

ORIGINAL PAPER

Clinical and histopathological aspects in otomastoiditis

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Abstract

We aimed to establish correlations between the clinical manifestations and histopathological changes occurring in otomastoiditis. To this effect, we have made a retrospective clinical and statistical study on a number of 146 patients diagnosed with otomastoiditis, admitted in the Otorhinolaryngology Clinic of the Emergency County Hospital, Craiova, during 2003–2007. Of the 146 patients, 128 (87.67%) were suggested to follow a radical surgical treatment (total petromastoidian evadation), in 10 cases (6.85%) a partial petromastoidian evadation was performed, and in eight cases (5.48%) there were made reappraisals of the petromastoidian evadation cavities. When the surgical procedures were performed, there were collected fragments of mucous from the middle ear or from the mastoid cavities, which were sent for examination to the Laboratory of Anatomical Pathology, where there were performed classical histological (Hematoxylin–Eosin and trichromic Van Gieson) and immunohistochemistry staining. The clinical and statistical study emphasized the fact that the onset of the disease was chronic in 143 patients (97.95%) and of acute type in three patients (2.05%). Taking into account the medical history of the patients, repeated episodes and incorrectly treated of acute infections of the middle ear (otitis) were found in most cases, amounting to a percentage of 97.95%. The distribution of the patients on the five years was relatively uniform, in 2003 – 24 cases (16%), in 2004 – 36 cases (25%), in 2005 – 28 cases (19%), in 2006 – 25 cases (17%), in 2007 – 33 cases (23%), and the most affected age groups were 21–30-year-old (19.86%) and 51–60-year-old (21.92%). Analyzing the cases included in the studied group emphasized the fact that for a relatively large percentage of patients (87.67%) it was required as an immediate necessity the surgical procedure of total petromastoidian evadation, due to the extensive damages, the negligence of the patients that did not contact in proper time a medical specialist. The most frequent histopathological diagnose was of cholesteatoma in 60 cases (41.10%), fact which also grounded the surgical procedure. Immunohistochemical and microscopic study highlighted in the epithelium areas of necrosis, associated with areas of reactive hypertrophy and hyperplasia, and in the chorion, the existence of a chronic inflammatory infiltrate made up of lymphocytes, plasmocytes and macrophages. The immunohistochemistry studies stressed the preponderant presence of T-lymphocytes and macrophages in the chorion of the mucous of the middle ear, confirming the presence of an immune reaction, predominantly of cellular type.

Keywords: otomastoiditis, otalgia, cholesteatomas, petromastoidian evadation.

Introduction

The otomastoiditis is an inflammatory process that includes the middle ear and the mastoid cells. Most often, the otomastoiditis appears as a complication of a chronic otitis media, incorrectly treated. The introduction of antibiotics in the treatment of otitis media reduced the incidence of occurrence of otomastoiditis as a complication of the acute otitis media, from 50% to 0.4% [1, 2]. Before antibiotics were introduced, about 50% of the otitis media evolved to acute otomastoiditis, associated or not with severe intracranial complications, which often required surgical procedures [3]. After the emergence of antibiotics, the otitis media have become diseases treatable with medicines, the surgical procedure being recommended only in case of complications [4], its recommendation decreasing to less than 1% [3, 5].

Recently, several studies reported an increase in the incidence of acute mastoiditis, which suggests there might be a correlation between the incorrect use of anti-

biotic therapy and the increase of mastoiditis cases [6].

The factors influencing the onset of mastoid infections are: the type and virulence of the microbial germs, the intensity, the immune response of the patient, the accuracy or inaccuracy of the antibiotic treatment, the presence of some associated chronic diseases, and so on. Most often, the otomastoiditis affect children because of the poor immune system and the anatomical particularities of the otomastoid region at this age. Taking into account these considerations, we aimed to evaluate the clinical and histopathological aspects in people with acute and chronic otomastoiditis.

Patients and Methods

The study group consisted of 146 patients with acute otomastoid pathology, admitted in the Otorhinolaryngology Clinic of the Emergency County Hospital, Craiova, during 2003–2007. The research method was the classical one, consisting in analyzing the hospital admission register and the clinical medical records,

the surgical procedure register, the anatomical and pathological reports, and the laboratory reports, the imaging examinations (the mastoid X-ray – Shuller and Chausse incidences; the computed tomography examinations), thus allowing an efficient selection of the patients. The methods used for diagnosing histopathologic lesions of the mucous within the tympanum sampled during the surgical procedure were Hematoxylin–Eosin staining, trichromic Van Gieson and immunohistochemistry techniques. We identified the cells of the immune system present in the inflammatory infiltrate: CD3 (DAKO clone, F7) for T-lymphocytes, CD20 (DAKO clone, L26) for B-lymphocytes, and CD68 (DAKO clone, KP1), for macrophages.

