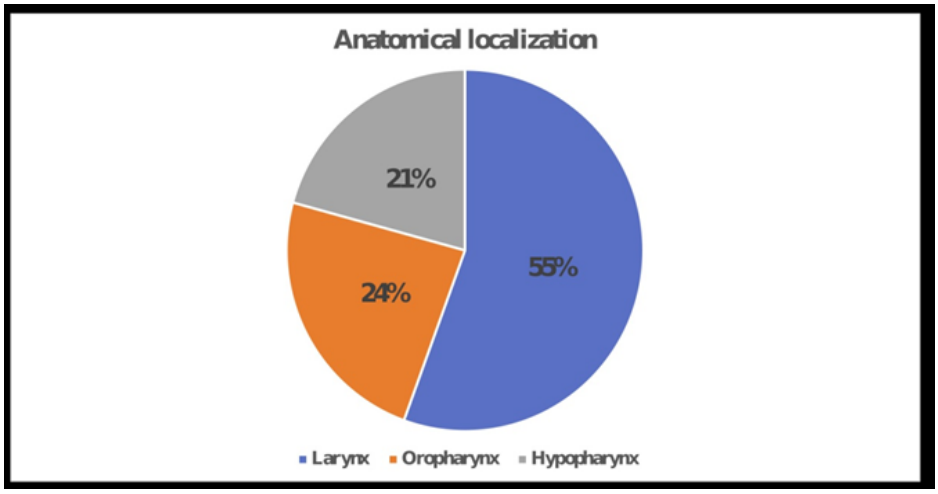

Figure 6. Anatomical localization.

Discussion

Squamous cell carcinoma of the larynx and hypopharynx is the second most common respiratory tract cancer, after lung cancer. According to the literature the tumors are more common in men, although the male-to-female ratio is decreasing in some regions [11]. In our study 95% of the diagnosed patients were males. But also, the total number of female patients has been doubled over the examined period. It might be possibly due to increased incidence of smoking among women over the past couple of decades. Tobacco and alcohol consumption are the most important risk factors for laryngeal and hypopharyngeal cancer development [12].

According to the literature this type of carcinoma most frequently occurs in the sixth and seventh decades of life. Our patient population was slightly different, the diagnostic peak of HNSCC was between 60 and 69 years. But the second most frequent incidence was in the 50-59 age group [13].

There are geographical differences in the topographical distribution of HNSCC in different countries. At our clinic we found to be the most common localization in the larynx (75%), followed by oropharyngeal (24%) and hypopharyngeal presentation (20%) [14].

Conclussions

In this case study, most cases of HNSCC developed at the larynx and the hypopharynx. The incidence of these lesions showed a continuous increase in female sex during the study period, the most frequent risk factor being smoking. Most cases have been diagnosed in advanced stages and have a moderate or poorly differentiated histological appearance.

Our results correlate with those presented in literature.

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ANTIBACTERIAL ACTIVITY OF FIVE ESSENTIAL OILS ON REPRESENTATIVE BACTERIAL PATHOGENS

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Abstract

Aim. *The aim of the study was to evaluate antibacterial properties of commercial essential oils (thyme, ginger, orange, lemongrass, rosemary) against Gram-positive and Gram-negative bacteria.*

Material and method. *Essential oils from two different companies with two opposite price ranges were purchased from local retailers. To evaluate the antimicrobial activity, agar diffusion method was used to test the essential oils activity on Gram-positive Staphylococcus aureus ATCC 29213 (MSSA), methicillin resistant Staphylococcus aureus ATCC 43300 (MRSA), Enterococcus faecalis ATCC 29212, and Gram-negative Escherichia coli ATCC 25922, Klebsiella pneumoniae ATCC 13883 and Pseudomonas aeruginosa ATCC 27853. Muller-Hinton agar plates were inoculated with the bacterial strains. Sterile paper disks were dispensed on the inoculated media and loaded with 5 µl of each essential oil. After incubation, the inhibition zone diameters were noted.*

Results. *Based on the inhibition zone diameter, the highest antibacterial properties had thyme essential oil on MSSA (44-46 mm) and on MRSA (38-40 mm) and lemongrass essential oil on MSSA (30-33 mm) and MRSA (26-30 mm). On Pseudomonas aeruginosa, almost none of the essential oils tested expressed antibacterial properties, except for the thyme essential oil which showed a small inhibition area (9-10 mm). The orange essential oil had the lowest antimicrobial activity (6 mm). The lowest antimicrobial effect/price index was shown by lemongrass essential oil on MSSA (0.1) and the maximum index by ginger essential oil (2.08) on E. coli, K. pneumoniae and P. aeruginosa.*

Conclusions. *the essential oils showed a higher antibacterial effect on Gram positive bacteria compared to Gram negative bacteria. The highest antibacterial properties presented thyme essential oil. The results confirmed the inhibiting effect of commercial essential oils and provide a scientific background for further research. These essential oils may find their use as natural antibacterial agents, useful for treating different types of infections.*

Keywords: thyme essential oil, lemongrass essential oil, rosemary essential oil, ginger essential oil, antimicrobial activity

Introduction

Essential oils are highly complex, volatile, natural compounds that are characterized by their strong fragrances and are synthesized by aromatic plants as secondary metabolites. The chemical composition of essential oils includes complex mixtures of organic substances, especially terpenoids. **Thyme** (*Thymus vulgaris*) is an herbaceous plant that is native to southern Europe, where it is often cultivated for its culinary properties and used as a spice in the food industry. The volatile oil has many effects including antibacterial, antiviral and antifungal [1].

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Citronella (lemongrass) (*Cymbopogon citratus*), a tall perennial grass, with about 55 species, grows in tropical and subtropical regions. The main active constituents of volatile citronella oil (citral, neral and geraniol) give its specific aroma. As a bactericidal agent, lemongrass essential oil was found to be effective against many bacterial species including *Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Salmonella enterica or Proteus vulgaris* [2-4]. **Rosemary** (*Rosmarinus officinalis*) is a plant belonging to the Labiateae family that is widely used in many areas, including aromatherapy, as adjuvant to improve circulation or in case of rheumatic pains. The main components of rosemary essential oil are 1,8-cineole, alpha-pinene and camphor. The properties of rosemary as antibacterial against Gram-positive and Gram-negative bacteria have already been highlighted by other studies [5-7]. **Ginger** (*Zingiber officinale*) is a well-known spice used in many Asian countries and is cultivated especially in South-east Asia, China, Austria, America, Jamaica and Africa. In addition, the main compounds of ginger essential oil are α-zingiberene, beta-sesquiphelandrene, which give it numerous properties including antioxidant, anti-inflammatory and antitumoral properties. Antimicrobial effects of ginger have been reported against *E. coli*, *Proteus*, staphylococci, streptococci and *Salmonella* spp. [8,9]. **Sweet orange** (*Citrus sinensis*) is a tree of the *Rutaceae* family, whose essential oil is known for its strong antiseptic effect but also its antispasmodic and tonic effects. The main components of the oil are alpha-pinene, limonene, and neral [10-12].

The aim of the study is to evaluate antibacterial properties of commercial essential oils (thyme, ginger, orange, lemongrass, rosemary) against representative Gram-positive and Gram-negative bacteria, in order to get a better view on their possible use as antibacterial agents. Nowadays, there is an increasing trend for aromatherapy and usage of essential oils on different purposes, and the retailing price represent for many people a main criterion for purchasing. Nevertheless, we hypothesize that the price is not highly correlated with the quality (at least with the antibacterial effect), considering that all the products are natural and the extraction method is the same. Thus, the evaluation of price/quality ratio is a second aim of this study.

Material and methods

Essential oils from two different companies (A, respectively B) with two opposite price ranges were purchased from local retailers. The manufacture method, the provenance of each essential oil were noted (Table I), as well as the price / ml in Euros (€).

The inhibitory effect was assessed by disk diffusion. Bacterial inoculums of 0.5 McFarland units (~1.5 x 10^8 CFU/ml) were prepared from the following bacterial strains: Methicillin sensitive *Staphylococcus aureus* ATCC 29213 (MSSA), methicillin resistant *Staphylococcus aureus* ATCC 43300 (MRSA), *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 13883 and *Pseudomonas aeruginosa* ATCC 27853. Muller-Hinton agar plates were inoculated with bacterial inoculums. Sterile paper disks with the diameter of 6 mm (Bioanalyse Ltd, Turkey) were dispensed on the medium surface. Five µl of essential oils were pipetted on corresponding disks. After 10 minutes (time needed for a proper diffusion of active components), the plates were incubated in normal atmosphere at 37°C. After 24 hours of incubation, the inhibition zone diameters were read and noted in spreadsheet software, aside the average price in €/ml of essential oil. For better visualization of the results, heat maps were created; an antibacterial activity (inhibition zone diameter)/price ratio index was also calculated, in order to offer a proper view on the quality-price relation regarding the antibacterial effect.

Table I. Essential oils used in the study and their origin.

Producer	Essential oil	Country of origin	Extraction method	Source
A	Thyme	Germany	Steam Distillation	Leaf
	Lemongrass	India	Steam Distillation	Leaf
	Rosemary	Morocco	Steam Distillation	Flower, leaf
	Ginger	Madagascar, Indonesia	Steam Distillation	Root
	Orange	Dominican Republic, Brazil	Cold Pressed	Peel
B	Thyme	France, South Africa	Steam Distillation	Flower, leaf
	Lemongrass	Nepal, India, South Africa	Steam Distillation	Leaf
	Rosemary	France, South Africa	Steam Distillation	Flower, leaf
	Ginger	Madagascar	Steam Distillation	Root
	Orange	USA, Mexico	Cold Pressed	Peel

Results

Of all the studied essential oils from both companies, thyme essential oil had the greatest efficacy, at the opposite end being orange essential oil. (Table II), and Gram-positive bacteria were more susceptible than Gram-negative bacteria, as exemplified in Figure 1.

With regard to volatile oils from Producer A, ginger essential oil determined an inhibition zone between 6-12 mm, the weakest against *E. coli*, *K. pneumoniae* and *P. aeruginosa* (6 mm), and the strongest against MSSA (12 mm). Thyme essential oil presented inhibition zones ranged between 9-44 mm, with the weakest action against *P. aeruginosa* (9 mm) and the strongest against MSSA (44 mm). Rosemary essential oil determined inhibition zones between 6-16 mm, the most effective being against MSSA (16 mm) and at the opposite end being against *P. aeruginosa* (6 mm). Lemongrass essential oil determined inhibition zones between 6-30 mm, with a weak effect against *P. aeruginosa* (6 mm) and a maximum effect against MSSA (30 mm). Orange essential oil showed no antimicrobial activity against any of the studied bacteria (6 mm) (Table I).

With regard to volatile oils from Producer B, the inhibition zones diameters were slightly larger than those identified for Producer 1. Ginger essential oil determined inhibition zones between 6-12 mm, presenting the weakest effect against *E. coli*, *K. pneumoniae* and *P. aeruginosa* (6 mm) and better effect on MSSA (12 mm). Similarly to the other producer, thyme essential oil showed the strongest activity (10-46 mm) of all the essential oils, being the most effective against MSSA (46 mm) and the weakest against *P. aeruginosa* (10 mm). Rosemary essential oil presented an antibacterial activity ranging from 6-18 mm, the most effective being against MSSA (18 mm), the weakest being against *P. aeruginosa* (6 mm). Lemongrass essential oil showed variate antimicrobial activity, with diameters between 7-33 mm; the lowest inhibition zone was again for *P. aeruginosa* (7 mm) and the highest against MSSA (33 mm). Also, orange essential oil from Producer B, showed the weakest antimicrobial activity against all studied bacteria (6 mm).

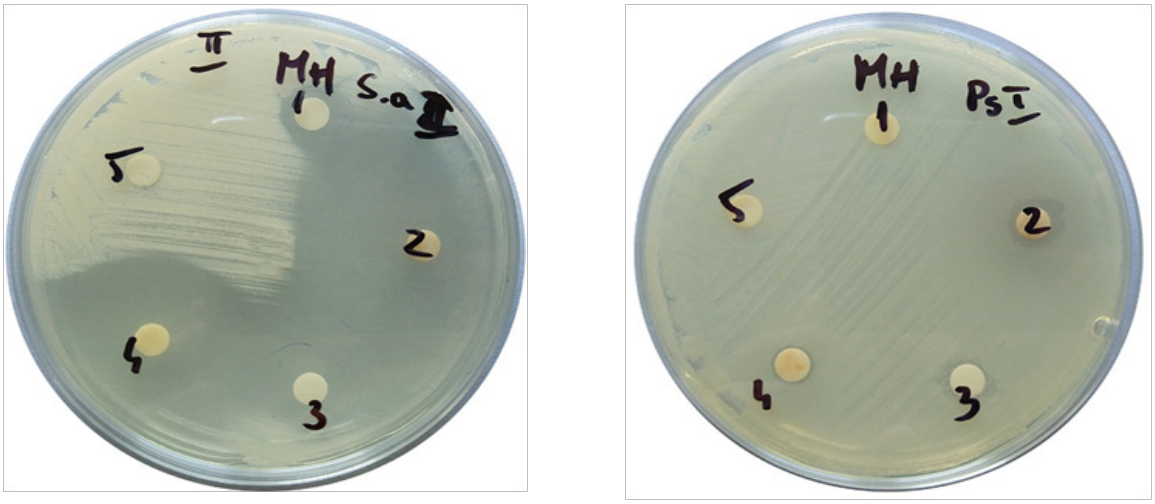

Figure 1. Suggestive images that show the good inhibition of S. *aureus* (A) compared with P. *aeruginosa* (B). High diameters are visible for thyme (2), rosemary (3) and lemongrass (4), while smaller diameters or no inhibition zone are visible for ginger (1) respectively orange (5) essential oils on S. *aureus*. No inhibition zones are present for all essential oils against P. *aeruginosa*.

Table II. Antibacterial effects of the tested essential oils on Gram-positive and Gram-negative bacteria.

	Inhibition zone diameters (mm)									
	Producer A (high price range)					Producer B (low price range)				
	ginger	thyme	rosemary	lemongrass	orange	ginger	thyme	rosemary	lemongrass	orange
MSSA	12	44	16	30	6	12	46	18	33	6
MRSA	8	38	10	26	6	12	40	13	30	6
E. faecalis	8	30	11	19	6	9	29	9	20	6
E. coli	6	31	13	20	6	6	33	12	20	6
K. pneumoniae	6	30	12	16	6	6	28	9	15	6
P. aeruginosa	6	9	6	6	6	6	10	6	7	6

Table III. inhibition zone diameter/price ratio indexes. Lower indexes denote better price/ quality ratio.

	Inhibition zone diameter/price ratio index									
	Producer A (high price range)					Producer B (low price range)				
	Ginger	Thyme	Rosemary	Lemongrass	Orange	Ginger	Thyme	Rosemary	Lemongrass	Orange
MSSA	1.07	0.35	0.54	0.15	0.77	0.58	0.15	0.22	0.1	0.55
MRSA	1.61	0.41	0.64	0.18	0.77	0.58	0.17	0.31	0.12	0.55
E. faecalis	1.61	0.51	0.58	0.24	0.77	0.78	0.24	0.44	0.17	0.55
E. coli	2.08	0.5	0.49	0.23	0.77	1.17	0.21	0.33	0.17	0.55
K. pneumoniae	2.08	0.51	0.54	0.29	0.77	1.17	0.25	0.44	0.23	0.55
P. aeruginosa	2.08	1.71	1.07	0.77	0.77	1.17	0.7	0.67	0.49	0.55

The prices for 1 ml of each oil from Producer A varied between 1-3.30 €/ml and those of Producer B varied between 0.7-1.5 €/ml. As presented in Table III, the obtained indices (inhibition zone diameter/price ratio) of each essential oil, both from Producer A and Producer B, were compared. In the case of Producer A, ginger essential oil presented the best index for MSSA (1.07) and the weakest for *P. aeruginosa*, *K. pneumoniae* and *E. coli* (2.08). Thyme essential oil had a maximum index against MSSA (0.35) at the opposite end being the index for *P. aeruginosa* (1.71). The best index for rosemary essential oil was for E. coli (0.493) and the lowest for *P. aeruginosa* (1.07). Lemongrass essential oil showed the best index for MSSA (0.154), at the opposite end being the index for *P. aeruginosa* (0.77).

