

Mastoiditis and facial paralysis as initial manifestations of temporal bone systemic diseases – the significance of the histopathological examination

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Abstract

Several systemic diseases, including granulomatous and infectious processes, tumors, bone disorders, collagen–vascular and other autoimmune diseases may involve the middle ear and temporal bone. These diseases are difficult to diagnose when symptoms mimic acute otomastoiditis. *Case reports:* The present report describes our experience with three such cases initially misdiagnosed. Their predominating symptoms were otological with mastoiditis, hearing loss, and subsequently facial nerve palsy. The cases were considered an emergency and the patients underwent tympanomastoidectomy, under the suspicion of otitis media with cholesteatoma, in order to remove a possible abscess and to decompress the facial nerve. The common features were the presence of severe granulation tissue filling the mastoid cavity and middle ear during surgery, without cholesteatoma. The definitive diagnoses was made by means of biopsy of the granulation tissue from the middle ear, revealing granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis) in one case, middle ear tuberculosis and diffuse large B-cell lymphoma respectively. After specific associated therapy facial nerve functions improved, and atypical inflammatory states of the ear resolved. *Conclusions:* As a group, systemic diseases of the middle ear and temporal bone are uncommon, but aggressive lesions. After analyzing these cases and reviewing the literature, we would like to stress upon the importance of microscopic examination of the affected tissue, required for an accurate diagnosis and effective treatment.

Keywords: mastoiditis, facial nerve palsy, systemic disease, infectious processes.

Introduction

Several systemic diseases, including granulomatous and infectious processes, tumors, bone disorders, storage diseases, collagen–vascular and other autoimmune diseases, may involve the middle ear and temporal bone. In some, the initial clinical symptoms may occur in the temporal bone and can be confused with other diseases limited to the middle ear and mastoid, such as chronic otitis media [1]. The common presentation of a draining ear is nearly indistinguishable from that of common otitis media. A high index of suspicion and knowledge about possible causes are required for accurate diagnosis and effective treatment [2]. Granulomatosis with polyangiitis (GPA), historically known as Wegener's granulomatosis, is a systemic vasculitis that affects small and medium vessels predominately in the kidneys, lungs, and the mucosa of the upper respiratory tract [3]. The majorities (73–93%) of patients with GPA have otorhinolaryngological (ENT) involvement at presentation and many of these patients see an ENT surgeon in their first visit to the hospital [4]. Otological manifestations appear in between 6% and 56% of patients suffering from GPA. The most frequent of middle ear lesions is serous otitis. Acute otitis media or chronic otitis media, which develop because of the

presence of granulation tissue affecting the Eustachian tube, middle ear or nasopharynx, are less frequent [5]. Facial paralysis, including bilateral cases, can also appear associated with the presence of otomastoiditis [6]. The diagnosis is achieved through clinical assessment, serological tests for ANCA (antineutrophil cytoplasmic antibodies) and histological analysis [7].

Tuberculosis of the middle ear is a rare disease and accounts for between 0.04–0.9% of all cases of chronic suppurative otitis media. It is difficult to diagnose because the disease presents like other chronic suppurative otitis media. The significant features of aural tuberculosis are abundant granulation tissue in mastoids with good pneumatization, cervical lymphadenopathy, profound hearing loss, facial palsy, and foci of tuberculosis elsewhere [8]. The diagnosis of middle ear tuberculosis may be delayed because of its similarity to other forms of otitis media in the early stages.

Lymphomas represent the second most frequent malignant tumor (incidence 2.5%) in the head and neck region [9]. Non-Hodgkin's lymphomas (NHLs) present with cervical lymph node involvement, but in 40% extranodal site could be primary involved: nasopharynx, the lachrymal sac, the temporal bone, or the other areas [10]. NHLs of the ear are rarely reported. These temporal bone

tumors are typically associated with facial nerve paralysis and hearing loss, and few cases have granulation tissue in the external auditory canal as well [11].

In this report, we present three such patients seen and treated within our institution. All patients had the same clinical features mimicking otomastoiditis with facial palsy as initial symptoms that proved to be later a systemic disease involving the temporal bone.