Results

The onset symptoms of acute otomastoiditis found in three patients were represented by: otorrhea, otalgia, hypoacusy, fever, asthenia and headaches. We found them in two children aged three, respectively 14, and in one patient aged 60 years. In the immediate history of the children with acute otomastoiditis, we observed repeated episodes of acute infections of the upper respiratory system. On the clinical examination, we found general signs of infection, noisy, with high temperature, inappetence, psycho-motive agitation, retroauricular edema with the trend to exteriorization, intense pains when palpating the mastoid region. The otoscopy revealed at the outer ear canal the presence of some abundant auricular discharges with a direct festering aspect. We only found one case recorded as a complication the presence of a retroauricular abscess.

The third patient aged 60 years had dimmer clinical symptoms, due to the slow setting of the inflammatory process. The patient presented obnubilation, asthenia, insomnia, transmission deafness, and the clinical examination revealed the infiltration of the eardrum, auricular and retroauricular pains, otorrheas and the radiologic image of the mastoid revealed lesions of bony destruction within the mastoid.

The most cases (143) were diagnosed with chronic otomastoiditis. The clinical symptoms were dominated by auricular and retroauricular pains of medium and moderate intensity, gradually set, after repeated episodes of acute otitis media or acute infections of the upper respiratory system. The general condition of all the studied patients was altered, the patients presenting fever, insomnia, pallor, fatigue. Sometimes the auricular pains were accompanied by temporo-parietal hemicranias, with nocturnal paroxysmal attacks. On the local clinical examination, we encountered the presence of auricular suppuration. It had variable aspect and quantity from one patient to another. We also encountered the reduction in size of the outer ear canal, the presence of a perforation of the timpani, through which it was discharged fetid pus, the congestion of the retroauricular tissues. Alteration of the auditory function, with the predominance of the transmission deafness was also encountered. The deep palpation

of the mastoid points was accompanied by pain. The radiologic examination revealed the reduction of the pneumatic process of the mastoid cells, up to the total opacity of the mastoid, in some patients presenting areas of local osteolysis. The tonal audiogram emphasized transmission deafness on the damaged side, up to a loss of about 30 db and an intact bony leading in patients without neurosensorial damage of hearing during their medical history.

The clinical and statistical study of the studied group revealed a relatively constant number of patients suffering from otomastoiditis, annually admitted to hospital. Their number ranged between 24 and 36, with a relatively uniform distribution of the cases: in 2003 – 24 cases (16%), in 2004 – 36 cases (25%), in 2005 – 28 cases (19%), in 2006 – 25 cases (17%), in 2007 – 33 cases (23%). It is noticed, however, a higher preponderance in 2004 (36 cases – 24.66%) (Figure 1).

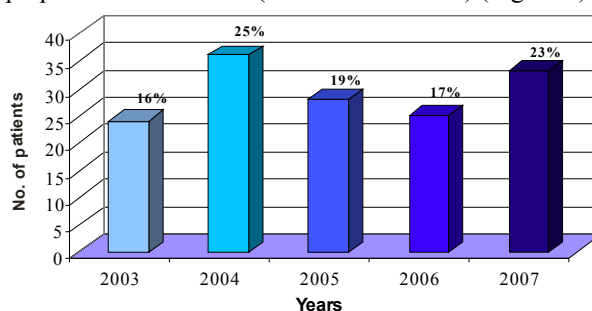


Figure 1 – Distribution of otomastoiditis on years of study.

We found chronic otomastoiditis in all age groups. Most cases were found in the age groups of 21–30-year-old (29 cases, representing 19.86%), and of 51–60-year-old (32 cases – representing 21.92%) (Figure 2).

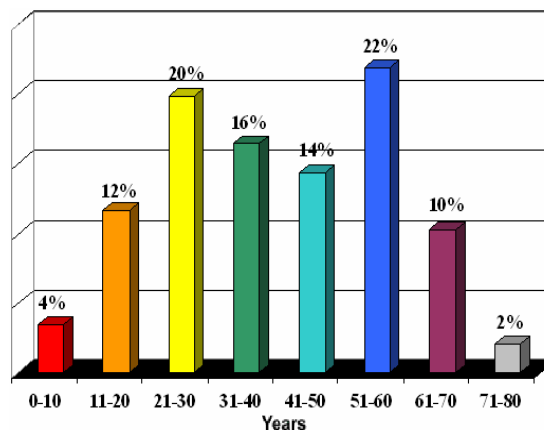


Figure 2 – Distribution on age groups.