In the same table are shown indices obtained from the essential oil used by company B. Thus, ginger essential oil had the best index against MSSA and MRSA (0.58) and the lowest for *E. coli*, *K. pneumoniae* and *P. aeruginosa* (1.17). Thyme essential oil showed the highest index for MSSA (0.15) and the lowest for *P. aeruginosa* (0.7). Rosemary essential oil recorded the best index for MSSA (0.22) and the lowest for *P. aeruginosa* (0.67). The best index of lemongrass essential oil is 0.1 for MSSA, at the opposite end being the lowest index (0.49) against *P. aeruginosa*. Producer A, similarly to Producer B, obtained the same index for orange essential oil (0.55) for all studied bacteria (Table III).

Discussion

Some studies have shown that Oregano, thyme and rosemary essential oils are among the most active antimicrobials (Dimitrijević et al.) [13]. According to Moreira et al. [14], the lipophilic compounds of the oils bind the phospholipidic bilayer of the cell membrane, increasing its permeability, spreads to the intracellular content and damage the enzymatic system of the cell. As a result of our study, the essential oils were found to be more active against Gram-positive bacteria than against Gram-negative ones, a conclusion that Naik et al. [15] also highlighted in their study on the antibacterial efficacy of lemongrass essential oil against several bacteria, including *E. coli*, *K. pneumoniae* and *P. aeruginosa*. However, we noticed a minimal activity of lemongrass essential oil against *P. aeruginosa*, compared to data obtained by Naik et al., where no effect was observed. Gupta et al., studying the antimicrobial effects of lemongrass essential oil, obtained a high inhibition zone against *Pseudomonas* (29-32 mm) compared to ours (6 mm), but with a similar effect against MSSA (28-32 mm), which is consistent with our data (30-33 mm). The slight differences in efficacy obtained between the two lemongrass essential oils may be due to their different citral components, the volatile effect and lipolysis contributing to the penetration into the cell membrane of the pathogen and the cause of cell lysis [16]. Studying the antimicrobial activity of thyme essential oil against selected microorganisms such as *E. coli* K-12 and *K. pneumoniae*, Anzlovar et al. found that they inhibited the growth of ESBL-producing *E. coli*, and less efficiently ESBL-producing *K. pneumoniae*. Because of the geographic origins and the harvesting period, the age of the distilled essential oils and their compositions can be different and this will affect the degree of activity against Gram-positive and Gram-negative bacteria [1].

In a recent study [17] the antibacterial capacity against *E. coli* and *S. aureus* of thyme essential oil was highlighted, obtaining an inhibition zone of approximately 55 mm for *S. aureus*, being much higher than that obtained by us (44-46 mm), and approximately 25 mm for *E. coli*, being slightly lower than in our study (31-33 mm). This could be though, to the variance in the type of the bacterial strains that were used.

Antibacterial properties of rosemary essential oil have been reported by Abdullah et al., in a study based on

agar well diffusion method; the essential oils were shown to have good activity against four multidrug resistant strains: Acinetobacter baumannii (35mm), *P. aeruginosa* (34mm), *S. aureus* (30mm) and *E. faecalis* (32mm), discovering their high potency against microorganisms when using a concentration of 10% v/v. Decreasing the concentration below 5% v/v, they showed almost no antimicrobial effect. The results of this study are not in complete accord with ours, as the rosemary essential oil had only a slight antimicrobial activity against *P. aeruginosa* (6 mm), and slightly higher against Enterococcus (9-11 mm) and MSSA (16-18 mm) [18]. Kwiatkowski et al. showed in their study that at a concentration of 1 mg/g of rosemary essential oil totally inhibited *E. coli* and *S. aureus*, instead using a concentration of 5 mg/g, they proved an antibacterial effect against *S. aureus* [19].

Another study reported that ginger essential oils had an inhibitory effect against a wide range of pathogenic bacteria and fungi, and the effect was probably due to the major components but also depended on the chemical structures of these components [20]. Regarding ginger essential oil, the results obtained by us indicate that it had a minimal effect (6 mm) against Gram-negative bacteria and slightly positive (8-12 mm) against Gram-positive bacteria. These results are slightly different from those reported by Hassan et al., obtaining a slightly increased inhibitory activity against *E. coli* (21 mm), *S. aureus* (23 mm), *K. pneumoniae* (15 mm) [8].

The antimicrobial activity of *Citrus sinensis* and *Citrus aurantium* were studied by Madhuri et al., using *Klebsiella* strains, concluding that *Citrus sinensis* (14 mm) had a higher inhibition zone compared to *Citrus aurantium* (13 mm); however, both inhibition zones were much higher than those we obtained in our study (6 mm) [21]. Our study highlighted that *Citrus sinensis* had a low antimicrobial activity against both Gram-positive and Gram-negative bacteria.

In this study, the quality of the antimicrobial effect in relation to the retail price of the product was evaluated, in the hypothesis that a high price isn't always equivalent to a superior product. We proved that Producer B, with significantly lower prices and globally slightly better antibacterial activity than Producer A, presented most of the indices subunitary for the majority of the bacteria, except for ginger essential oil for Gram-negative bacteria. The higher price isn't justified for ginger essential oil from Producer A, because the antimicrobial effect against the same Gram-negative bacteria studied is also low and the index exceeded the value of 2.

Conclusions

1.The essential oils studied had better antibacterial effect against Gram-positive bacteria compared to Gram-negative bacteria.

2.Regardless of the producer, thyme essential oil had the most powerful antimicrobial effect, while orange essential oil had the weakest antimicrobial effect.

3.Almost all the essential oils had a weak or no effect against *Pseudomonas aeruginosa*.

4.The retail price of the essential oils is not correlated with their antimicrobial activity.

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ROBOTIC SURGERY FOR RECTAL CANCER

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Abstract

Objectives. *The aim of the study was to assess the postoperative results of robotic surgery for rectal cancer.*

Method. *We conducted a study on a total number of 10 patients with rectal cancer undergoing robotic surgery at the 5th Surgery Clinic of the Municipal Clinical Hospital in Cluj-Napoca between January 2010 and December 2013.*

Results. *Of these, 6 were men and 4 women, and median age was 62 ± 11 years. Five anterior rectal resections, three lower rectal resections and two abdominoperineal resections were performed. Most tumors were stage III (6 cases). Conversion to open surgery was performed in a single case of significant intraoperative hemorrhage.*

Conclusions. *Robotic surgery may be an alternative to laparoscopic surgery in the treatment of rectal cancer, especially with regard to the identification and preservation of nerve plexuses and dissection in a narrow pelvis.*

Keywords: rectal cancer, robotics, surgery, minimally invasive, complications

Introduction

Laparoscopic surgery is now accepted as an approach for the treatment of colorectal cancer with superior results in terms of immediate postoperative recovery but with survival rates that are comparable to open surgery [1]. Many authors have demonstrated that total mesorectal excision can be performed laparoscopically, with patients benefiting from the advantages of minimally invasive techniques [2,3,4].

The da Vinci surgical system has been specifically developed to compensate for the technical limitations of laparoscopic instruments. The system offers a three-dimensional image, an ergonomic position, a steady camera, improved movement dexterity, the elimination of physiological tremor, the endowrist - a seven degrees of freedom instrument, with 180° of articulation and 540° of rotation, the ability to safely perform intracorporeal suturing, the ability to perform precise finite movements, thorough dissection of the mesorectum in the narrow pelvic space with the preservation of the pelvic nerve plexuses [5].

Nevertheless, the da Vinci surgical system has some technical disadvantages. First of all, there is a lack of tactile sensation. As a result, tissue damage can easily occur during robotic arm traction and during the movement of robotic instruments. Moreover, the suture material can be cut because there is no stretching feedback while performing the suture. These technical drawbacks can be overcome by visual feedback if the surgeon has sufficient experience [6].

The aim of our study is to present the experience of the 5th Surgery Clinic in Cluj-Napoca in the robotic surgical treatment of rectal cancer, emphasizing the indications, the technique, the intraoperative and postoperative complications, as well as the short-term results.

Material and method

We carried out a retrospective study on patients undergoing robotic surgery for rectal cancer at the 5th Surgery Clinic of the Municipal Clinical Hospital in Cluj-Napoca between January 2010 and December 2013. A database was created including patient characteristics, diagnosis, tumor location, type of surgery, operating time, hospitalization period, intraoperative and postoperative complications and postoperative progression. All patients

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included in the study signed the informed consent form and the study was approved by the Ethics Committee of the Cluj-Napoca Municipal Clinical Hospital.

Results

During the study, a total of 10 patients underwent surgery for rectal cancer using the da Vinci surgical system. Of these, 6 were men and 4 women, and median age was 62 ± 11 years. The body mass index was 28.20 ± 3.92 kg/m2. Tumor localization was in the upper rectum in 5 cases (>11 cm), in the middle rectum in 3 cases (6-11 cm) and in the lower rectum in 2 cases (>6 cm). None of the patients had history of surgery and 2 patients received preoperative radiotherapy. The following procedures were performed: 5 anterior rectal resections, 3 lower rectal resections with mechanical colo-anal anastomosis and two abdominoperineal resections. Total operating time including connecting time was 270 ± 50.73, decreasing once the learning curve is traversed. Most tumors were stage III (6 cases), 2 cases were stage II and 2 cases were stage I. The main intraoperative complications were significant hemorrhage that determined the conversion to open surgery and 1 case of technical difficulty during mesorectal excision. Postoperative complications were represented by 1 case of anastomotic fistula. The main characteristics of the study group are presented in Table I.

Table I. The main characteristics of the study group.

Characteristics	Number
Gender	
men	6
women	4
Age	62 ±11
BMI	28.20±3.92
Stage	
Stage I	2
Stage II	2
Stage III	6
Preoperative radiotherapy	2
Type of surgery	
Anterior rectal resection	5
Lower rectal resection	3
Abdominoperineal resection	2
Total operating time	270±50.73
Intraoperative complications	1
Postoperative complications	1
Conversion	1

Discussion

We showed that total mesorectal excision for rectal cancer can be safely done using the da Vinci surgery system. The method is safe and feasible, as confirmed by other studies in the literature [7,8].

Total mesorectal excision (TME) is a standard technique in rectal surgery. The correct dissection of the mesorectum is an important prognostic factor affecting the postoperative outcome. The da Vinci surgical system is best suited for mesorectal dissection, both due to the three-dimensional image and the possibility of a precise dissection in the narrow space of the pelvis enabled by the robotic surgical instruments. Several studies that compared the results of robotic rectal surgery versus laparoscopic surgery showed the obvious utility of robotic dissection, especially when performed under difficult conditions (narrow pelvis) [9,10].

Studies have shown that there are no significant differences between robotic and laparoscopic surgery of the rectum in terms of: operating time, blood loss, postoperative recovery. However, the dexterity and flexibility of the da Vinci robotic system have proven useful in certain situations and especially in the mobilization of the splenic flexure, the dissection of the lower mesenteric artery, the identification and preservation of nerve plexuses, the dissection in a narrow pelvis (especially in men). The main drawbacks of robotic surgery are the high cost and the need for staff with special training.

Conclusions

Robotic-assisted rectal surgery using the da Vinci surgical system is technically feasible and safe, and total mesorectal excision (TME) can be performed via robotic surgery, resulting in excellent outcomes, even under difficult conditions (narrow spaces, post-radiotherapy), being an alternative to laparoscopic surgery, especially in what concerns nerve-sparing surgery. However, oncological safety, functional outcomes, postoperative quality of life in patients undergoing surgery using this technique should be evaluated and demonstrated in extensive studies before being widely accepted as an option for the surgical treatment of rectal cancer.

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THE PERITONEUM. SURGICAL ANATOMY AND CLINICAL APPLICATIONS

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Abstract

Introduction/Objective. *In order to understand the way the intraperitoneal malignancies spread into the peritoneum we brought into discussion the embryological development, intra abdominal organization and histology of this structure. We also described the surgical applications of peritonectomy during the management of cancerous patients with peritoneal metastasis.*

Material and method. *Peritoneal carcinomatosis, as a sign of an advanced intra abdominal cancer, must be differentiated from other peritoneal pathologies, that have other therapeutic conduct. The literature describes different paths of cancer cells dissemination into the peritoneum based on the primary tumor histopathological origin. The intra abdominal malignancies have an aggressive treatment that will combine extensive surgery with intraperitoneal chemotherapy for better survival rates.*

Results. *Peritonectomies have an important role in cytoreductive surgery (CR) followed by intraperitoneal hyperthermic chemotherapy (HIPEC) in the radical treatment of selected cancerous patients with peritoneal carcinomatosis.*

Conclusions. *Implementing an accurate surgical approach based on anatomical dissections of peritoneum during the CR followed by HIPEC in radical treatment of intra abdominal malignancy with peritoneal carcinomatosis, will only improve the outcome of this procedure, by reducing the blood lost, shorter operative time and oncological radicality.*

Keywords: peritoneum, peritoneal carcinomatosis, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy

Introduction

The peritoneum is an important serous membrane that has a complex arrangement and divides the abdomino-pelvic cavity into compartments. The communications between these compartments and the circulation of a small amount of peritoneal fluid explains the limitations and the extension of intraperitoneal pathological processes. In order to understand the path of intraperitoneal malignancy spreading into this structure, it must be brought into discussion the embryological development, intra abdominal organization and histology of the peritoneum.

Also the peritoneal carcinomatosis, as a sign of an advanced intra abdominal cancer, must be differentiated from other peritoneal pathologies, that have other therapeutic conduct. Different types of tumors have different patterns of peritoneal metastasis.

As for clinical aplications in abdominal malignancies, peritonectomies have an important role in Cytoreductive surgery (CR) followed by Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in the radical treatment of selected cancer patients complicated with peritoneal carcinomatosis.

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Objective

The aim of this paper is to draw attention to the importance of the anatomical dissection of the peritoneum involved in abdomino-pelvic cavity malignancies during CR followed by HIPEC.

Methods

The embryological development of the peritoneum is complex and starts early in the intrauterine life.

During the third gestational week the blastodisc consists of ectoderm, mesoderm and endoderm. In this period the embryo starts to fold craniocaudal and lateral leading to the formation of endodermal tube. Paraxial mesoderm is segmented into somites and the lateral plate mesoderm divides into somatopleuric and splanchnopleuric mesoderm. The parietal peritoneum that covers the walls of the body cavity derives from somatopleuric mesoderm, while the visceral peritoneum that derives from splanchnopleuric mesoderm will envelop the organs.

The intraembryonic coelom it is at first one cavity that has the peritoneal, pericardial and pleural cavities connected trough pleuroperitoneal canals. The formation of the diaphragm will split the peritoneal cavity by the other three.

The primitive gut develops inside the peritoneal cavity and is connected with the posterior abdominal wall trough primitive mesentery. Inside the two peritoneal reflections are the arterial, venous, lymphatic vessels and nerves that supply the abdominal and pelvic organs.

Throughout the fetal life the mesenteric plane will suffer rotations and resorption that will lead to the complexity of peritoneum distribution in adult [1,2].

The peritoneum is a serous membrane that covers the walls of the abdominopelvic cavity and the abdominal and pelvic organs. It has a free surface, smooth, that is formed by flattened epithelium and lubricated by a small amount of fluid which permits the viscera to glide inside the peritoneal cavity. Mesotelium also reabsorbs the peritoneal fluid trough peritoneal stomata (pores) and sites of lymphoid clusters or 'milky spots' present in the omentum. The attached surface, rough, is connected through the subserous areolar tissue to the internal surface of the abdomino-pelvic wall and its containing viscera (Figure 1) [3,4].

The subserosal tissue is a conjunctive and vascular layer that contains fatty tissue, lymphocytes, resident macrophages, fibroblast-like cells, collagen and elastic fibres, blood vessels, lymph vessels and lymph nodes [1].

The parietal peritoneum has some loose sites of connection with the fascia of the muscles of the abdominopelvic wall and some closely adherent sites such as diaphragmatic surface [1].

The peritoneal cavity is a virtual cavity situated between parietal and visceral peritoneum. It is a complex structure that is organized in ligaments, omentum, mesenteries and peritoneal folds (Figure 2).