Case presentations

Case No. 1

A 26-year-old male presented with left-side facial nerve palsy, intense otalgia and fullness in the right ear. He had been previously diagnosed with bilateral serous otitis media and treated accordingly. After one month of conservative treatment, the symptoms worsened. The left tympanic membrane appeared to be perforated with granulating tissue and purulent effusion and the right tympanic membrane was inflamed. Audiometry tests showed moderate to severe mixed hearing loss in the left ear and conductive ear loss on the right side. Temporal bone computed tomography (CT) scans revealed opacification involving the left middle ear and mastoid cells without signs of osteolytic injury (Figure 1). A tympanomastoidectomy canal wall up procedure was performed under the

suspicious of chronic otitis media with cholesteatoma. During surgery granulating friable soft tissue, somewhat hemorrhagic, was removed and submitted for histological review (Figure 2). Additional medical therapy with antibiotics (Ceftriaxone) and intravenous steroids was associated for 10 days. Hearing loss improved and facial nerve palsy regressed almost entirely. The serology tests for HIV (human immunodeficiency virus), hepatitis B and C viruses, VDRL (venereal disease research laboratory), rheumatoid factor, cytoplasmic (c)-ANCA, and perinuclear (p)-ANCA came back negative. The patient was discharged after spending 10 days in hospital and was sent home with an antibiotic prescription. He returned after seven days for the histopathology result, with a newly installed dry cough. The histopathological exam from the ear revealed granulomas with aggregates of activated macrophages, multinucleated giant cells and a peripheral accumulation of lymphocytes (Figure 3, a and b).

Taken into consideration the clinical features, histological pattern suggested a Wegener's granulomatosis. We repeated c-ANCA test, which this time came back positive (1/20 titer). Chest CT scans revealed the presence of lung parenchymal nodules. Therapy with Methylprednisolone and Cyclophosphamide was initiated, and the patient partially recovered his hearing thresholds, as inflammation in the middle ear was controlled.

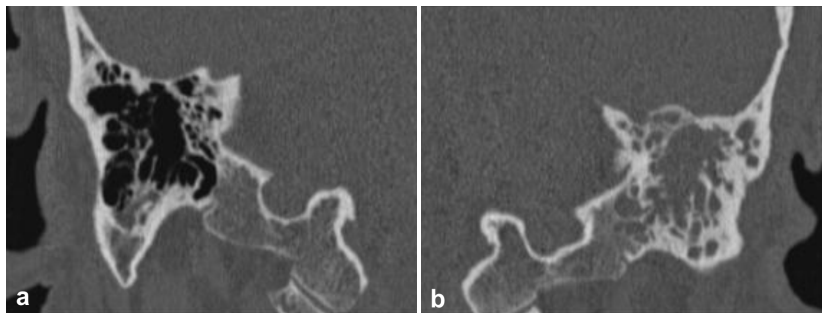


Figure 1 – (a) High-resolution CT scanning without contrast – coronal planes–right ear – shows normal pneumatization of the mastoid cells; (b) High-resolution CT scanning without contrast – coronal planes–left ear – shows opacification of the mastoid cells without signs of septal osteolytic injury.

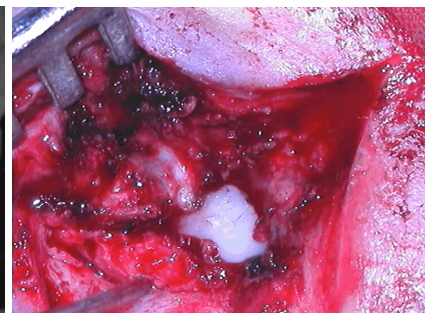


Figure 2 – View during surgery of the left ear revealing granulation tissue and puss in the middle ear.