Regarding the environment of origin, we noted that the patients are mainly from the urban areas (60.27%) and less from the rural areas (39.73%) (Figure 3).

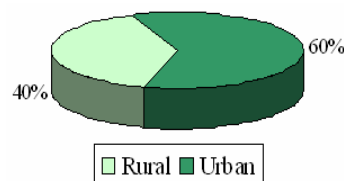


Figure 3 – Distribution of cases on origin environments.

The distribution on genders of the patients showed a preponderance of the otomastoiditis in men (55.48%), compared to women (44.52%) (Figure 4). The preponderance on the male gender is explained by the fact that they are exposed to cold, moisture, pollutants, more than women are.

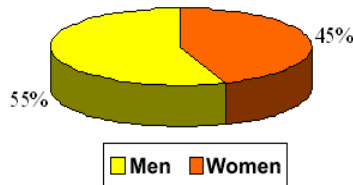


Figure 4 – Distribution on genders.

In our study, the otomastoiditis were accompanied by complications of the outside of the neurocranium, of the inside of the neurocranium and of the inside the temporal bone in 38 patients (26.02%).

Of these, the complications of the outside of the neurocranium represented by various liquid exteriorizations were diagnosed in 15 cases (10.27%), being represented by: retroauricular abscesses in 12 cases (8.21%), temporo-zygomatic abscesses in two cases (1.36%), and a case of Bezold's abscess (0.68%).

The complications of the inside of the neurocranium were present in 10 patients, being represented by thrombophlebitis of lateral venous sinus in seven cases (4.79%), otogenic meningitis in two cases (1.37%), and cerebral abscess in one case (0.68%).

Complications of the inside the temporal bone were diagnosed in 11 patients:

- Facial nerve paralysis in four cases (2.74%);
- Peri-lymphatic fistula with peripheral vestibular syndrome in seven cases (4.79%) (Figure 5).

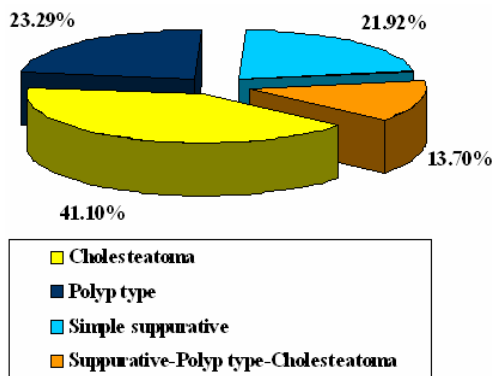


Figure 5 – Anatomical and clinical forms of otomastoiditis.

In our study, 32 patients had one complication and five patients had two concomitant complications. Thrombophlebitis of lateral venous sinus with the retroauricular abscess was found in four cases and CSF (cerebrospinal fluid) otic fistula with facial paralysis in one case). One patient had three concomitant complications (otogenic meningitis, cerebral abscess and thrombophlebitis of lateral venous sinus).

The anatomical and clinical forms of the otomastoiditis (Figure 6) found within the study were:

- Cholesteatoma forms in 60 cases (41.10%);
- Polyp-type forms in 34 cases (23.29%);
- Simple suppurative forms in 32 cases (21.92%);

- Mixed forms (suppurative, polyp-type, cholesteatoma forms) in 20 cases (13.70%).

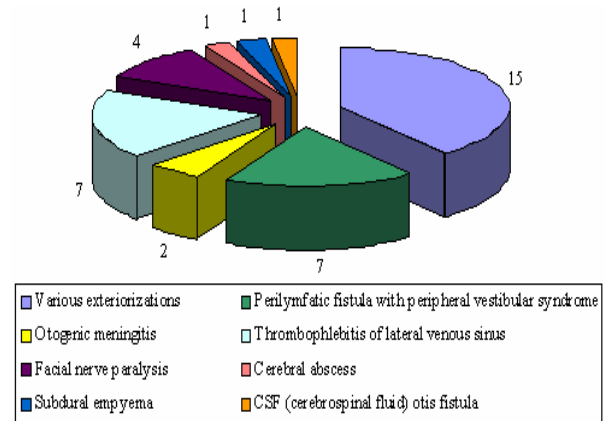


Figure 6 – Complicated forms of otomastoiditis.