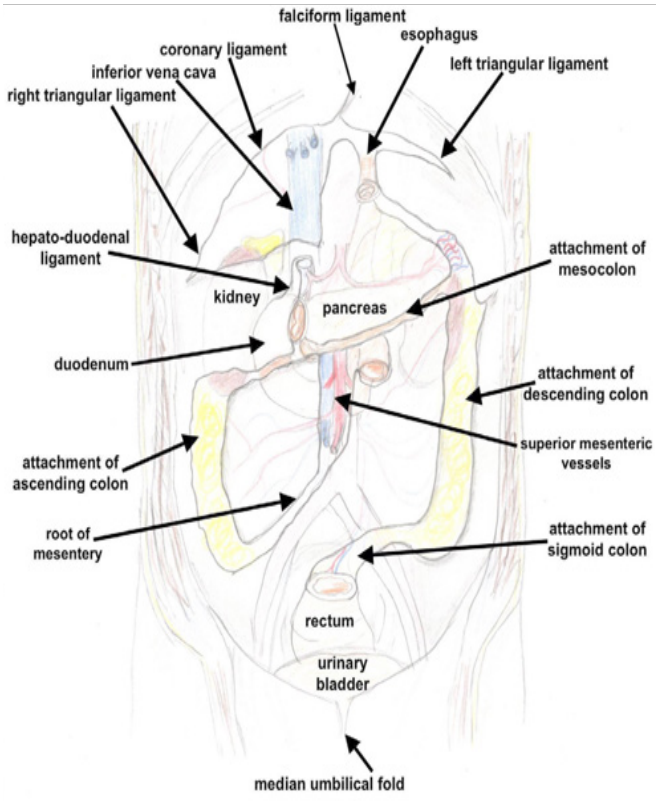

Figure 1. Attachments of peritoneum (from Bartos Dana Monica, Bartos Adrian et al with permission) [5].

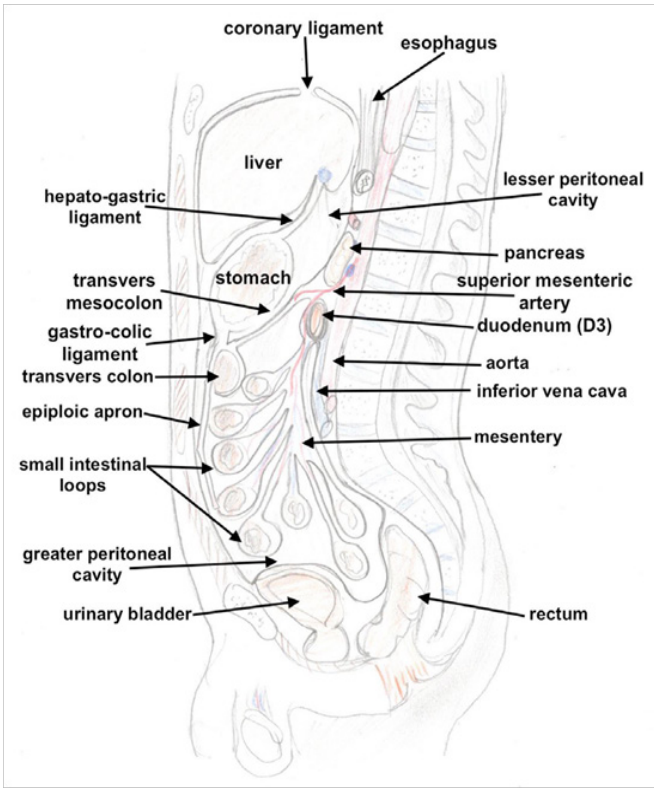

Figure 2. Peritoneal cavity (from Bartos Dana Monica, Bartos Adrian et al with permission) [5].

In order to understand the paths of dissemination of intraperitoneal malignancies is important to know the communications of different compartments of the peritoneal cavity [6].

The transverse colon and its mesentery divides the peritoneal cavity into the supramesocolic and inframesocolic compartment.

Further on, the supramesocolic compartment is divided into right and left peritoneal space. The right supramesocolic space has three subspaces. The right subphrenic space and the right subhepatic space communicate with the right paracolic gutter. The lesser sac is situated posterior to the stomach, anterior to the pancreas and communicates with the rest of the peritoneal cavity through epiploic foramen (Winslow hiatus) (Figure 3). The left supramesocolic space has four communicating spaces: the left anterior perihepatic space, the left posterior perihepatic space, the left anterior subphrenic space and posterior subphrenic space (perisplenic) [1].

The inframesocolic compartment is divided by the insertion of the root of the mesentery from the duodenojejunal flexure to the ileocecal valve into right and left infracolic space. The right and left paracolic gutter are situated between ascending and descending colon and the lateral abdominal wall. The right one communicates superior with right subhepatic and right subphrenic space. Inferior both paracolic gutters are continuous with the pelvic cavity [1].

The peritoneum is reflected from the posterior surface of the urinary bladder to the anterior surface of the uterus in females forming the uterovesical pouch, and also reflected from the posterior surface of the uterus to anterior surface of the superior rectum forming the rectouterine pouch (Douglas) (Figure 4). In males there is just the rectovesical pouch [1].

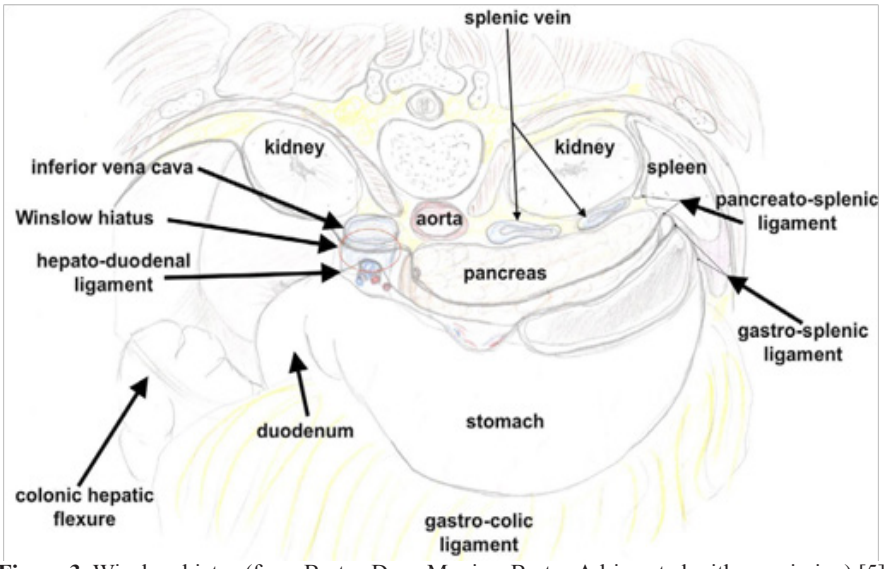

Figure 3. Winslow hiatus (from Bartos Dana Monica, Bartos Adrian et al with permission) [5].

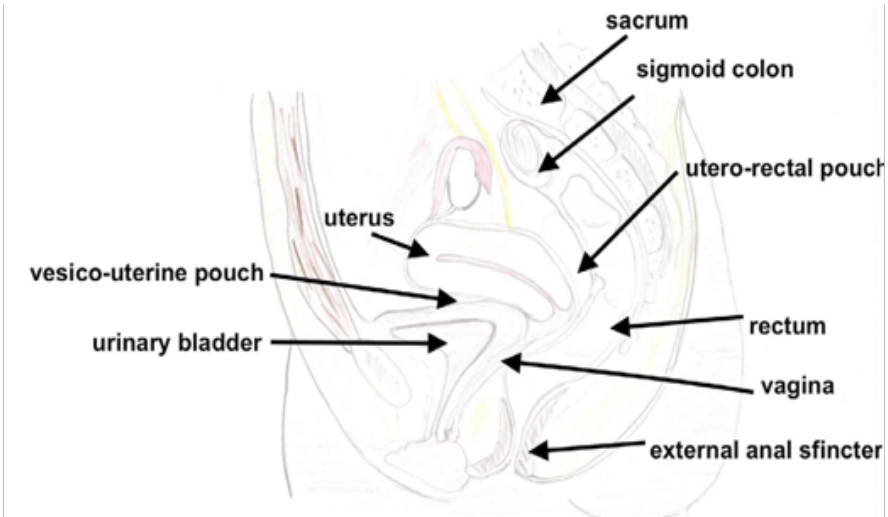

Figure 4. Mid sagittal section female pelvis (from Bartos Dana Monica, Bartos Adrian et al with permission) [5].

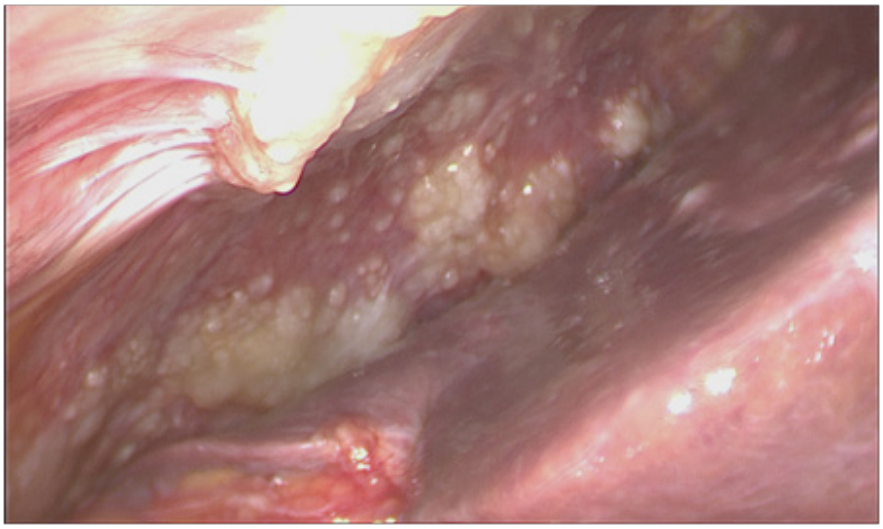

Figure 5. Parietal peritoneal carcinomatosis (from Bartos Adrian et al with permission) [7].

There is a continuity of the subserosa that will facilitate the spread of pathological process between intraperitoneal organs but also between intra- and extraperitoneal spaces [6].

Peritoneal carcinomatosis represents parietal or visceral peritoneum dissemination of ovarian or gastrointestinal cancers (Figure 5). It consists of tumoral deposits at the level of visceral or parietal peritoneum, with the localization depending on the primary tumor origin, circulation of intraperitoneal fluid and the histology of the cancer. Macroscopically the differential diagnosis of peritoneal carcinomatosis is sometimes difficult to make with the peritoneal tuberculosis or the primary malignancy of the peritoneum (mesothelioma), but the microscopic examination establishes the positive one.

The histopathology of peritoneal carcinomatosis is represented by gastric adenocarcinoma, pancreatic adenocarcinoma, colorectal adenocarcinoma, serous ovarian carcinoma, pseudomixoma peritoney with appendix or ovarian origin, with different degree of tumor cells differentiation and biological aggressiveness.

Primary metastatic route of ovarian cancer is the intraperitoneal dissemination due to ovaries position in the abdomen, but also due to the tumor's biology [1]. Unfortunatelly almost two-thirds of patients are diagnosed with an advanced stage cancer because of the lack of symptoms or diagnostic methods of detection, making the epithelial ovarian cancer the most malignant gynecological carcinoma [8].

Colorectal cancers develop peritoneal carcinomatosis at some point. Between 7-15% is discovered during the surgical intervension with radical treatment intent of the primary tumor. Furthermore, 4-19% of the colorectal cancer patient operated will develop peritoneal metastasis. In locally advanced cases the percentage is higher, reaching 50-60 % in the first 6 months from the surgical procedure [9].

There are two ways of intraperitoneal tumor cell spread. One is transversal growth, when tumor cells detach from the primary tumor into the peritoneal cavity spontaneously. The second one is the intraperitoneal spread after surgery due to the tumor cell release from the primary tumor or trought blood and lymph vessels resection. Regardless of the detachment of the tumor cells, they are transported by the intraperitoneal fluid and spread through peritoneal cavity [10].

The basic steps of dissemination of peritoneal tumors are: tumor cell exfoliating from the primary tumor, attachment to peritoneum, invasion into subserosa, proliferation and vascular neogenesis [10].

The tumor cell adhesion has some predilect areas of the peritoneum where the peritoneal carcinomatosis occurs spontaneously. The greater omentum and the 'milky spots' is one of these areas because it does not have a continuous mesothelial layer [1].

Postoperative, tumor cell adhesion occurs predominantly in the areas where the mesothelium is traumatized and the subserosa is exposed. Also the inflammatory cytokines (TNF- α, IL-1β) released after surgery or secreted by the tumor will make the mesothelial cell to retract, exposing furthermore extracellular matrix [1].

Results

The peritonectomy represents the surgical removal of all or a part of parietal peritoneum that is affected by peritoneal carcinomatosis during an intraperitoneal malignancy.

Peritoneal cancer index (PCI) is an important assessment of peritoneal malignancy, together with the histopathology of the primary tumor and preoperative imaging, in order to make the best terapheuthical decision for the patient. It consists in intraoperative evaluation of

peritoneal carcinomatosis of the entire peritoneal cavity, including distribution and size (Figure 6) [11].

The most important prognosis factor of peritoneal surface malignancy is the completeness of cytoreductive score. This assessment is done after removal of intraperitoneal tumors. Only a CC-0 cytoreduction is considered a complete cytoreduction, when there are no macroscopical visible tumors. In order to acquire these results the surgeon must perform an extensive surgery, with multiorgan resections if necessary (Figures 7 and 8) [1,12].

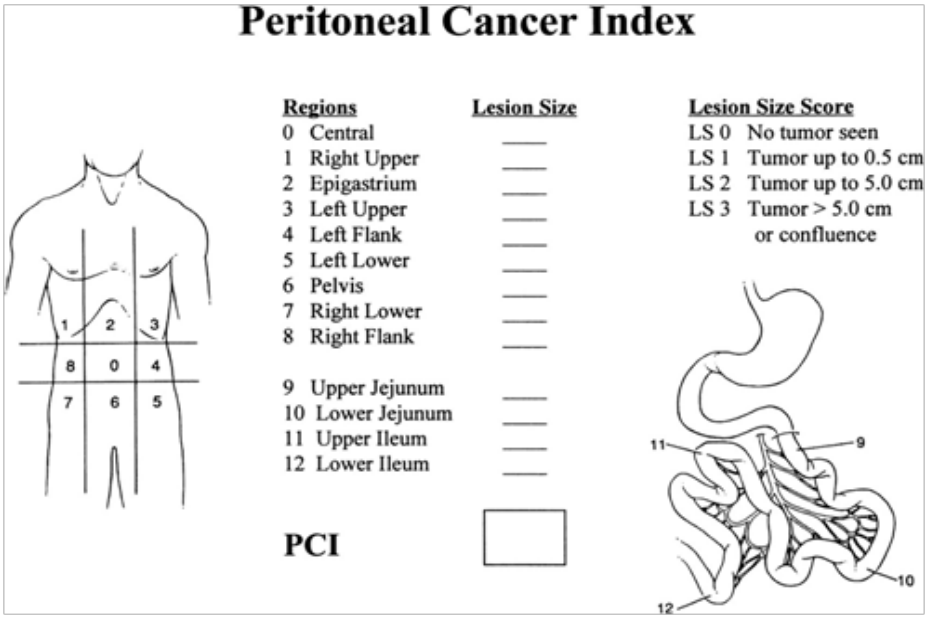

Figure 6. Peritoneal Cancer Index (from Sugarbaker PH et al) [11].

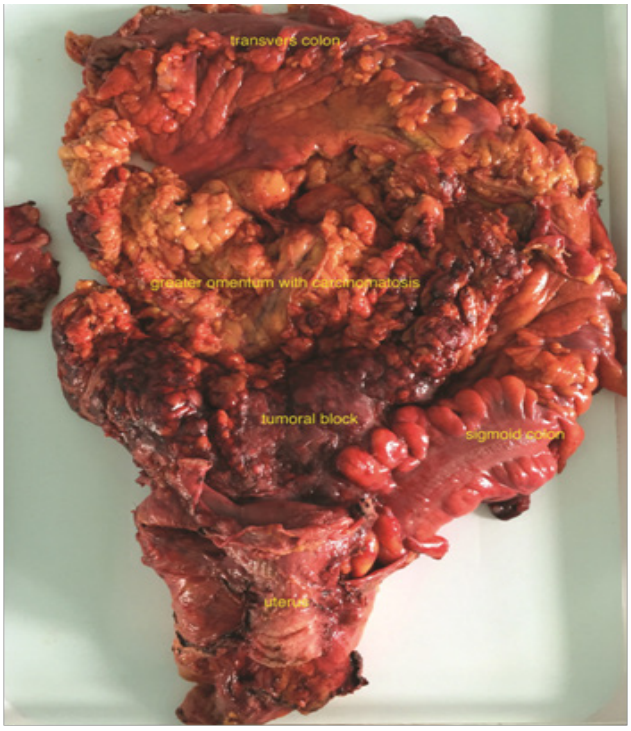

Figure 7. Operative piece after 'En bloc' extensive organ resection for intraperitoneal malignancy (from Bartos Adrian et al with permission) [7].