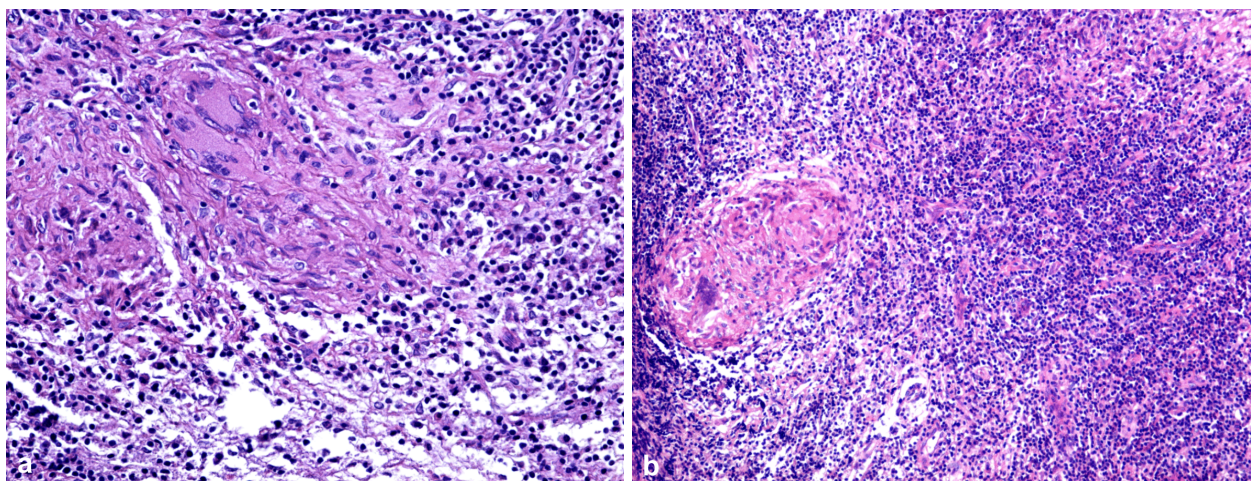


Figure 3 – (a) Biopsy specimen showing accumulation of lymphocytes and multinucleated giant cells; (b) Biopsy specimen showing granuloma with aggregates of activated macrophages, multinucleated giant cells and a peripheral accumulation of lymphocytes. HE staining: (a) $\times 200$; (b) $\times 100$.

Case No. 2

A 5-year-old female child came into the Department of Otorhinolaryngology with persistent painless otorrhoea for two months, resistant to conventional treatment. One week prior to admission, she associated a right-sided lower motor neuron facial palsy. On examination there was bulging of eardrum with granulation tissue presence. Temporal bone high-resolution CT scans demonstrated the entire tympanum and mastoid air cells were occupied by soft tissue, bone destruction and sequestra. The patient was taken to surgery. A cortical mastoidectomy was performed and the florid granulation tissue was scraped out (Figure 4). Histopathology examination revealed granulation tissue with epithelioid cells and multinucleated giant cells, areas of central necrosis, lymphocytic infiltration, ulcerations and superficial resorption of the involved bone (Figure 5, a and b). A diagnosis of the granulomatous

type tuberculous mastoiditis was made. The child was referred to the Department of Pneumology for standard systemic antituberculosis chemotherapy.

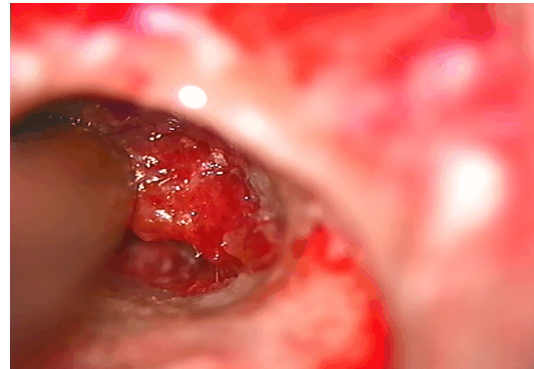


Figure 4 – View during surgery of the right ear revealing granulation tissue in the mastoid.