The histopathological study revealed a much modified mucous, consisting of a keratin squamous epithelium, much alike in structure to the skin in 41.10% of the cases of the studied group. The thickness of the epithelium was variable from one case to another and even from one area to another in the same case. In the structure of the epithelium, there were emphasized four layers of cells:

- A basal layer consisting of a row of cubic-cylindrical cells, ordered on a thin basal membrane. The dimensions of the cells, as well as those of the nuclei of this layer were varied, which showed that the cells were reactive, occurring as a response form to the local irritation factors. Some cells have been caught during the division. In addition to the keratinocytes, other cells we found round cells, with clear cytoplasm, possibly Langerhans' cells (Figure 7);

- A layer of polyhedral cells composed of 3–14 rows of superposed cells, similar to the spiny layer of the skin. The cells had a slightly acidophilous cytoplasm, with round, hypochromic nuclei and nucleoli. Between the cells, we identified emphasized wide intracellular spaces, crossed by numerous desmosomes;

- A layer consisting of 2–5 rows of rhomboidal cells, with basophil granules of keratohyaline (Figure 8);

- A horny layer, with variable thickness from one area to another and from one patient to another, composed of anucleate cells, elongated, slightly acidophilous, arranged in the form of bands, separated by wide, acellular spaces (Figure 9).

Within the chorion of the mucous, we found numerous round cells, belonging to the immune system, of lymphatic plasma cells type and macrophage type, numerous fibroblasts, mast cells, fibers of collagen and blood vessels.

In 23.29% of cases, the histopathological study stressed the microscopic structures of polyp type. Thus, on the histological sections we identified several conical, prominent formations, bound to the periphery by a cylindrical pseudo-bedded epithelium, with a dense cellular stroma, highly vascular, with numerous vessels of angiogenesis (Figures 10 and 11). In some cases, we revealed small areas of necrosis in the stroma of these formations of polyp-type.

In 21.92% cases, in accordance with the forms of simple suppurative mastoiditis, the histopathological study has revealed the presence of a mucous with a modified epithelium, with many cells of apocrine type and a chorion highly infiltrated with lymphocytes and plasma cells (Figure 12). Sometimes, we revealed extensive areas of epithelial necrosis or contrariwise, areas of hyperplasia and hypertrophy of the covering epithelium.

In the immunohistochemical study, we have sought

to emphasize the types of cells present in the stroma inflammatory infiltration. Among the present cells of the immune system, the most numerous were the T-lymphocytes, and then the B-lymphocytes, and the less numerous were the macrophages. The distribution of the cells in the inflamed chorion was inhomogeneous, which showed a varied distribution of the antigens. In addition, the immunohistochemical study showed that in chronic otomastoiditis the cellular immunity appears to be dominant (Figures 13–16).

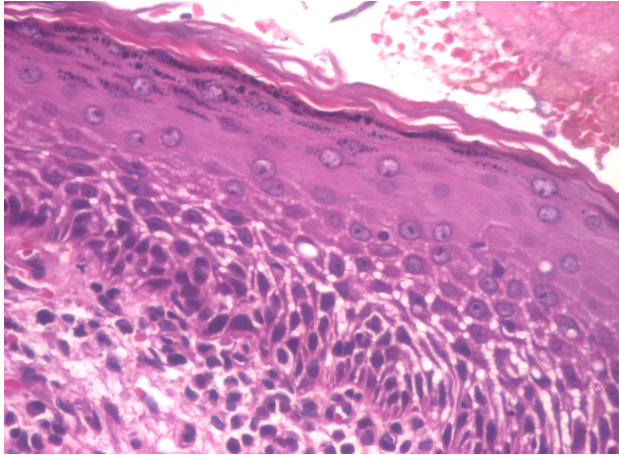


Figure 7 – Cholesteatoma (HE stain, ob. ×20).

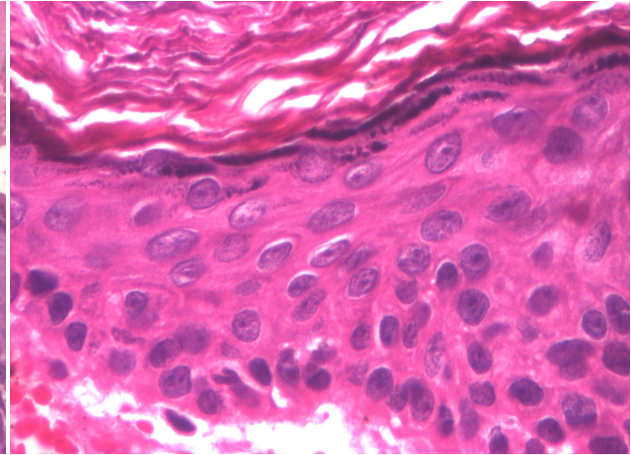


Figure 8 – Cholesteatoma (HE stain, ob. ×40).