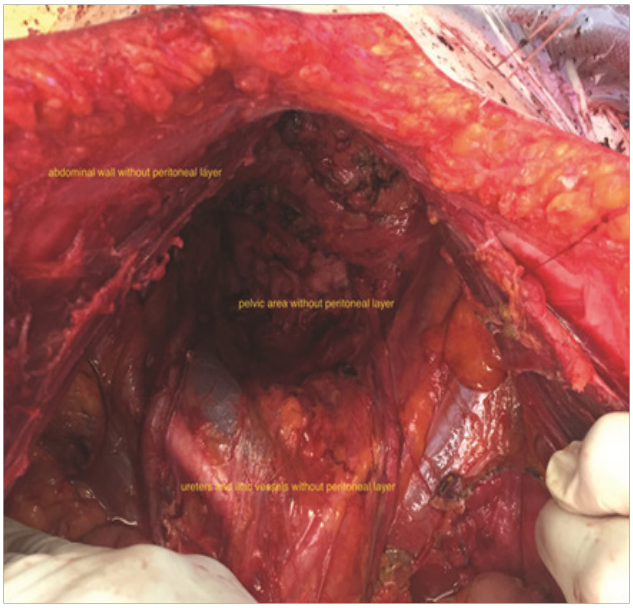

Figure 8. Abdominal wall and pelvic space after 'En bloc' extensive organ resection for intraperitoneal malignancy (from Bartos Adrian et al with permission) [7].

Cytoreductive surgery with parietal peritonectomy procedures and visceral resection, followed by hyperthermic intraperitoneal chemotherapy, have an important role in achieving a curative intent of selected cancer patients.

After entering the abdominal cavity trough a midline incision from xiphoid to pubis and assessing the extension of tumoral lesions, the skin will be fixt onto autostatic retractors in order to begin the peritonectomy from the free edge of the incision. The correct anatomical dissection in the subserosal areolar plane underneath the peritoneum is done with an electrosurgical hand-piece, preferable with a ball-tipped. This surgical approach is important for reduced bleeding, lesser operative time and oncological radicality (Figure 9). Of course, if the peritoneal carcinomatosis is invasive, the tissue infiltrated by the tumor must be resected (eg: abdominal wall fascia or muscle, retroperitoneal fatty tissue, portion of the hemidiaphragm) [1].

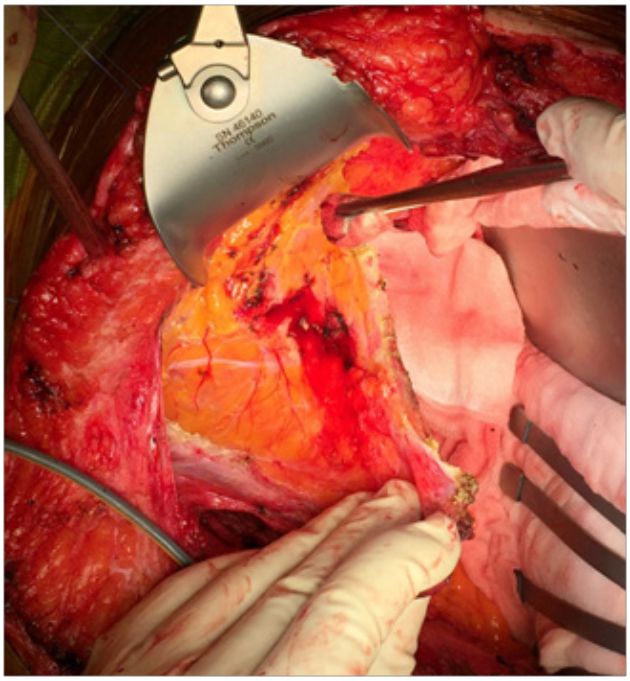

Figure 9. Peritonectomy (from Bartos Adrian et al with permission) [7].

Hyperthermic intraperitoneal chemotherapy follows the cytoreductive surgery and consists in intraperitoneal administration of chemotherapeutic agents as a solution, at 41-43 degree C, for a certain amount of time, using a pump that will heat and circulate the solution, maintaining the circuit in equilibrium. Depending on the histology of the primary tumor and the extension of the peritoneal malignancy, the chemotherapeutic agents, time of the intraperitoneal exposure and association with intravenous chemotherapy will be different [1].

The peritonectomy does not eliminate the transport role of the peritoneal membrane and it is recommended that after cytoreductive surgery intraperitoneal delivery of chemotherapy should follow [1].

Discussion

The advantage of intraperitoneal administration of chemotherapy is represented by the lower systemic toxicity of the agent, that can allow a longer exposure time of the tumoral cells to the chemotherapy solution and a higher dose of it. Also the hyperthermia associated with it increases the absorption and the tissular penetration of the cytotoxic drug [13,14].

Cytoreductive surgery hyperthermic intraperitoneal chemotherapy has shown better results than systemic chemotherapy or surgery alone. Although the mortality is situated below 10% and the morbidity between 20-50%, this combined treatment has led to significant increase in median survival of 19.2- 38.4 month and 5 years survival of 19-51% in advanced colorectal cancer [15,16].

Starting with 2017 both National Comprehensive Cancer Network guidelines and European Society for Medical Oncology has change the attitude towards the CR and HIPEC procedure, recommending it in selected colorectal cancer patients with peritoneal carcinomatosis in experienced centers [17,18].

Conclusions

Implementing an accurate surgical tactic based on anatomical dissections of peritoneum during the CR followed by HIPEC in radical treatment of intra abdominal malignancies complicated with peritoneal carcinomatosis, will only improve the outcome of the cancer patient therapy by reduced bleeding, lesser operative time and oncological radicality.

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ASSESSMENT OF THE INDICATIONS FOR UROLOGICAL INTERVENTIONS IN RENOURETERAL ANOMALIES IN CHILDREN. RESULTS. PERSPECTIVES

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Abstract

Objectives. *The aim of the study was to assess the indications for urological interventions in renal and ureteral anomalies in children and to evaluate the results obtained by modern treatment of kidney malformations.*

Method. *We carried out a retrospective study on a total number of 101 pediatric patients with renal and ureteral malformations undergoing surgery at the Department of Pediatric Urology of the Urology Unit at the Municipal Clinical Hospital in Cluj-Napoca between 2007 and 2012. We recorded the types of diagnostic procedures performed in the preoperative assessment, the type of surgery performed (conventional or minimally invasive), the number of patients undergoing surgery, the results obtained.*

Results. *The median age of children with renal and ureteral malformations undergoing surgery was 5 years, with a minimum of 1 year and a maximum of 18 years. Of these, 68% were from urban areas and 63% were male pediatric patients. There were 47 patients with congenital hydronephrosis secondary to ureteropelvic junction obstruction, 14 children with primary obstructive megaureter, 3 cases of pyeloureteral duplication and 3 cases of horseshoe kidney. Vesicoureteral reflux was diagnosed in 22.7% of cases. Of the 16 nephrectomies performed, 7 were for multicystic dysplastic kidney, 2 for hydronephrosis secondary to ureteropelvic junction obstruction, 2 for hydronephrosis in horseshoe kidney, 1 case for hydronephrosis in kidney malrotation and 1 case for primary congenital hydronephrosis.*

Conclusions. *The spectrum of indications for urological interventions has followed a more conservative tendency in recent years, with a decrease in the number of nephrectomies and an increase in the number of pyeloplasties. Robotic-assisted minimally invasive surgery represents a valuable perspective into the treatment of various pediatric urological disorders.*

Keywords: renal anomalies, urinary malformations, pediatric urology

Introduction

Congenital anomalies of the urinary tract are associated with an increased mortality rate in children, especially in case of structural abnormalities of the kidney. Renal anomalies often require surgical treatment and generally have a favorable prognosis [1,2].

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In the last decades, the understanding of the anatomical and ontogenetic pattern of renal and ureteral anomalies has paved the way for improved preoperative diagnosis, surgical technique and postoperative management of pediatric patients [3,4]. Although the percentage of prenatally diagnosed kidney anomalies has improved in recent years, there is little data in the literature in terms of indications and optimal timing for urological interventions in anomalies of the kidney and the urinary tract in children.

Conventional urologic surgery still retains an important role in the treatment of kidney and ureteral anomalies in the child, but new minimally invasive techniques - laparoscopy, interventional endoscopy and robotic assisted surgery - are gaining ground in pediatric urology.

The purpose of the study is to evaluate the indications for urological interventions in renal and ureteral anomalies in children. Another aim was to evaluate the results obtained through the modern treatment of kidney anomalies and the future prospects for diagnosis and treatment in pediatric urology.

Material and method

Treatment of children with renoureteral anomalies was performed at the Department of Pediatric Urology of the Urology Unit at the Municipal Clinical Hospital in Cluj-Napoca, between January 2007 and January 2012.

We recorded the types of diagnostic procedures performed for the preoperative assessment to determine the indication for urological intervention, the type of surgery performed (conventional or minimally invasive), the number of patients undergoing surgery, the results obtained and future prospects for the development of laparoscopic and robotic surgery. The study was approved by the Ethics Committee of the Municipal Clinical Hospital in Cluj-Napoca.

Preoperative diagnostic protocols included the following investigations: abdominal ultrasound, renal scintigraphy, urography, retrograde cystography, urethrocystoscopy, diagnostic laparoscopy. Surgical interventions were performed within the operating block of the Municipal Clinical Hospital in Cluj-Napoca.

Results

During the study, 153 patients with anomalies of the urinary tract underwent surgery at the Department of Pediatric Urology of the Municipal Clinical Hospital in Cluj-Napoca, of which 101 (66%) children with congenital anomalies of the kidney and ureter. Median age of children with renoureteral anomalies undergoing surgery was 5 years, ranging between 1 year and 18 years. Of these, 68% were from the urban area and 63% were male pediatric patients (Table I).

In the present study, 47 pediatric patients with congenital hydronephrosis in the course of ureteropelvic junction obstruction were treated at the Department of Pediatric Urology of the Municipal Clinical Hospital in Cluj-Napoca. Cases of hydronephrosis in the course of ureteropelvic junction obstruction in which the affected kidney showed potential usefulness in the future (differential renal function >10%, parenchymal index >2 mm) were treated in a conservative manner by performing pyeloplasty. When the kidney was compromised at the time of diagnosis (differential renal function <10%, parenchymal index <2 mm, pyonephrosis), nephrectomy was performed [3,4].

Of the 47 cases of pediatric patients diagnosed with hydronephrosis, a total of 45 children underwent pyeloplasty (2 cases of retroperitoneal laparoscopy, 1 case of robotic-assisted laparoscopic pyeloplasty and 42 cases of conventional lumbar approach) and lumbar nephrectomy was performed in 2 patients.

Of the 16 nephrectomies performed, 7 were for multicystic dysplastic kidney, 2 for hydronephrosis secondary to ureteropelvic junction obstruction, 2 for hydronephrosis in the horseshoe kidney, 1 case for hydronephrosis secondary to renal malrotation and 1 case for primary congenital hydronephrosis. Partial nephrectomy for pyeloureteral duplication was performed in 3 cases. Mean age of nephrectomized patients was 7 years, ranging between 2 years and 16 years.

Renal dysplasia was diagnosed in 6.9% of children with renoureteral anomalies undergoing surgery. The diagnosis of multicystic dysplastic kidney was established by abdominal ultrasound [7]. In cases where renal scintigraphy or urography revealed reduced or absent renal function, the therapeutic indication was for nephrectomy of a non-functional kidney175. In our study, total nephrectomy by the lumbar approach was performed in 5 cases of multicystic dysplastic kidney and total nephrectomy by the retroperitoneal laparoscopic approach was performed in 2 cases of multicystic dysplastic kidney. Laparoscopy was performed in older children.

Table I. Type of surgery performed at the Department of Pediatric Urology of the Municipal Clinical Hospital in Cluj-Napoca.

Type of surgery	Conventional	Laparoscopic	Endoscopic	Robotic surgery	Total
Pyeloplasty for hydronephrosis secondary to ureteropelvic junction obstruction	42	2		1	45
Ureteral reimplantation for vesicoureteral reflux	23				23
Treatment of primary obstructive megaureter	14				14
Nephrectomy for renal dysplasia	5	2			7
Nephrectomy for decompensated hydronephrosis / pyonephrosis	6				6
Partial nephrectomy for pyeloureteral duplication	3				3
Endoscopic placement of ureteral stent			2		2
Nephrolithotomy for coraliform lithiasis in horseshoe kidney	1				1
Total	96	2	1	1	101

A total of 14 children were diagnosed with primary obstructive megaureter, with a mean age of 4 years at the time of surgery; 61.5% were children with megaureter on the left side and 15.3% with bilateral obstructive megaureter. The percentage of patients with primary obstructive megaureter was of 76.9%. The indication for surgery in primary obstructive megaureter was established based on the scintigraphic or urographic evidence of urinary obstruction. Surgery consisted of ureteroplasty and anti-reflux ureteral reimplantation.

Of the 101 children with renouretrral anomalies undergoing surgery, 3 were diagnosed with pyeloureteral duplication and underwent partial nephrectomy. The indication for surgery in pyeloureteral duplication was motivated by the presence of obstruction in the upper pole ureter and subsequent hydronephrosis [3].

In the present study, the diagnosis of horseshoe kidney was established in 3 pediatric patients, 2 undergoing nephrectomy for decompensated hydronephrosis and 1 nephrolithotomy for associated coraliform lithiasis.

Vesicoureteral reflux was diagnosed in 22.7% of children with renoureteral anomalies. The diagnosis was established by micturating cystography and the indication for ureteroneocystostomy was determined by the association of urinary infection and the degree of reflux [4].

There were no intraoperative complications. Postoperative complications in patients who underwent pyeloplasty were represented by urinary fistula in the lumbar region in 4 cases treated in a conventional manner, 1 case of subcapsular kidney urinoma treated with nephrectomy, and 1 case of acute postoperative appendicitis; there were no cases of anastomotic stenosis requiring reintervention. Another postoperative complication was vesicoureteral anastomotic stenosis in 1 of the cases treated for primary obstructive megaureter, which required reintervention one year postoperatively.

Discussion

In the last 20 years there has been a significant increase in the total number of nephrectomies for multicystic dysplastic kidney, while the number of nephrectomies for vesicoureteral reflux has remained constant. The emergence of new surgical techniques has led to an increase in the number of partial nephrectomies as compared to the percentage of total nephrectomies in patients with localized disease of the kidney, with an attractive alternative to preserve functional kidney parenchyma. There is little data in the literature on the indications for nephrectomy in children. The decrease in the number of nephrectomies performed for ureteropelvic junction obstruction can be explained by the improvement in the management and assessment of prenatal diagnosis of hydronephrosis [8,9]. In the adult population, 67% of nephrectomies are performed for kidney malignancies. In children, the most common indication for nephrectomy is in congenital anomalies of the kidney, neoplastic diseases accounting for only 43.6% of the indications for nephrectomy in pediatric patients. In our study, the most common partial nephrectomies were performed for pyeloureteral duplication, which is consistent with other data in the literature. Ultrasonographic monitoring of children with prenatally diagnosed hydronephrosis has shown that most cases of congenital hydronephrosis can spontaneously regress, surgery being indicated in only 20% of cases [10].

The most common congenital anomaly of the kidney diagnosed in our study was congenital hydronephrosis secondary to ureteropelvic junction obstruction (44.5%), followed by vesicoureteral reflux (22.7%) and primary obstructive megaureter (13.8%). In recent years, there has been a decrease in the number of nephrectomies performed for hydronephrosis secondary to ureteropelvic junction obstruction in children undergoing surgery at the Department of Pediatric Urology. The tendency to adopt a more conservative attitude in clinical practice guidelines resulted in the performance of nephrectomy for pyonephrosis or non-functional hydronephrotic kidney alone, otherwise being replaced by pyeloplasty.

Reflux nephropathy is the third major indication for nephrectomy in children. The indication for surgical therapy in children with vesicoureteral reflux has become more selective in recent years, endoscopic treatment being an alternative of the modern therapeutic arsenal. In children with severe ureteral dilation and subsequent hydronephrosis, it is important to establish the moment to perform surgery prior to the occurrence of recurrent acute pyelonephritis and of a high degree of vesicoureteral reflux [11].

Children diagnosed with multicystic dysplastic kidney have an increased incidence of contralateral or ipsilateral congenital renal abnormalities, mainly vesicoureteral reflux (15%) and ureteropelvic junction obstruction (3-12%) [12].