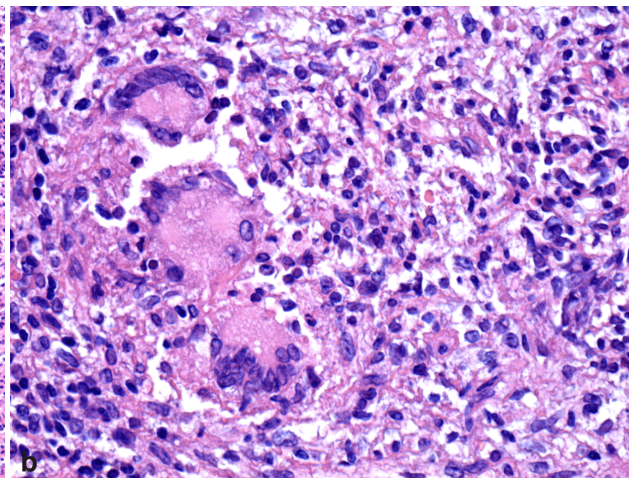
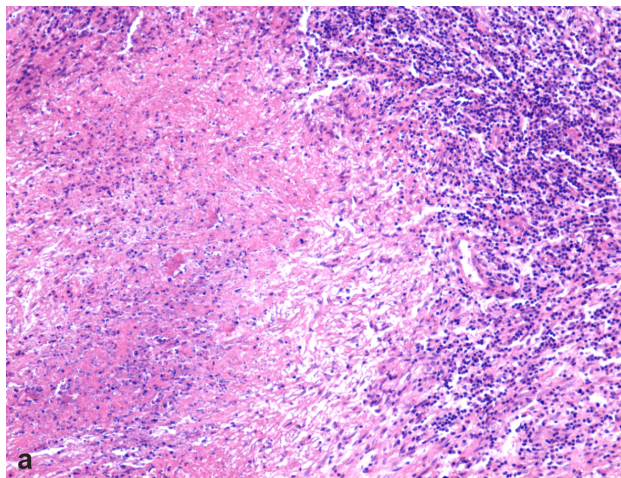


Figure 5 – (a) Biopsy specimen showing granulomas with central area of necrosis, activated epithelioid macrophages, Langhans giant cells, and a peripheral accumulation of lymphocyte; (b) Biopsy specimen under high-power view showing granulomas with areas of caseating necrosis, activated epithelioid macrophages, Langhans giant cells (multinucleated giant cells with abundant eosinophilic cytoplasm and nuclei forming an horseshoe arrangement), and a peripheral accumulation of lymphocytes. This distinctive histological pattern suggests an inflammatory process specific for tuberculosis. HE staining: (a) $\times 100$; (b) $\times 400$.

Case No. 3

A 4-year-old female child with left facial palsy and retroauricular swelling presented to our institution after being seen at another hospital for the facial palsy, installed two weeks prior. She had been previously treated for acute otitis media, but his symptoms were not improved and retroauricular swelling developed on the same side three days before he came to our attention (Figure 6). On physical exam, the posterosuperior part of the external auditory canal (EAC) showed marked bulging and the tympanic membrane was not visible (Figure 7). Pure-tone audiometry showed a left-side conductive hearing loss of 35 dB. A CT scan of the temporal bone showed a soft-tissue density filling the mastoid antrum and middle ear. The soft tissue had eroded the mastoid cortex and seemed to extend to the wall of the EAC.

Given these findings, the patient underwent a right tympanomastoidectomy. The mastoid cavity contained copious amounts of necrotic bone, mastoid cells filled with some whitish amorphous material and granulating tissue. Biopsies were taken.



Figure 6 – Right ear (preoperative image): it can be noted the presence of a retroauricular abscess.

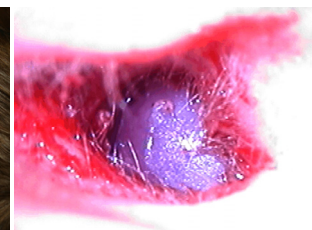


Figure 7 – Otoscopy of the right ear. The posterosuperior part of the external auditory canal (EAC) showed marked bulging and the tympanic membrane was not visible.