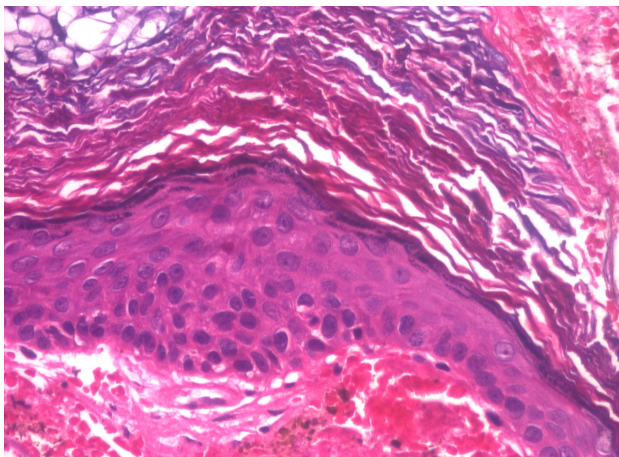


Figure 9 – Cholesteatoma (HE stain, ob. ×20).

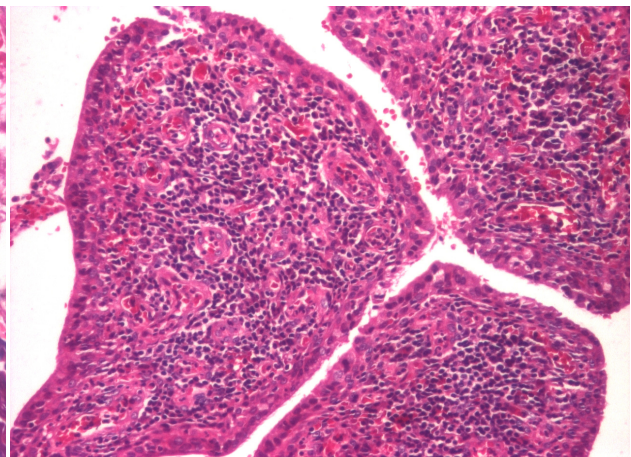


Figure 10 – Polyp (HE stain, ob. ×10).

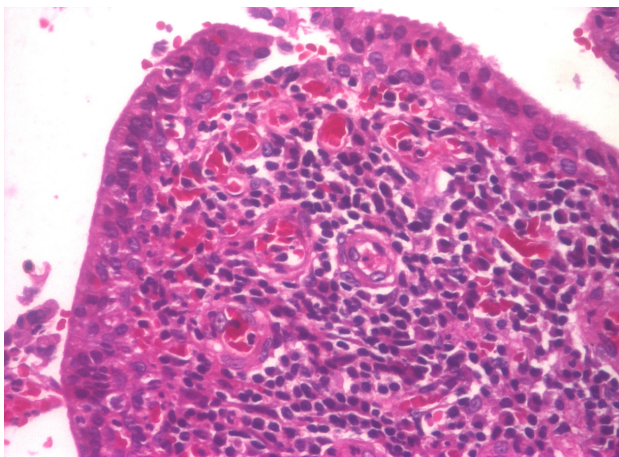


Figure 11 – Polyp. Detail (HE stain, ob. ×20).

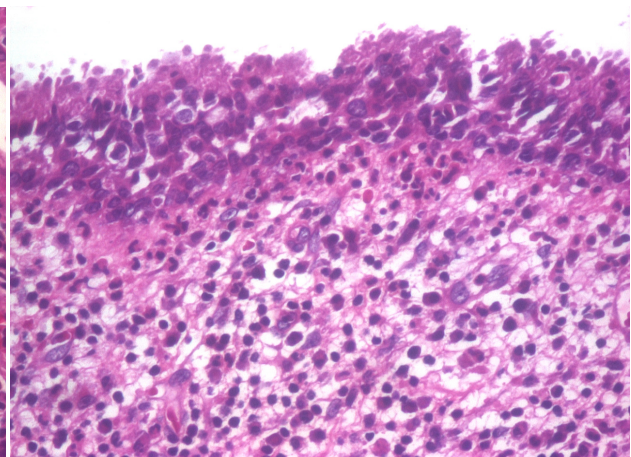


Figure 12 – Mucous within the tympanum, epithelium with cells of apocrine-type and chronic inflammatory infiltrate (HE stain, ob. ×20).