Abnormalities such as the horseshoe kidney due to the position of the pelvis and aberrant vasculature may be associated with other renoureteral anomalies such as ureteropelvic junction obstruction, renal lithiasis, pyeloureteral duplication and vesicoureteral reflux [7]. In our study, children diagnosed with horseshoe kidney had associated hydronephrosis requiring nephrectomy (2 cases), coraliform lithiasis, vesicoureteral reflux and ureteropelvic junction obstruction (1 case).

Laparoscopic nephrectomy in children has become a routine surgical procedure in some pediatric urology centers. Laparoscopic pyeloplasty is an alternative treatment in ureteropelvic junction obstruction, but there are some limitations that derive from the particularity of pediatric patients; this can not be safely performed at younger age (under 7 years) due to insufficient working space and the degree of difficulty of intracorporeal suturing [13]. The first series of robotic assisted urological interventions in children were performed in 2004, the same year when the first complex

reconstruction (Mitrofanoff appendicovesicostomy) and the first bilateral partial nephrectomy [14] were performed. Robotic assisted minimally invasive surgery offers better conditions for intracorporeal suturing [15]. Other facilities offered by robotic surgery include the elimination of physiological tremor, the ability to perform precise movements, the ability to perform microanastomoses, to perform laborious dissections in limited spaces, the reduced risk of visceral or vascular lesions in the reduced working space, safe intracorporal suturing, low intraoperative and postoperative complications, reduced intraoperative blood loss, and significant reduced hospitalization. The main robotic approaches to pediatric urology are nephrectomy, pyeloplasty, antireflux procedures and pyelolithotomy. In the Department of Pediatric Urology of the Municipal Clinical Hospital in Cluj-Napoca, there were laparoscopic approaches for hydronephrosis secondary to ureteropelvic junction obstruction and multicystic dysplastic kidney. Robotically assisted minimally invasive pyeloplasty was also performed in a 16-year old pediatric patient. Excellent results of minimally invasive surgical techniques have improved the complex problem of the therapeutic approach to anomalies of the kidney in children.

The antenatal diagnosis of renoureteral anomalies in children undergoing surgery at the Department of Urology of the Municipal Clinical Hospital in Cluj-Napoca was established in a low percentage (2.9%): 1 case of multicystic dysplastic kidney, 1 case of left-sided ureteropelvic junction obstruction with third degree hydronephrosis, and a1 case of right-sided ureteropelvic junction obstruction with right-sided hydronephrosis and right-sided Hutch type diverticulum. The low proportion of prenatal diagnosis of renoureteral anomalies suggests the need for routine ultrasound examination both prenatally and postnatally prior to discharge from the maternity hospital.

Conclusion

The spectrum of indications for urological interventions has followed a more conservative tendency in recent years, with a decrease in the number of nephrectomies performed for congenital hydronephrosis secondary to ureteropelvic junction obstruction and an increase in the number of pyeloplasties.

The conditions with indication for minimally invasive techniques were ureteropelvic junction obstruction, multicystic dysplastic kidney and ureteral stenosis. The procedures performed were laparoscopic nephrectomy, endoscopic placement of ureteral stent, laparoscopic pieloplasty, and robotic assisted minimally invasive pyeloplasty.

Renal anomalies with the highest incidence that were surgically treated in our study were congenital hydronephrosis secondary to ureteropelvic junction obstruction (44.5%) and vesicoureteral reflux (22.7%). The rate of postoperative complications was very low, with only 2 children (1.9%) undergoing surgical reinterventions.

Robotic assisted minimally invasive surgery is a valuable perspective into the treatment of various pediatric urological conditions such as pyeloplasty and ureteral reimplantation for vesicoureteral reflux, allowing for laborious dissections in limited spaces and the ability to perform microanastomoses.

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THE ANATOMICAL LANDMARKS FOR THE IDENTIFICATION OF THE LARYNGEAL NERVE IN THYROID SURGERY

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Abstract

Objectives. *The purpose of the study was to demonstrate the anatomical landmarks for the identification and preservation of recurrent laryngeal nerves in thyroid surgery, as well as to know their anatomical variations.*

Method. *We carried out a retrospective analysis of the anatomical landmarks for the identification of the recurrent laryngeal nerve in patients with thyroid diseases admitted and undergoing surgery at the 5th Department of Surgery in Cluj-Napoca between 2012 and 2017, and we also studied inferior laryngeal nerves by anatomical dissection within the Department of Anatomy and Embryology of Iuliu Hatieganu University of Medicine and Pharmacy.*

Results. *We studied 308 patients with total thyroidectomy, of which 210 women (68.2%) and 98 (31.8%) men, and median age was 43.6 years. In 254 cases (82.5%) the interventions were performed for benign thyroid diseases. In 81% of cases, the inferior laryngeal nerve was posterior to the inferior thyroid artery on the left side. The ramification of the recurrent laryngeal nerve starts at a distance of 3.2 mm (median) from the entry point into the larynx and presents a unique trunk in 253 cases (82.1%). The recurrent laryngeal nerve was posterior to Zuckerkandl's tubercle in 287 cases (93.2%). In one case we found one non-recurent laryngeal nerv.*

Conclusions. *Knowing the anatomical positions and accurately identifying the inferior laryngeal nerve help decrease the incidence of complications occurring after total thyroidectomy.*

Keywords: inferior laryngeal nerve, thyroidectomy, Zuckerkandl's tubercle, Berry's ligament

Introduction

The identification of recurrent laryngeal nerves is of great importance for thyroidectomy. In thyroid surgery, both the recurrent laryngeal nerves and the outer branches of the superior laryngeal nerves must be preserved. Lesions of the inferior laryngeal nerve on one side lead to the paramedian positioning of the vocal cord located on that side, but phonation is preserved. In case of bilateral injury, the median positioning of both vocal cords occurs, accompanied by respiratory obstruction, requiring temporary or permanent tracheostomy.

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The thyroid gland develops during the fourth week of gestation from the foramen cecum and migrates inferiorly from the hyoid bone and the thyroid cartilage. The ultimobranchial body derives from the fifth pharyngeal pouch and contains cells derived from the neural crest that will give rise to calcitonin-producing parafollicular cells (C cells). During the 5th week of intrauterine development, the ultimobranchial body fuses with the thyroid with Zuckerkandl's tubercle forming at the fusion site [1,2]. The recurrent laryngeal nerve derives from the 4-6 pharyngeal arches. Thus, the embryological development explains the anatomical relations of the recurrent laryngeal nerve with Zuckerkandl's tubercle and the fact that it never passes through the thyroid parenchyma, as well as the anatomical

variations encountered (Figure 1).

The objectives of this study were to demonstrate the anatomical landmarks for the identification and preservation of recurrent laryngeal nerves in thyroid surgery, as well as to recognize their anatomical variations.

Material and method

We carried out a retrospective analysis regarding the anatomical landmarks for the identification of recurrent laryngeal nerves in patients with thyroid diseases admitted and undergoing surgery at the 5th Department of Surgery in Cluj-Napoca during 2012-2017, and we also studied inferior laryngeal nerves by anatomical dissection within the Department of Anatomy and Embryology of Iuliu Hatieganu University of Medicine and Pharmacy. Thus, we evaluated the relationship between the recurrent laryngeal nerve and the inferior thyroid artery, the branching of the recurrent laryngeal nerve, the distance to which it branches from the entry point into the larynx, the relationship between the laryngeal nerve and Berry's ligament and Zuckerkandl's tubercle. The study was approved by the Ethics Committee of the Cluj-Napoca Municipal Clinical Hospital.

Results

Between 2012 and 2017, 722 total thyroidectomies were performed at the 5th Department of Surgery of the Municipal Clinical Hospital in Cluj-Napoca, 308 of them, performed by one surgical team, were considered in the present study, as well as dissections performed within the Department of Anatomy and Embryology of Iuliu Hatieganu University of Medicine and Pharmacy. There were 210 women (68.2%) and 98 men (31.8%) with a median age of 43.6 years. In 254 (82.5%) cases, the interventions were performed for benign thyroid diseases, and in 54 (17.5%) cases, for malignant thyroid diseases.

The following were observed regarding the relationship between the inferior laryngeal nerve and the inferior thyroid artery: inferior laryngeal nerve located posterior to the trunk or arterial branches in 162 cases on the right side (52.5%) and 81% on the left side (Figures 1, 2); the inferior laryngeal nerve passes through the arterial branches in 56 cases (18.8%) on the right side and 61 cases (19.8%) on the left side.

The recurrent laryngeal nerve presented a unique trunk in 253 cases (82.1%) or two branches in 52 cases (16.9%), three branches in three cases (0.97%) and in one case we found one non-recurrent laryngeal nerve.

There was no case with four branches in our study. Ramification of the recurrent laryngeal nerve begins at a variable distance from the entry point into the larynx. In our study, the calculated median distance was 3.2 mm.

The recurrent laryngeal nerve was located posteriorly to Zuckerkandl's tubercle in 287 cases (93.2%). The tubercule was absent (grade 0) in 15 cases (4.92%). In 5 cases (1.62%), the recurrent laryngeal nerve was identified laterally to the tubercle, and in one case (0.26%) anteriorly to the tubercle.

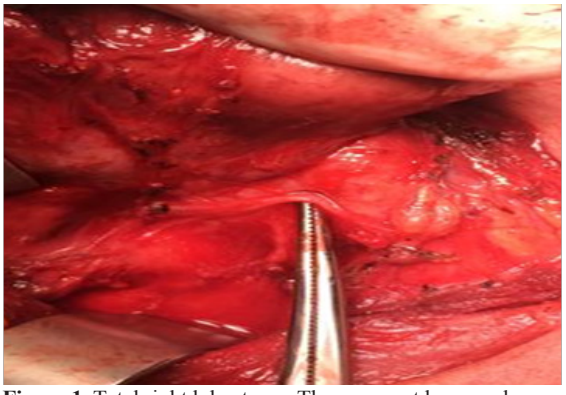

Figure 1. Total right lobectomy. The recurrent laryngeal nerve located anteriorly to the inferior thyroid artery (5th Department of Surgery archive).

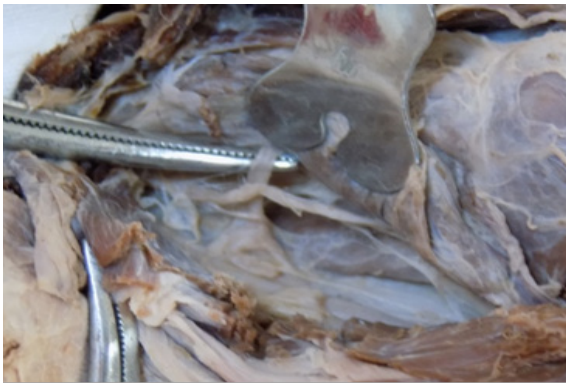

Figure 2. Left recurrent laryngeal nerve located anteriorly to the inferior thyroid artery. (Department of Anatomy and Embryology of the University of Medicine and Pharmacy in Cluj-Napoca).

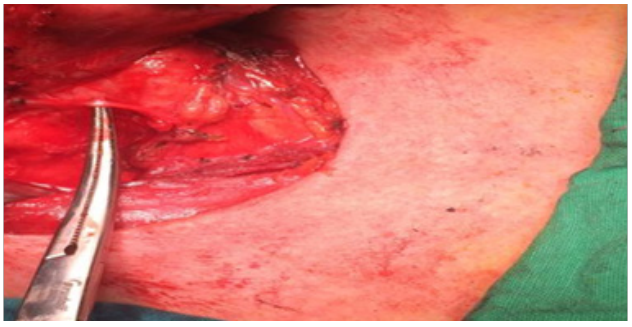

Figure 3. Right recurrent laryngeal nerve with three terminal branches (Archives of the 5th Department of Surgery, Cluj-Napoca).

Discussion

The relationship between the inferior laryngeal nerve and the inferior thyroid artery represents an important anatomical landmark in identifying the recurrent laryngeal nerve, with a multitude of studies describing these anatomical relationships [3,4]: type A - the inferior laryngeal nerve located superficial to the trunk or arterial branches (50% on the right side) (Figures 2, 3); type B - the inferior laryngeal nerve passes through the arterial branches in (14% on the right side and 16% on the left side); type C - the inferior laryngeal nerve passes posteriorly to the artery (56% on the left side); type D - the artery passes through nerve branches (12% on the right side and 3% on the left side); type E - arterial and nerve branches intersect (2% on the right side and 14% on the left side).

Branching of the recurrent laryngeal nerve also presents numerous anatomical variations [1,5,6,7]. The recurrent laryngeal nerve can have between one and four branches (Fig. 3). Most frequently, it has a unique trunk (92%-8%) or two branches (92%-18%). The presence of left-right symmetry is not mandatory and the left or right recurrent nerve caliber can be similar or different in the same patient. Ramification of the recurrent laryngeal nerve begins at a variable distance from the entry point into the larynx, ranging between 0 and 45 mm [1].

The recurrent laryngeal nerve is located laterally to Berry's ligament, at a variable distance of about 3 mm, but it can be located medial to the ligament or even penetrate it in very rare situations [8,9,10]. The relationship between the recurrent laryngeal nerve and Zuckerkandl's tubercle are also particularly useful in identifying the recurrent laryngeal nerve. Several situations may be encountered [11,12,13]: grade 0 - the tubercle is absent; grade 1 - the tubercle appears as a thickening (less than 5 mm) of the lateral part of the thyroid lobe; grade 2 - the tubercle is less than 1 cm in diameter; grade 3 - the tubercle is over 1 cm in diameter. The recurrent laryngeal nerve is located posteriorly (92% of the cases) to Zuckerkandl's tubercle, sometimes being identified laterally to it and very rarely anteriorly.

In the lateral approach, most commonly used in thyroid surgery, Zuckerkandl's tubercle is the most important landmark for the preservation of the recurrent laryngeal nerve [1]. In the inferior approach, the recurrent nerve is identified in the tracheoesophageal groove, on the left and lateral to it on the right, and in the superior approach the nerve is observed at the entry point into the larynx [1,14,15]. The rarest, but also the most dangerous situation is represented by the presence of a non-recurrent inferior laryngeal nerve.

Knowledge of the anatomical landmarks used to identify the recurrent laryngeal nerve (Zuckerkandl's tubercle, the anatomical relationship with the branches of the inferior thyroid artery, Berry's ligament, the tracheoesophageal groove, the relationship with the inferior or superior parathyroid glands, the identification of the laryngeal nerve at the entry point into the larynx), knowledge of the anatomical variations and possible differences in anatomical landmarks correlated with gender and the dissection of the left inferior laryngeal nerve, respectively the right inferior laryngeal nerve, are of particular importance in obtaining a low incidence of postoperative complications in total thyroidectomy.

Conclusions

The accurate identification of the inferior laryngeal nerve decreases the incidence of postoperative complications represented by postoperative transient dysphonia resulting from the elongation of the recurrent laryngeal nerve, as well as the unilateral or bilateral temporary or permanent injury to the recurrent laryngeal nerve.

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EMBRYO-FOETAL DEVELOPMENT OF THE EAR

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Abstract

Our paper presents moments in embryo-foetal development of the ear using microMRI and ultrasonographic studies and reveals also malformated ears on the autopsy of the aborted foetuses.

The microMRI study pointed out the details of the otic vesicles from the early ear development. The ultrasonographic study revealed the evolution of the auricle during the foetal development. The foetal autopsy identified cases of malformed ear from different pathologies, genetic or multiple malformations context.

The data are completed with a literature revision.

Keywords: ear, development, malformations

Introduction

The ears represent anatomical structures which have a role in hearing perception and in maintaining balance. The cochlea processes the auditory information, while the vestibular apparatus assures balance and sense of movement, orientation, and gravity [1]. The anatomical position, on either side of the head, allows very well localization of sounds in space by neural comparison in time and intensity of signals arriving each ear.

The human ear contains a complex architecture with different cell types. The development of the ear begins early by gestation week 4. The inner ear develops from the neuroectoderm (otic placode), but the middle and external ear develop from the first and two branchial arches and the first pharyngeal pouch [2]. Almost all of the inner ear structures reach an adult size and form by approximately 11 gestation week [3]. Thus, the most critical period is between the 4 -12 gestation week. The ossicles mature later, by 15–20 gestation week, and the tympanic cavity enlarges until approximately 37 gestation week. The external auditory canal attains its final form later, in the end of childhood [4].