Histological analysis showed a monomorphic infiltrate of intermediate sized lymphoid cells. These cells stained positively for CD20 and CD79a (a B-cell marker), and stained negatively for T-cell markers CD3, cyclin D1 and CD23. The lymphoid cells had a stippled chromatin pattern and a small rim of cytoplasm. Cell markers CD10 and TdT (terminal deoxynucleotidyl transferase) stained

positively. Mature cell markers were negative. Following immunohistological staining and flow cytometry, a diagnosis of immature lymphoblastic non-Hodgkin's B-cell

lymphoma was made (Figure 8, a and b). The child was referred to the Department of Pediatric Oncology and was started on a chemotherapeutic regimen.

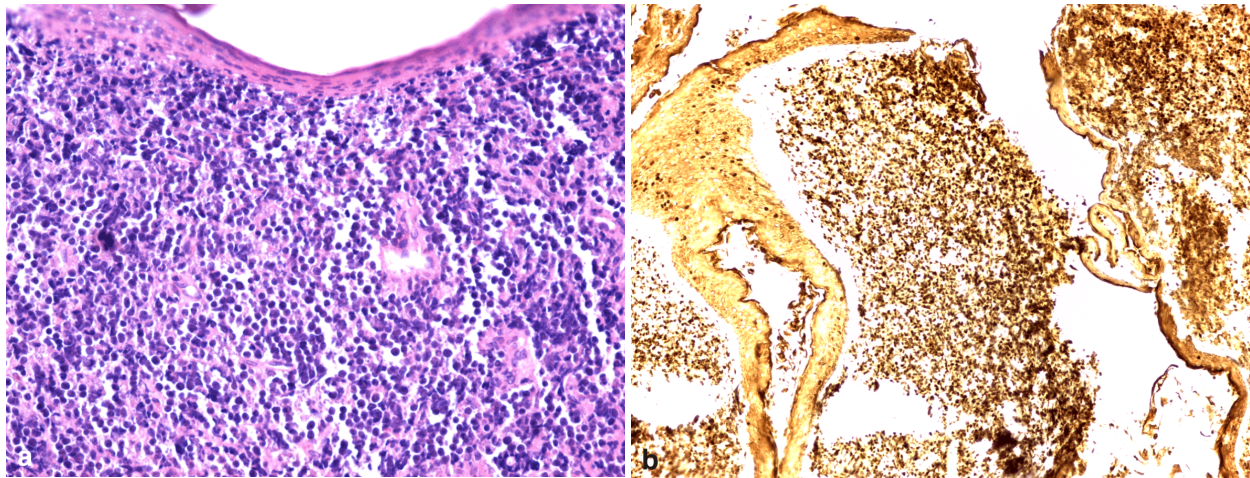


Figure 8 – (a) Biopsy specimen: a fragment of keratinized, stratified squamous epithelium and subjacent tissue infiltrated by a monotonous population of small lymphocyte-like cell (HE staining, $\times 200$); (b) Biopsy specimen: the monotonous population of small lymphocyte-like cells shows CD20 positivity (B-cell marker). Histological pattern and CD20 immunostaining positivity suggests a diffuse B-cell non-Hodgkin's lymphoma, $\times 100$.

Discussion

Systemic diseases are not easily diagnosed when the presenting symptoms mimic otomastoiditis, particularly in patients who do not have associated symptoms at disease onset. Granulomatosis with polyangiitis (GPA – the former Wegener's) is a relatively rare condition [5]. Current vasculitis assessment employs the Birmingham Vasculitis Activity Score (BVAS). It is divided into nine organ domains, and the ear, nose and throat (ENT) domain encompasses five items [12]. Most patients with GPA with ear involvement have chronic otitis media with effusion caused by Eustachian tube disorders and sensorineural hearing loss. Facial nerve palsy has been reported during the course of the disease, but it is extremely rare as the presenting feature [13]. Chronic otitis media occurs consequently to the direct involvement of the middle ear and the mastoid cavity by necrotizing granuloma, and may develop accompanied by effusion, mastoiditis and facial nerve palsy. Otomastoiditis associated with facial nerve palsy is seen in 10% of the cases [14]. In our case, the patient evolved this way, however without other previous symptoms, as rarely reported in the literature. The patient underwent urgent mastoidectomy with facial nerve decompression. Previous studies recommend a conservative approach to such complications in GPA [15], as the nerve function does not recover after surgery. However, in our case the histological examination was the key-point to produce the diagnosis, as c-ANCA was initially negative. However, a recent study confirmed that mastoid surgery is performed in 5% of the patients before the diagnosis of GPA is made [4]. Tuberculosis is a chronic bacterial infection caused by *Mycobacterium tuberculosis*, a slow-growing strict aerobic bacillus. It forms granulomas with caseous necrosis due to the cell response of involved tissues [16].