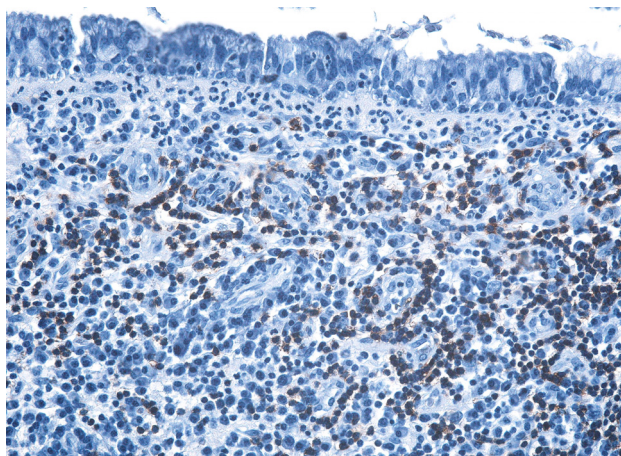


Figure 13 – Diffuse inflammatory infiltrate with B-lymphocytes. CD20-immunomarking, ob. $\times 20$.

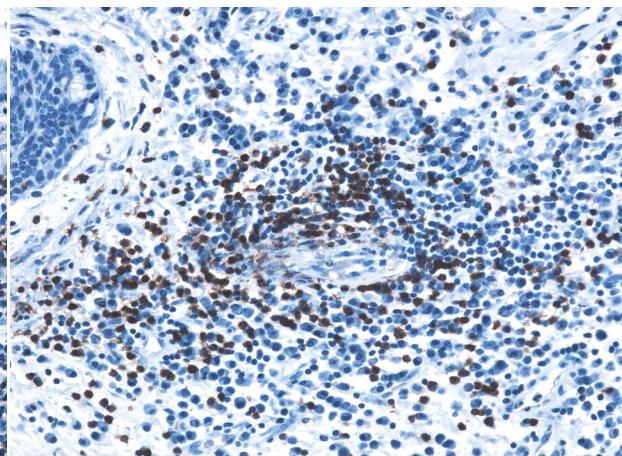


Figure 14 – T-lymphocytes with a predominantly perivascular disposition. CD3-immunomarking, ob. $\times 20$.

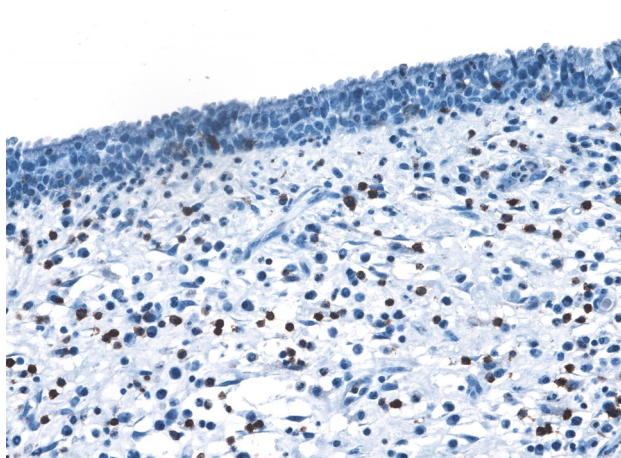


Figure 15 – Macrophages present both in the chorion and in the epithelium. CD68-immunomarking, ob. $\times 20$.

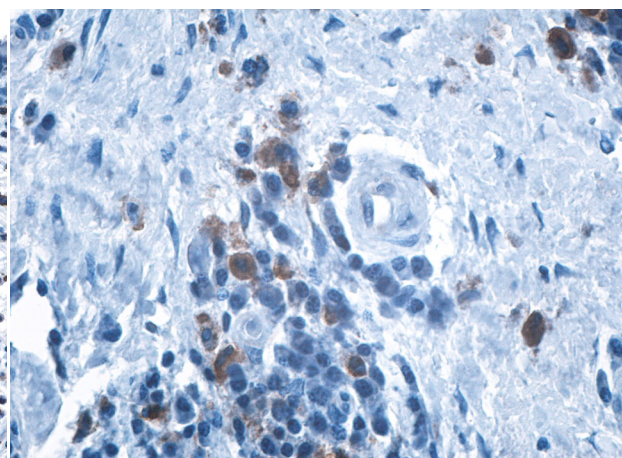


Figure 16 – Macrophages in chorion. CD68-immunomarking, ob. $\times 40$.