The good function of the hearing and vestibular apparatus is very dependent on the integration of the ear components during development. The formation and interaction of the tissues involved in ear development requires the involvement of reciprocal molecular signaling [1].

Because human labyrinth attains its adult morphology before birth, the postnatal influences on the morphology by environmental or behavioural factors are minimal [5].

We present the fundamental moments in embryo-foetal morphogenesis, using ear imagistic, emphasizing congenital malformations.

Material and method

On the microMRI study we used three human embryos, Carnegie stages 12 (CRL=4.5 mm), 13 (CRL=7 mm) and 16 (CRL=12 mm) kept in formalin solution 9%,

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from the collection of the Anatomy Department of the University of Medicine and Pharmacy Cluj-Napoca.

Magnetic resonance analysis was performed using a Bruker Biospec 7.04 Tesla scanner. The embryos were scanned when immersed in formalin solution 9 % at room temperature. Post-scanning processing of MR images was performed by employing ParaVision® software.

On ultrasound study we used the images from routine investigations of four pregnancies on different gestational weeks (GW): 22, 26, 35, 37.

The external exam was performed on three aborted foetuses (approximately 14, 15, 18 GW) from the IMOGEN - Centre of Advanced Research Studies, Cluj-Napoca.

Results

The microMRI study identified the early moments of the otic vesicles which can be seen on the embryo sections (Figure 1): on the 12 CS embryo (approximatley 28 days) the otic cup (represents the invaginated otic placode) can be observed on parasagittal and axial slices, with the evolution to otic vesicle which can be seen in both slices (C- parasagittal, D - axial) from 13 CS embryos (32 dys) and in axial slice from 16 CS (38 days).

The ultrasonographic study identified the evolution of the auricle from the external ear. The ultrasounds pointed out the position and the morphology of the auricle. The physiological evolution can be seen in the ultrasound images from the preganancies: 2D images from 22, 26, 37 GW (Figure 2) and 3D images from 35 GW foetus (Figure 3). These information cand be correlated with the pathological evolution of the auricle, evidence of single or pluri – foetal malformations. The exam of the external ear of the aborted foetuses revealed abnormal implantation of the auricle and modified morphology. Figure 4 represents a case of a Potter Syndrome with Potter face from a foetus of 14 GW – with low ears and pressed against the head. The 18 GW foetus with Down Syndrome (Figure 5) presents the low ears. Figure 6 represents images of a foetus with abnormal morphological aspects of the auricle on the context of multimalformative context.

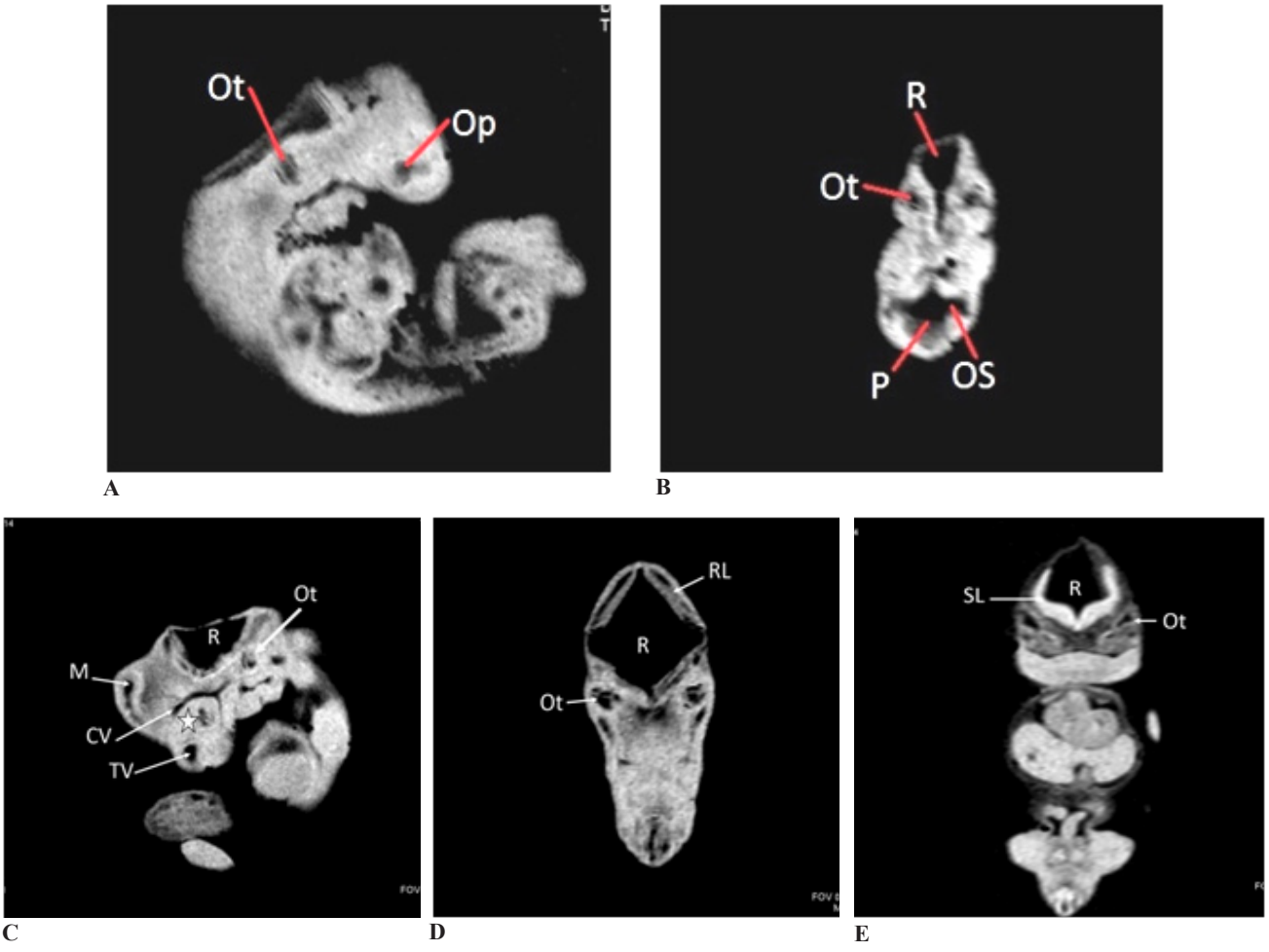

Figure 1. Human embryos imaged by microMRI: 12 CS: A - parasagittal slice; B – axial slice; 13 CS embryo: C - parasagittal slice; D - axial slice; 16 CS embryo: E - axial slice (RL: rhombic lips, Ot: otic cup/vesicle, R: rhombencephalon, SL: sulcus limitans, P: prosencephalon, Op: optic placode, M: mesencephalon, TV: telencephalic vesicles, OS – optic sulcus, CV: cardinal vein)

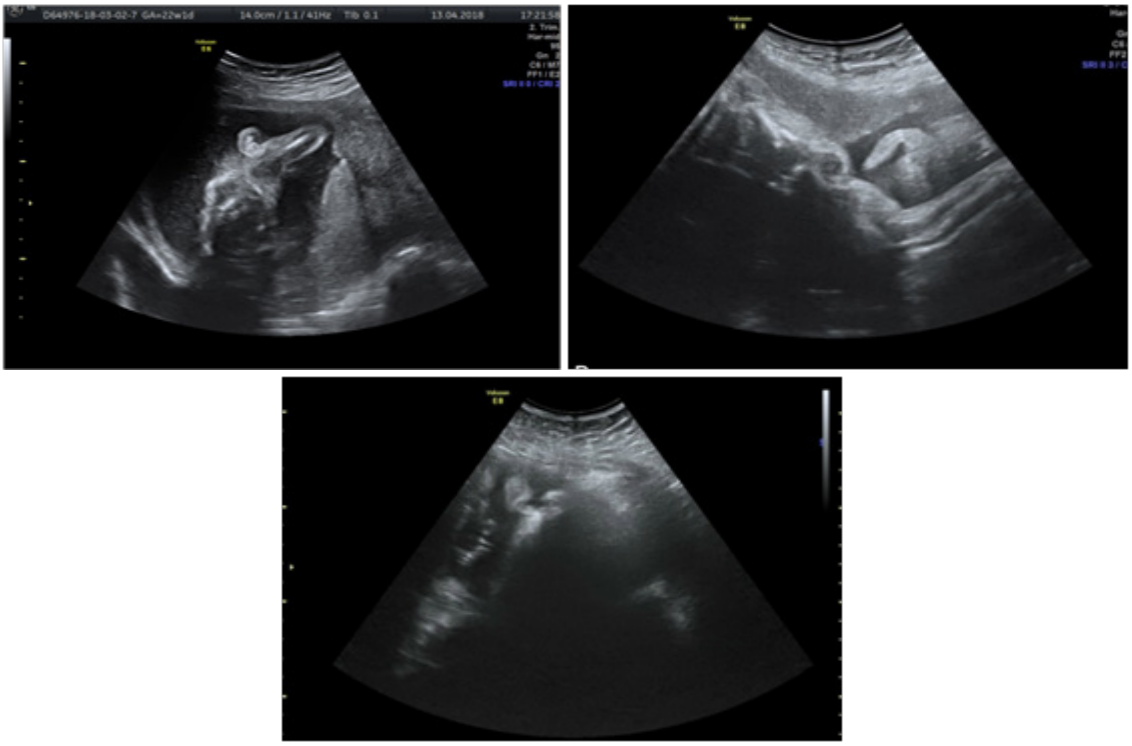

Figure 2. 2D Ultrasound images of the external ear in 22, 26 and 37 GW.

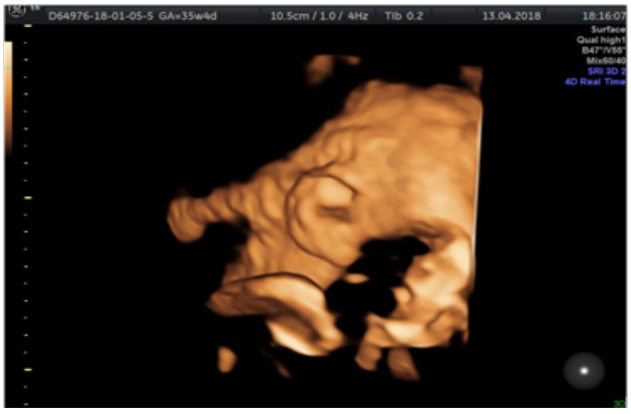

Figure 3. 3D Ultrasound image of the external ear of a 35 GW.

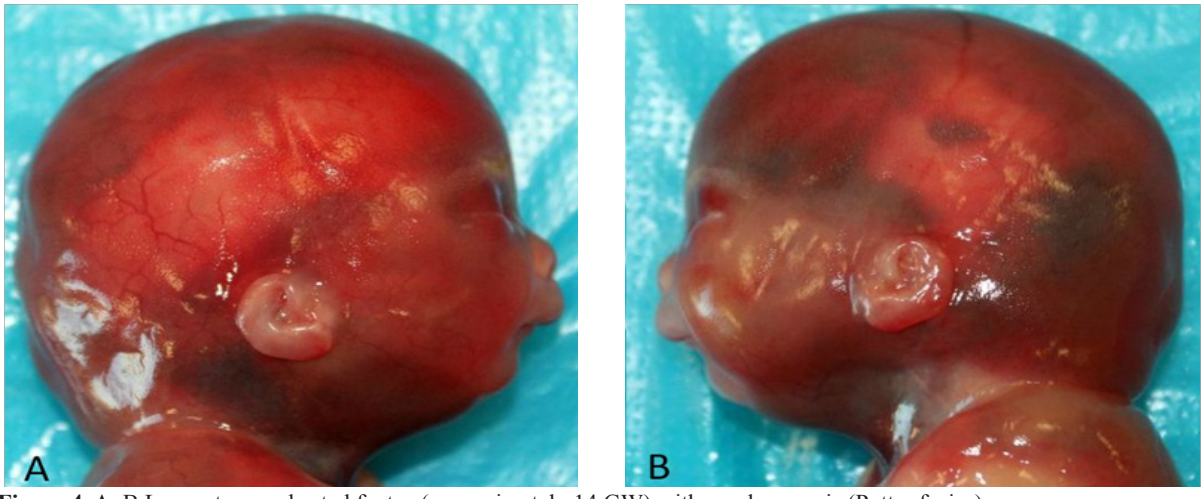

Figure 4. A, B Low set ears, aborted foetus (approximately 14 GW) with renal agenesis (Potter facies).

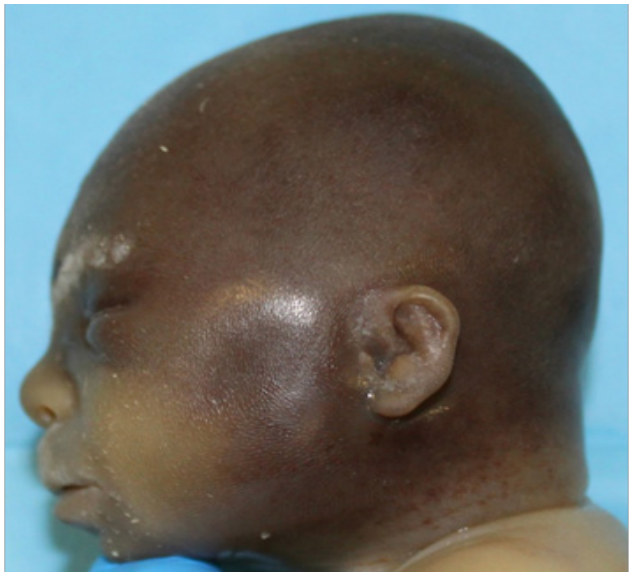

Figure 5. Low set ears, aborted foetus (approximately 18 GW) with 21trisomy, Down Syndrome.

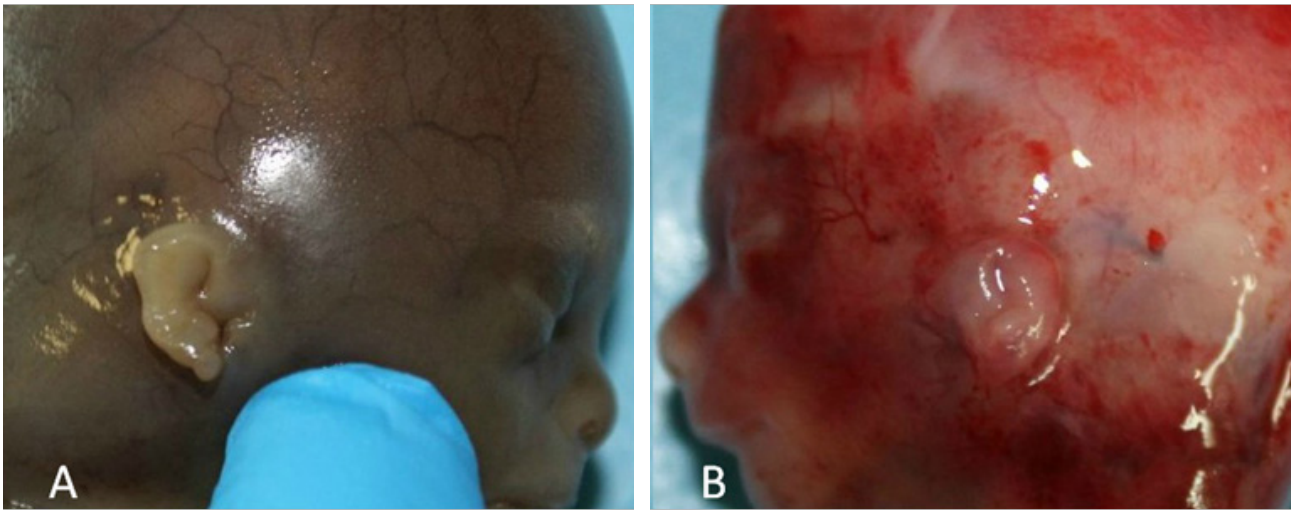

Figure 6. A, B Abnormalities of the external ear in a multiple malformations context, aborted foetus (approximately 15 GW).

Discussion

Prenatal ultrasound is the gold-standard for prenatal imaging, but foetal magnetic resonance imaging has become an important tool in prenatal imaging. Through prenatal ultrasonography can be seen local malformations of the auricle, but the visualization of the middle and inner ear is very difficult by ultrasonography [6]. Its capacity to rule out temporal bone pathology is limited. The foetal magnetic resonance imaging offers high spatial resolution and the possibility to delineate the cochlea, vestibular apparatus and the middle ear using magnetic resonance imaging with T2-weighted sequences, as early as at 13 gestation week, with good enough detail as to exclude major malformations [4]. Foetal magnetic resonance imaging is limited by foetal motions, thus the prenatal imaging of the ear become a very difficult task in clinical practice. For research purpose the microMRI studies offer images of the stuctures in different stages of the development. Being *in vitro* studies, the microMRI give the possibility to use embryos kept enough time in investigation to acquire detailed images of the structures.