Discussion

The inflammatory pathology of the middle ear is quite common today, especially at extreme ages, young children and the elders. Several articles from recent years have identified an increase in the incidence of the otomastoiditis, because of incorrect usage of antibiotics [6–8]. The acute otomastoiditis also currently represents the most frequent complication of acute otitis media in children, still having a high incidence, however much lower than in the pre-antibiotic era [4, 9]. The rate of mortality is still high [10, 11]. In recent years, despite all expectations, it was reported an increase in the incidence of the occurrence of otomastoiditis [8, 12, 13], while other studies have reported a relatively stable incidence [9]. The children under 2-year-old represent the most commonly affected age group, since at this age the acute otitis media is most frequent [14–16].

Involvement of the mastoid apophysis represents the most common complication of acute auricular suppurations. Along with the occurrence on the market of the antibiotics of high efficacy, the frequency of acute mastoiditis consecutive to acute otitis media has dramatically decreased. Currently, it is noted a recrudescence of the mastoid bone infections due to the occurrence of the post-antibiotic iatrogenic pathology on one hand, and of the infections with “opportunistic”,

“aggressive”, “resistant”, “of hospital” germs on the other hand, the osteitic lesions tending to become chronic.

In young and old patients, the risk factors multiply due to various reasons. Thus, in children, the ampler mastoid pneumatic process encourages the extensive and complicated clinical forms; in the elderly, the general status, with numerous organic failures such as cardiovascular diseases, hepatorenal failures, diabetes, aggravate the disease set in the otomastoiditis region [17].

In our study, against expectations, the age most affected by otomastoiditis was that of 21–30 years. This aspect can be explained by the incorrect use of the antibiotic therapy or by the negligence patients’ display regarding their disease.

Clinically, the diagnosis of acute otomastoiditis is suspected whenever, during an acute otitis media, it is not found any improvement after the treatment or when, after a temporary improvement, it occurs an aggravation of the local and general symptoms. In these cases, the otic spontaneous pains are predominant, with parietal, frontal, occipital irradiations, having a character of hemicrania. Sometimes it appears as a pulsatile painful sensation, which is pathognomonic due to the lack of drainage of the mastoid empyema.

A correct diagnosis of an otomastoiditis based on anamnesis, local and general clinical examination must

be supplemented by testing the auditory function, along with the imaging and laboratory examinations [17].

An increasing number of studies show that self-medicating with antibiotics or an incomplete medication has created a new pathology by transforming the acute otitis into latent otitis with an insidious development, which favors the emergence of complications, and primarily by extending the infection to the mastoid cavities. Frequently, otomastoiditis with extremely virulent germs appears after prolonged treatments with antibiotics, especially in the hospital environment. The increase of the resistance to antibiotics of the pathogenic microorganisms occurring in the ear area requires fresh attitudes in therapeutic environments otitis and their complications [18, 19].

The improvement of the pathological breeding grounds for disease of the otomastoiditis by appropriate surgical techniques leads both to the ceasing of the suppuration and to the avoidance of the complications. If it is not treated, the otomastoiditis may cause the occurrence of some local and regional complications, common with those of the suppurative otitis, represented by the facial paralysis, labyrinthitis, sinus-jugular thrombophlebitis, otogenic meningitis, epidural or cerebral and cerebellum abscesses. In a study of 335 complicated otomastoiditis, in 67% of the cases it was about intracranial abscesses, in 25% of the cases there were recorded meningitides and in 12% of the cases thrombophlebitis of lateral sinus [20].

In our study, on a group of 146 patients diagnosed with otomastoiditis, the complications of the inside of the neurocranium were encountered at a rate of 6.85% and were represented by thrombophlebitis of lateral venous sinus (4.80%), meningitides (1.37%) and cerebral abscess (0.68%).

The histopathological aspects noticed by us correspond to other data in medical literature. Normally, the mucous within the tympanum and of the mastoid cells consists of a simple columnar epithelium, pseudo-bedded in patches, with high, ciliary cells and mucus secreting cells (mostly arranged around the hole of Eustachian tube and a chorion quantitatively reduced, made of a lax conjunctive tissue with numerous round mononuclear cells, belonging to the immune system [21].

We consider that microscopic changes noted by us in otomastoiditis have also been generated by the inflammatory process, through the mediators released by the cells and the presence of microbial flora.

The macroscopic appearance of hypertrophy of the tympanum mucous corresponds from the microscopic point of view to hyperplasia and mucous metaplasia.