Inner ear. The inner ear is in the petrous part of the temporal bone and contains of the membranous labyrinth and the bony labyrinth. The beginning of ear development is reported in the 21-22 embryonic day through the appearance of symmetrical thickening of the surface ectoderm (the *otic placode*), on both sides of the rhombencephalon. Through the invagination of the otic

placode at 4 gestation week, is formed the *otic vesicle* [7]. Induction of the otic placode is dependant on signaling from the pharyngeal mesenchyme and signaling from the hindbrain [8].

Afterwards, each otic vesicle is divided into two components: the ventral one will give birth to the saccule and to the cochlear duct, and the dorsal one will form the utricula, the semicircular canals and the endolimphatic duct.

The membranous labyrinth consists of the semicircular ducts, the utricle, the saccule, the endolymphatic ducts, and the cochlear duct. As the membranous labyrinth is developing, there is a concomitant development of the sensory neuroepithelia [9]. A group of cells detaches from the wall of the otic vesicle and forms the *vestibulocochlear ganglion*. In this ganglion migrates also cells from the neural crest. During development, the ganglion will be divided into a cochlear portion - which forms the sensory cells of Corti's organ, and a vestibular portion, which forms the sensory cells of the utricula, sacula, and semicircular canals [7].

The membranous labyrinth grows with rapidity and arrives adult size by the middle of the gestation period [3]. The cochlear part gradually winds around its own axis towards the vestibular part, finish off 2½ windings at the 10 gestation week [10]. The semicircular canals emerge as disc-like out-pocketings, and touch their form at the 8 gestation week. The human foetal labyrinth as a whole attains an adult equivalent size between 17 and 19 gestation week and is fully encapsulated by bone a few weeks later [5].

So, the membranous labyrinth and vestibulocochlear nerve are derived from the otic placode [11].

The development of the inner ear depends temporally and spatially coordinated gene expression patterns. The homeobox genes are very important regulators of inner ear development. The Pax2 paired-homeobox gene is essential for the specification of the ventral otic vesicle derived auditory structures and the Dlx5 and Dlx6 homeobox genes for the specification of the dorsally derived vestibular structures [12]. The paracrine and autocrine signals, including fibroblast growth factor, retinoic acid, and bone morphogenetic protein regulate also fate determination, axis formation, and morphogenesis in the developing inner ear [11].

The bony labyrinth (Figure 7) inside the petrous temporal bone houses membranous labyrinth. The otic capsule is a term which refers to the dense osseous labyrinth of the inner ear that surrounds the cochlea, the vestibule and the semicircular canals. The otic capsule develops from a cartilage model. The ossification process of the otic capsule proceeds rapidly between 18 and 24 gestation week from multiple ossification centers [3,5]. The unique opportunity to see by ultrasonography the cochlea is in the early second trimester when the temporal bone is hypomineralized and offers an acoustic window for sonography of the cochlea [13].

Figure 7. Section through petrous temporal bone: the cochlea (From bones collection, Museum of the Department of Anatomy and Embryology, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca).

Comparative studies have demonstrated that the bony labyrinth of modern humans is morphologically distinct from that of other primates: anterior and posterior semicircular canals have a larger arc size than the great apes, but the arc of the lateral canal of humans is marginally smaller, and the cochlea is similar in size. These differences were explained by the functional adaptation to la modern human bipedal locomotion. However, the embryo-foetal changes and of correlations with the cranial base does not provide a clear ontogenetic basis for the evolutionary history of the human labyrinth [5].

Developmental defects in the inner ear cause congenital hearing loss and balance disorders.

Based on embryogenesis and radiological findings, the inner ear malformations can be classified as such: *cochlear malformations* include Michel deformity (complete absence of all cochlear and vestibular structures), cochlear aplasia (the cochlea is completely absent), common cavity (a cystic cavity without showing any differentiation into cochlea and vestibule), cochlear hypoplasia (the cochlea and vestibule are separate from each other, with smaller dimensions than normal, incomplete partition type I (the cochlea is whithout the entire modiolus and cribriform area, accompanied with a large cystic vestibule), and incomplete partition type II - Mondini deformity (the cochlea consists of 1.5 turns, in which the middle and apicalform a cystic apex). *Vestibular malformations* include Michel deformity, common cavity, absent vestibule, hypoplastic vestibule, and dilated vestibule. Semicircular canal malformations can be hypoplastic or enlarged. Internal auditory canal malformations can be narrow or enlarged [14].

Developmental malformations in the inner ear and

its nearby structures are often diagnosed in paediatric patients with sensorineural hearing loss. 50% of the congenital sensor neural hearing loss cases are caused by environmental exposures during pregnancy, and 50% from patients have genetic mutations [15]. The internal auditory meatus malformations can be narrow, or enlarged, with *the absence of the vestibulocochlear nerve or the underdeveloped cochlear branch*. Magnetic resonance imaging examinations are needed preoperative and for prognostic evaluations of patients with these malformations who are candidates for cochlear implantation [16,17]. The cochlea, vestibule, and semicircular canals are very prominent and easily recognized on magnetic resonance images [3].

In 1863, Michel described a complete absence of differentiated inner ear structures associated with other skull base anomalies, including an abnormal course of the facial nerve and jugular veins [18,19]. This is complete labyrinthine aplasia or Michel deformity.

CHARGE syndrome is a congenital anomalies group, including ocular coloboma, heart defects, choanal atresia or stenosis, retarded growth, genital hypoplasia, and inner and external ear anomalies. Semicircular canal dysplasia has been included as a major diagnostic criterion for CHARGE syndrome [20].

Middle ear. The tympanic cavity and middle ear ossicles (malleus, incus, and stapes) are parts of the middle ear. The middle ear with Eustachian tube and tympanic membrane is produced by all three germ stratums and the neural crest of the pharyngeal apparatus [1].

The *tympanic cavity* is formed from the first pharyngeal pouch endoderm. This develops laterally: from the distal side, the primitive tympanic cavity will form, and the proximal part will remain narrow and will form the Eustachian tube [7]. The middle ear bones (ossicles) are derived from separate origins in the first and second pharyngeal arches: from first arch – malleus and incus, and from second arch cartilage – stapes. The presumptive ossicles will differentiate into cartilage. Initially, the malleus and incus form a single cartilaginous condensation that splits into two parts. The mesenchymal tissue within the middle ear cavity and around the ossicles will retracts, leaving the ossicles in a space filled with air [1].

The studies about middle ear development during the foetal period using high-resolution magnetic resonance imaging indicated that the middle ear ossicles are morphologically similar during foetal development and adulthood. In each middle ear ossicles, ossification spread outward from a single center [21]. The bony tympanic ring does not begin to ossify until the 3rd month [22] (Figure 8).

The congenital anomalies of the middle ear have a frequency of 1 la 3000–20000 newborns. By change of the normal anatomy, these anomalies cause the alteration in the hearing function [23].

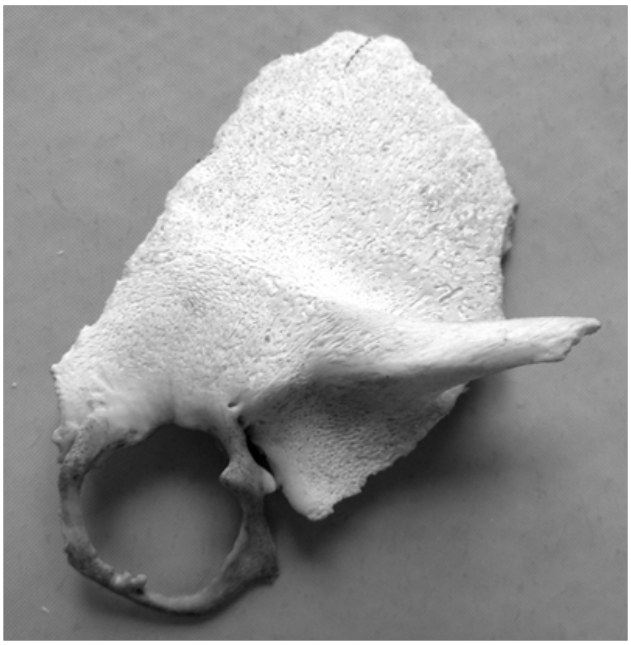

Figure 8. Child temporal bone with preparation of the bony tympanic ring (From bones collection, Museum of the Department of Anatomy and Embryology, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca).

The impairment of embryonic development before 6 gestation weeks determines injury to the immature primordium and malformation of the external and middle ear. The injuries that occur after 3 months do not appear to cause middle ear malformations [24].

There is a variety of malformations in the middle ear. The middle ear malformation can be unilateral or bilateral, minor (only involvement of the middle ear) and major (associated with an involvement of the external ear) [25]. The minor middle ear anomalies include *morphological changes of the tympanic cavity* or fixated ossicles (stapes ankylosis). In the major anomalies, the ossicles are often involved (*aplasia* or *hypoplasia*, *thickening*, *thinning or fusion* of the stapes crura). The surgeon is obligated to estimate if deformed ossicles can perform a normal transmission function or should be replaced [26].

Also, the *ear windows* may be involved in middle ear malformations (mobile stapes footplate or dysplasia/ aplasia of the round or oval window). Other anomalies of the middle ear are *dehiscence* or *displacement* of the facial nerve, a *missing antrum*, *apneumatized mastoid*, and *aberrant vascular courses* [26,27].

Visualization of the foetal middle ear is is very difficult with prenatal ultrasonography. Ossicle (incus and malleus) can be observed only in the second half of pregnancy, as a bright echo within the upper part of the tympanic ring [13]. Middle ear malformations are usually associated with mandibulofacial dysostosis [28]. The middle ear cavity can be visualized with foetal magnetic resonance imaging and it is recommend the use of this

imaging method in the diagnosis of middle ear anomalies.

External ear. The external ear show a multiple movement during craniofacial morphogenesis. Initially, the external ears are contained in the lower neck region. With the development of the face structure and of the mandible, the external ear ascend to the side of the head at the eyes level [29].

In 36-38 embryonic day, the precursors of the *auricle* are presenting. The auricle develops from 6 mesenchymal protuberances from the first and second branchial arch [7,22]. Because the fusion process of auricular buds is complicated, the developmental anomalies of the auricle is frequently.

The *external meatus* contains an epithelial stopper until the month 7, when it resolves [7].

Generally, the auricle will grow with the rest of the body up to 7 to 10 years of age. However, the developmental anomalies remain in their birth form [22].

The malformations of the auricle occur in 1 out of 12 500 births and can occur alone or can be associated with genetically syndromes. These malformations can relate to pharyngeal arch development or may be part of a wider spectrum of anomaly associated with a genetic or environmental factors [22].

The *anomalies* of the auricle include anotia, microtia [30] (from decreased development of the auricular hillocks or from a defect of fusion of the parts), proeminent ear, lop ear, cryptotia (there is a skin deficiency of the superior part of the auricle, resulting the adherence of the ear to the head) [22], low set ears (Figures 2-3).

The *anomalies* of the external canal are classified into four categories: aplasia, atresia and stenosis (the external auditory meatus can fail to canalise, stenosis is frequently seen in Down's syndrome), and duplication [22].

The abnormalities of the external ear can occur also in a multiple malformations context.

Conclusions

The understanding of the fundamental of ear development is important for the diagnosis and management of patients with congenital ear malformations. The malformations of the ears may be a part of complex foetal malformations.

The microMRI studies are very powerful tools for research purpose, being a technique for *in vitro* investigations, giving possibility to point out detailes of the developmental structures.

The prenatal imaging of the ear remain a difficult task in clinical practice in the attempt to have an early detection of the possible anomalies. The routine examination of the pregnancy evolution is the ultrasonography, giving us sufficient information of the foetal evolution.

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THE IMPORTANCE OF POWERPOINT PRESENTATIONS IN TEACHING ANATOMY. THE STUDENTS' PERSPECTIVE

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Abstract

Background and aims. *The aim of this study was to evaluate the students' perspective regarding anatomy teaching methods (oral speaking/blackboard vs. PowerPoint PPT presentation) in 1st year medical students.*

Methods. *This was a cross-sectional descriptive questionnaire-based study on 1st year medical students. A total of 90 (n=90) french section medical students were included in the study. A 14-questions questionnaire regarding anatomy teaching methods was used. Students were asked to fill in the questionnaire according to their perception of the anatomy classes. The results were analyzed using MS Excel 2016.*

Results. *PowerPoint PPT presentation is the preferred teaching method for most of the interviewed students - 64 (71.1%), considering it more attractive - 71 (78.8%), able to clearly present the subject - 75 (83.3%) and that facilitates and improves individual study - 84 (93.3%). Oral speaking/blackboard presentations are preferred by 60 (66.6%) of the students for a better teacher-student interaction.*

Conclusion. *PowerPoint PPT presentation is the best preferred anatomy teaching method along with the dissection technique. Blackboard teaching methods can be used additionally to improve drawing techniques and for better teacher-student interaction.*

Keywords: anatomy, teaching methods, PowerPoint presentations

Background and aims

Studying anatomy involves many notions that need to be understood and memorized in a relatively short period of time. Moreover, students from first years find it difficult to aquire basic anatomy notions due to high volume material and lack of ability in distinguish essential information. Thus, the learning process must be student-centered and must always come to his aid. The role of the anatomy teacher is to facilitate the learning process of the student both through active involvement and also by developing student's interest in the subject matter. The study of anatomy is essential for understanding future clinical subjects and for medical practice, as well [1]. Compared to active learning methods like (problem based learning or bedside clinics), teaching anatomy through passive methods (oral speaking/blackboard or PowerPoint PPT presentations) may represent a disadvantage regarding student's interest in the subject [2]. Thus, the anatomy teacher has to overcome this possible inconvenience and must transmit students the information by means of modern communication.

Classical methods of teaching anatomy include oral speaking/blackboard presentations along with cadaver dissection [3]. The increasing use of PowerPoint PPT presentations came as a normal response to the technological evolution we are witnessing. So nowadays, not only they are widely used in medical universities, but are also considered to be some of the most effective methods of teaching anatomy [4,5]. PowerPoint PPT presentations expose the information in an interactive manner, using various audio-visual components that can be attractive to the audience. One of the biggest advantages of PowerPoint PPT in anatomy classes is that they allow the image-text association for each

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aspect to be mentioned, contributing to the understanding of anatomical details. Moreover, the students can review the presentation during individual study, aspect that would allow for a better assimilation of the anatomy notions.

This paper aims to evaluate medical student's perspective regarding the use of PowerPoint PPT presentation in teaching anatomy.

Methods

This was a cross sectional study conducted on students from the Iuliu Hatieganu University of Medicine and Pharmacy of Cluj – Napoca, Romania. First year medical students after completion of one semester of study were invited to ask a 14-questions questionnaire regarding preference of teaching in anatomy classes. Students were selected randomly from 1st year French section medical students, 2017-2018 batch. The results were based upon the data obtained from 90 students. Analysis of the questionnaires was performed using MS Excel 2016.

Results

The response of students are presented in Table I.

Table I. Students perspective regarding orally/blackboard and PowerPoint PPT teaching methods in anatomy classes.