The hyperplasia of the mucous is interpreted by the increase of the cells number both of the covering epithelium and the underlying chorion. This cellular hyperplasia transforms in a very short time, an average of 15 days, the normal epithelium in an epithelium with a new structure and different function, through mucous metaplasia. At the chorion, the hyperplasia caused the appearance of the lymphatic plasma-type infiltration and the angiogenesis vessels. The mucous metaplasia occurs due to the transformation of the

one-bedded epithelium into a cylindrical pseudo-bedded epithelium of respiratory type.

In our study, the most numerous anatomical and clinical forms of otomastoiditis were the cholesteatoma ones. This form of otomastoiditis may be encountered both in children and in adults, but it seems that there are differences related to clinical manifestations, evolution and recurrence, depending on age [22]. Thus, Sudhoff H *et al.* [23] consider that in children, the secondary cholesteatoma is more aggressive and has a much greater power of expansion.

The cholesteatomas can be considered as benign tumors, characterized by an abnormal growth of the cells of the covering epithelium, which decorate the middle ear and the mastoid cavities, associated with complex and dynamic changes of the cells of the chorion and of the extracellular matrix [24]. According to some authors [25] the occurrence of the chronic cholesteatoma otomastoiditis might be due to a lack of control of the cellular proliferation in the covering epithelium, which determines the development of an epidermoid cyst (cholesteatoma) characterized by the appearance of a squamous stratified keratin epithelium inside the pneumatic processed areas of the temporal bone.

The fact that some cholesteatomas are congenital, made some authors to consider that the lack of control of the cellular proliferation could be caused by abnormalities in genes that control the proliferation. In addition, in the emergence of the cholesteatoma, the cytokines issued by the inflammatory cells because of some recurrent otitis media seem to be involved [26].

The cholesteatoma otitis frequently produces complications. Meningitis, encephalitis or cerebral abscesses represent intracranial complications, which may put life in danger [27]. In our study, the complications of the inside of the neurocranium and of the outside of the neurocranium were found in about 26% of the studied patients. In addition to local inflammatory processes, an important role in the emergence of the complications seems to have the cholesteatoma itself, as by the bone enzymatic resorption, it allows the extension of the infection outside the ear, causing suppurative complications inside the temporal bone, outside or inside the neurocranium.

The mechanisms of bone destruction by the cholesteatoma are yet to be fully elucidated. Until now, there are incriminated as possible mechanisms: the pressure necrosis, the operation of the inflammatory perimatrix granuloma, chronic osteomyelitis and the operation of the osteoclasts and osteocytes stimulated by various local factors, produced by the cells of the inflammatory process. Thus, histochemistry studies have shown the fact that in the inflammatory breeding grounds for disease and the cholesteatoma, the local activation of the collagenase, phosphatase, proteases and changing the local pH plays an important role in the mechanisms of bone destruction. The collagenases are placed in the category of metalloproteinases. They were outlined in the perimatrix of the cholesteatomas and it seems that they are the main factor responsible for the osteolysis process [28].

Even since 1969, Abramson M [29] mentioned the fact that in the perimatrix of the cholesteatoma there is a collagenase with a very high collagenolytic power, superior to that of the normal skin. This, along with other local factors, would cause the bone lesion and the propagation of the infection from the middle ear and mastoid in the surrounding tissues, including inside of the neurocranium.

Other microscopy studies performed on the perimatrix have showed an intense activity of this tissue, by increasing the local cellularity but also of the vessels' density of the angiogenesis. This angiogenesis encourages the proliferation of the keratinocytes, the increase of the enzymatic activity at this level and the activation of the osteoclasts, thus explaining the bone resorption and the centrifugal proliferation of the cholesteatoma [23].

The osteolytic processes are met both in the mastoid as well as in the ossicular chain from the middle ear. The total or partial destruction of the ossicular chain is met in approximately 80% of the patients with cholesteatomas and it seems to be the main factor responsible for the reduction of the auditory perception.

Conclusions

In our study, the highest incidence of the otomastoiditis was for the age group of 21–30-year-old.

The otomastoidites were accompanied by complications of the outside of the neurocranium, of the inside of the neurocranium and of the inside the temporal bone in 38 patients, representing 26.02% of all studies cases.

We encountered otomastoiditis with cholesteatoma formation in 60 cases, representing 41.10%, of polyp-type in 34 cases (23.29%), and simple suppurative forms in 32 cases (21.92%).

The histopathological study of the cholesteatoma forms emphasized the presence of an epithelium of Malpighian-type with keratin, having the structure similar to the skin, and a chorion dominated by a chronic inflammatory infiltrate, made up of lymphocytes, plasma cells and macrophages.

The immunohistochemical study showed the fact that most lymphocytes were of T-type, so the immune reaction was of cellular type.

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