Question number	Questions	PowerPoint PPT presentation (n,%)	Orally/Blackbord presentation (n,%)
	Part A		
1.	**Which method of teaching do you prefer?**	64, 71.1	26, 28.8
2.	**Which method of teaching is more attractive?**	71, 78.8	19, 21.1
3.	**Which method is able to keep you more attentive?**	60, 66.6%	30, 33.4
4.	**Which method helps you better understand the subject?**	75, 83.3	15, 16.7
5.	**Which method helps you memorize the subject better?**	84, 93.3	6, 6.7
6.	**What method inspires you more?**	49, 54.4	41, 45.5
7.	**Which method covers more topics?**	68, 75.5	22, 24.4
8.	**Which method better permits you to take notes?**	48, 53.3	42, 46.6
9.	**Which method allows for a better student-teacher interaction?**	30, 33.3	60, 66.6
10.	**Which method should be used?**	54, 60	36, 40
11.	**Part B (Yes/No)**	Yes (No.)	No (No.)
12.	**Did you noticed any differencess in your learning process between subjects that were presented in PPT vs orally?**	73, 81.1	17, 18.9
13.	**Was the text - image association in PPT useful to remember the subject when needed?**	88, 97.8	2, 2.2
14.	**Do you find it useful to have all the information from your theme in your PPT presentation, with an explicit image alongside?**	87, 96.6	3, 3.4
15.	**Do you find it useful to have the possibility to acces topics from the theme electronically?**	90, 100	0, 0

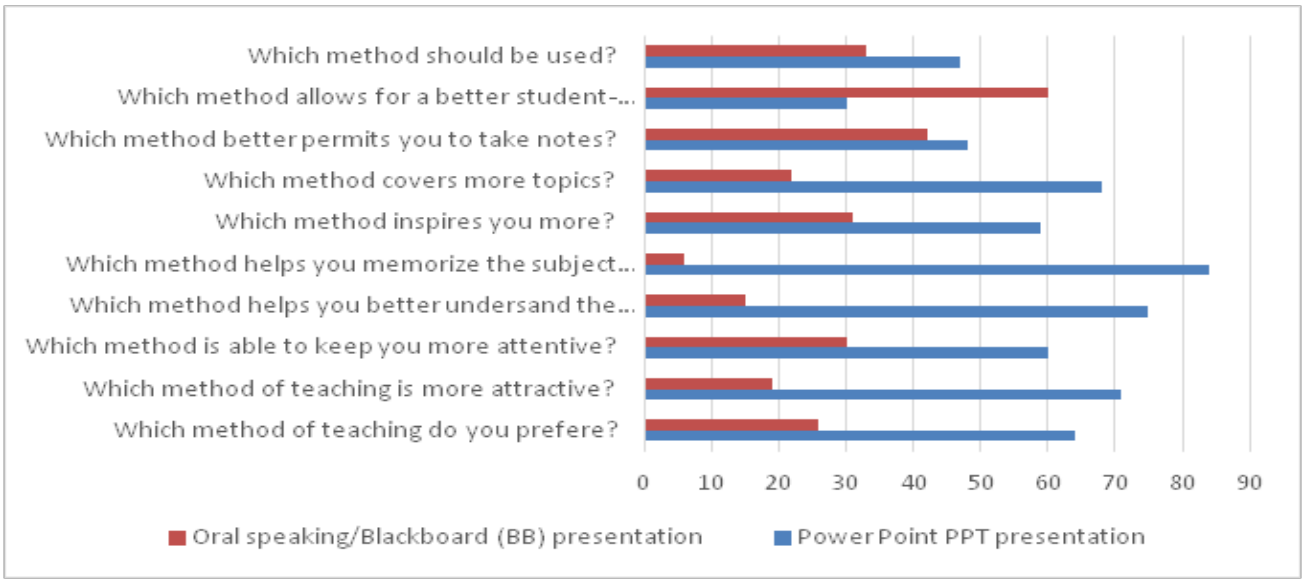

Figure 1. Percentage distribution in orally/blackboard and PowerPoint PPT presentations.

Discussion

Along with the cadaver dissection technique, didactic lecturers have been used for long time in teaching anatomy, usually in form of orally and blackboard presentations. Nevertheless, as a result of technological evolution, modern teaching techniques, including the use of PowerPoint PPT presentations have appeared. The majority of the students in our study prefer PowerPoint PPT presentations in anatomy classes, most considering them a more attractive teaching method. A high percentage of students consider that PowerPoint PPT presentations allows them to better understand anatomy concepts, emphasizing that the most important aspect is the text – image association, thus confirming that anatomy is a visual science. Nevertheless, the possibility to review the PowerPoint PPT presentations at home gives them the chance for a better individual study and avoids having oral subjects thought in the class to be forgotten. PowerPoint PPT presentations are able to transmit information in an interactive way, using images, animations and videos and are thought to be the best teaching method in anatomy classes also according to some recent studies [4,5].

Even if more than haf of the students interviewed consider PowerPoint PPT presentations the method that should be used in teaching anatomy, they recognize the disadvantage of not allowing for a good teacher-student interaction. The results are similar to those obtained in other studies [2,6,7]. In terms of methods that inspire the student, the percentages are close in our study, so we tend to believe that this parameter is more related to the teacher himself/herself and not necessarily to the teaching method. Another aspect to be considered is that all of the students interviewd signaled the importance of having the possibility of electronically accessing of the taught subjects, which can be achieved if PowerPoint PPT presentations are being used. The importance of using electronic means is underlined in other papers as well [3,4].

Anatomy may be difficult to assimilate at first, before having a general perspective of the anatomy of the entire human body. Students may be temped to try to learn as many ideas as possible from the first courses, but to memorize them without basic anatomical knowledge and without realizing correlations and association with visual information is not appropriate. It is specifically important for the students to understand every anatomical notion presented and not to learn the information ”by heart” and so the teacher must adapt the learning methods to current, modern requirements.

Conclusions

All in all, PowerPoint PPT presentations are the best preferred anatomy teaching method. Blackboard teaching methods can be used additionally to improve drawing techniques and for better teacher-student interaction.

Limitations: the study was conducted in only one institution.

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THE LEGAL SITUATION OF THE DEPARTMENTS OF HUMAN ANATOMY: BETWEEN PARADOX AND UNLAWFULNESS!

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Abstract

Taking into consideration the current legislative issues in the fields of health and education, it is desirable to make a review of the existing laws with applicability in the field of education, for the departments of Human Anatomy. The relevant laws for medical practice in laboratories are taken into account, as well as references to wage rights for both teaching staff and auxiliary staff. When observing the methodological norms of application, however, a paradoxical situation between the human anatomy chairs and the other departments of anatomy arises, if not illegal for the departments of human anatomy. And these aspects can be observed both in terms of employment for special conditions or salaries, but also as regards the right of medical practice in the laboratories of both physicians and laboratory staff. The major problem that arises is the existence of a legislative void that requires urgent completion and for which the Universities of Medicine in the country should have been involved so that the members of these departments would not be vulnerable before the law.

Keywords: Law 104/2003, methodological norms for law enforcement 104/2003, the legislation on the Departments of Anatomy, Framework Law no. 153 of 28 June 2017

Introduction

The main approach underlying the initiation and presentation of this article was the findings on medical practice, which were subsequently transposed for the laboratories in the departments of human anatomy of the medical universities.

One can notice that over time the legal problems of physicians have increased and are likely to increase in the years to come. Even if the human anatomy legislation on medical practice loses interest at first sight, after we reviewed issues related mainly to the remuneration of teachers and auxiliary staff, we found that problems transcend these unique views.

The issue raised in the course of time has been linked to several aspects. One of these was represented by the work categories and the placement of the personnel in the human anatomy departments. As expected, due to the conditions of working, as well as the existence of harmful substances, respectively carcinogens represented by formaldehyde mainly, this personnel was introduced into the category of work under special conditions. Only in the course of time will we notice that it has changed and not due to changing working conditions.

A second issue raised was that relating to the remuneration. And in this regard we will see in the following that they have also changed in a paradoxical and non-unitary way, with different interpretations depending on aspects more circumstantial than legal.

Last but not least, the legal protection of doctors and laboratory staff has suffered dramatically over time. If the right to dignity is well-defined, even after death, the same cannot be said about the rights and restrictions that doctors and lab staff have in the anatomy laboratories.

Taking into account the evolution of the last period of judicial practice and the need to know precisely the rights that the teaching and auxiliary staff have in relation to the practice of their profession, it is found that this

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jurisprudence is currently extremely limited if not vanished altogether.

The Framework Law which has been the basis for clarifying all these problems and which presently makes its presence felt is Law No 104/2003 on the manipulation of human corpses and organs and tissues from bodies in the view of transplants.

The methodological norms for the application of this law were subsequently elaborated, but they only had the quality to restrict the applicability of the framework law the way the legislator meant it and to render its applicability unclear if not completely confusing with respect to the departments of human anatomy.

These methodological rules were subsequently abrogated and others hvae been introduced instead. Additionally last year, a new law on education was drafted, to which we will make reference.

However, in order to be able to unravel this countless approved, abrogated and reintroduced laws, I have turned to lawyer Patricia Gherman, who has over 20 years of experience in labor law and in connection with labor conflicts. I also turned to lawyer Ciprian Paun, an international law expert, to see to what extent the Romanian legislation can be found in that of the European Union. Last but not least, I contacted the Union of Medicine and Pharmacy University of Cluj-Napoca, and through it Iulia Dumitru, lawyer and jurist of the union.

The purpose of the study

The objectives of this article are to answer the following questions:

1.Are there gaps in terms of current legislation when defending the rights of the members of anatomy departments and what are they?

2.What are the possible consequences of maintaining the current legislation?

3.Are there jurisprudence implications in the activity of human anatomy laboratories?

Thus, through the answers given above, the main purpose of this article is to find the existing anomalies as well as to raise awareness in all the responsible actors, but especially in all the anatomy departments in the country regarding the current legislation in view of a collaboration and joint involvement in order to restore the rule of law.

Methodology

In order to observe the current legal implications, a review of the existing legislation was made by highlighting the most important aspects.

Thus, the existing legislative situation for each point of interest was synthesized in the following, most often involving the same laws but with different articles. They searched for and found a series of laws, Government Emergency Ordinances, international laws as well as rulings of the High Court of Cassation and Justice with relevant implications in the presented issues, even some that were later abrogated or completed, but which had effects on decisions or laws subsequently issued, as follows:

A) Law 104/2003 on manipulation of human corpses and organs and tissues from bodies for transplants:

- Article 2 The right to manipulate human corpses for diagnosis or didactic and scientific activities belongs to the pathological anatomy and prosecution services of hospitals and legal medicine institutions, to the university disciplines of anatomy and the pathological anatomy of the state or private medical institutions of higher education, accredited or licensed, which organize services for the use of corpses.

- Article 4 (1) Corps services are functional structures of the university anatomy disciplines in human medical higher education institutions which have the attribution of handling them, for the purpose of collecting and preserving human tissues and organs for didactic and scientific activity.

- Article 13 The services for the use of corpses within the university disciplines of anatomy have the following attributions:

a) take corpses on a protocol basis between medical higher education institutions and pathological anatomy and hospital prosecution services;

b) prepare and preserve the corpses for dissection, providing anatomic and surgical education teaching material;

c) perform anatomical preparations;

d) prepare skeletons;

e) preserve tissues and organs.

- Article 21 (2) The financing of services for the use of corpses within the university disciplines of anatomy is made from the state budget allocated to the higher medical institution and from the institution's own income.

- Article 22 The personnel working in pathological anatomy and hospitalization services, as well as the staff of the university disciplines of anatomy, histology, pathological anatomy and department of cell biology fall into the category of work places under special working conditions.

B) The decision of the High Court of Cassation and Justice No 33 of 9 June 2008

C) The Governmental Decision 1093/2006

D) Law 19/2000 art. 20

E) Law 263/2010 art. 29 and art. 30

F) Convention of the International Labor Organization no. 95/1949

G) Government Emergency Ordinance no. 115 of November 24, 2004, subsequently approved by Law 125/2005

H) Law no. 47/2013

I) Law no. 153 of 28 June 2017.

Results

1. To answer the first question, whether there are any

legal loopholes, started off with Law 104/2003 on Handling Human Corpses and Organ and Tissue Collection of Corpses for Transplantation re-published 2014. Regarding Article 27 of this law, it provides that "Any other provisions contrary to this law shall be abrogated".

In other words, all laws issued until that time which have provisions contrary to it are null and void. This law was reapproved in 2014 and it is in force nowadays. In Article 26 of the same law it is provided that: "Within 60 days of the entry into force of this law, the Ministry of Health, the Ministry of Environment and Climate Change and the higher medical education institutions will submit to the Government the methodological norms for the application of this law."

And these methodological norms came through GEO no. 115/2004 approved with amendments and completions by the Law no. 125/2005. From this moment, all legislative references have provided scope thereof, namely in the health, educational field we are a part of, having been completely forgotten since then with repercussions nowadays.

It can therefore be seen that the methodological norms applicable and currently referring to the implementation of Law 104/2003 are made exclusively in the sanitary field. Regarding the educational environment and implicitly the university, there is a legislative void.

1.Maintaining the current legal framework prevents the entire staff of the anatomy departments from benefitting from being appointed to the particularly dangerous working conditions group, as is, rightfully so, the staff of the other departments of pathological, legal anatomy etc. Thus, all the rights that would result from the correct employment in the work group are canceled together with its benefits both during and after retiring.

2.The implications of jurisprudence in human anatomy laboratories.

The legislative void referred to in point 1 has as an effect the fact that an anatomo-pathologist has clear rules of attributions and responsibilities, as well as well-established salary benefits as well as employment in particularly dangerous conditions work group. Instead, an anatomist, whose working conditions are similar, and who was initially included in the same group as anatomo-pathologists, has no clearly defined rules, salary benefits or employment.

For the lab employees, the situation is strange, even paradoxical: thus, a practitioner of pathological or legal medicine has clear job responsibilities, being precisely defined the legal framework in which he can carry out his activity and this is done in order for a deceased person to be incinerated or buried. However, a human anatomy lab employee, who is required to prepare human bodies and tissues so that they can be used by teachers and students, does not have any methodological norm to carry out their activity. And of course there is no additional pay or special working categorizing.

The Universities of Medicine and Pharmacy prevail over the existing legislative void in order not to offer adequate employment or salary benefits because there are no methodological norms for applying Law 104/2003. But in the absence of these rules, it would make the law non-applicable in the university environment, which leads to the absence of a legal framework for working with human bodies or tissues in the university environment, as this is referred to by that law: "The Law on Handling Human Corpses and Removing Organs and Tissues from Corpses for Transplantation". Viewed in this way, the doctors and lab staff working in the anatomy departments manipulating human tissues would be conducting their activity illegally!

Discussion and conclusions

In the Romanian law there is a clear principle that the special law derogates from the general law, and the special law is STRICTLY INTERPRETED. Hence, it is clear that whenever there is a case in which the special law applies, this law is the PRIORITY, as to the general law, thus the general law can never circumvent the special law (there is also the Decision 33 of the High Court of Cassation and Justice on this subject, from 9 June 2008).

Thus, Law 104/2003 would have priority over other general laws, and automatically placing these activities under the special conditions category should be a priority, just as the other departments of legal anatomy, pathological anatomy, etc. have benefited. The condition is due to the existence of the rules for the application of that law.

The way in which the Universities of Medicine and Pharmacy understood to apply salary increases in the country was completely uneven, having different percentages and taking into account circumstantial reasons, even if Law 104/2003 provides in Article 21: "The financing of services for the use of corpses within the university disciplines of anatomy is made from the state budget allocated to the higher medical institution and from the institution's own income."

Regardless of the percentage allocated for salary increase, the categorizing in special conditions is withdrawn, which will be felt acutely when retiring from the activity, because the remuneration at that time is completely different depending on the employment of the person in question.

Last but not least we have to ask ourselves the question: does the department where the anatomists work have a functioning authorization? And if so, under which law? On the other hand, the workbook states that these teachers and lab staff work with these "teaching materials", which inherently means dissection on molded parts. But is it legal to do so if there are no methodological norms in education for law 104? Because Article 25 of this law provides: **"The manipulation of corpses in violation of the provisions of the present law constitutes a contravention and is sanctioned by a fine from 500 lei to 3,000 lei."**

In conclusion it is imperative to take all possible measures for these activities to become legal. The methods by which this can be achieved must start at the level of trade unions, by lobbying through the lawyer of the people, but also by lawmakers, who also have the legislative levers at hand. Last but not least, Medical Universities have at their disposal the necessary levers, and they even are obliged to use them, as stipulated by Article 26 of the same law: "..The Ministry of Environment and Climate Change and the higher medical institutions will submit to the Government the methodological norms for the application of this law."

Basically, the ultimate goal is in fact to follow the elaboration of the methodological norms for enforcing law 104/2003 in the academic environment as well as in the health departments. The responsibility for their elaboration lies with the Ministries of Education and Labor, to which reports must be submitted directly or by mobilizing all the responsible actors: MPs, trade unions, etc.. Only in this manner can we hope that people with training and similar working conditions should have similar wage conditions. And in this way we can look at the anatomy-pathologists who benefit from these rules of application. Thus for the person working in **pathological anatomy services**:

- **The provisions of Law no. 104 of March 27, 2003 are applicable to them, so that they fall into** the category of work in special conditions

- In this case, Article 7 letter h) of the Framework Law 153/2017, which provides for an increase of 15% !!, but letter b) of the same article provides that the particularly dangerous activity of the pathological anatomy establishes an increase of up to 85%.

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