Tuberculosis is one of the major infectious diseases

with predominant involvement of lung and lymph nodes, but tuberculosis of the middle ear is uncommon [17]. Very few cases of tuberculous otitis media (TOM) are reported in the literature. Mills' study mentioned that the incidence of TOM has fallen dramatically since the beginning of the last century [18]. The classic clinical features of TOM were described by Wallmer in 1953 as painless otorrhoea, multiple tympanic membrane perforations, pale granulation tissue, ipsilateral facial nerve paralysis, and early severe hearing loss and bone necrosis [19]. However, these classical features are rarely observed today. Recently, a review of all TOM reports in the English literature by Skolnik *et al.* refuted these findings. Their research showed that facial palsy is present in only 16% of cases and multiple tympanic perforations are equally rare [20]. In the series described by Nishiike *et al.*, none of the patients had multiple perforations, facial nerve palsy or bone erosion [21]. Therefore, in our case the patient did not present with the classic symptoms of middle ear tuberculosis. The classically described painless otorrhoea was painful, due to granulation tissue in the middle ear and possible bacterial super infection. Due to the atypical clinical presentation a left mastoidectomy was performed. The diagnosis was based on the histology following middle ear exploration for acute mastoiditis. TOM should be considered in the differential diagnosis of chronic middle ear discharge that does not respond to usual therapy. Delay in diagnosis can lead to complications. When surgery is combined with adequate chemotherapy, there is a fair chance of healing with a dry ear and a good prognosis.

Lymphoblastic lymphomas (LBLs) are precursor lymphoid neoplasms with less than 25% lymphoblasts in the bone marrow [22]. More than 60% of patients with LBLs are younger than the age of 18, and they account for one fourth of all childhood non-Hodgkin's lymphomas in industrialized countries [23]. The majorities

of LBLs are of T-lineage and frequently present with a mass in the anterior mediastinum, whereas precursor B-cell (pB)-LBLs constitute less than 10% of LBLs and predominantly involve extranodal sites including the skin, soft tissue, and bones. A pB-LBL of the ear is extremely rare [24]. In our patient, the acute onset of conductive hearing loss and retroauricular swelling accompanied by facial palsy suggested an acute otomastoiditis and a tympanomastoidectomy canal wall up procedure was performed. Otitis media with effusion and cholesteatoma are relatively common in children, even in the absence of acute middle-ear inflammation. In contrast, less frequent middle ear tumors can cause symptoms and signs that are identical with those of otitis media [25]. In our case, the histopathological examination was crucial to make the diagnosis.

We would like to emphasize that systemic diseases might be etiological factors in patients presenting with otomastoiditis, facial nerve paralysis and unilateral hearing loss. It is appropriate for an otorhinolaryngologist to consider complete blood count, peripheral blood smear, and temporal bone imaging and exclude any other systemic diseases such as: granulomatosis with polyangiitis, middle air tuberculosis, leukemia or temporal bone malignancy, especially before steroid administration for facial nerve paralysis treatment. Our cases showed how radiological semiology and CT sometimes are not enough to diagnose the nature of the disorder. Moreover, all patients were in good general condition at the time of the examination; they did not show history of previous immunodepression or other risk factors. Biopsy of granulation tissue in the middle ear rarely offers a diagnosis because of the limited amount of sample taken for diagnosis, except for those performed in the context of mastoidectomy [26]. In our cases, surgical treatment was considered to be the best opportunity for the patients, as long as they seemed to be medical emergencies. Surgery also aimed to provide the samples required for bacteriological and histological examinations, allowing subsequently early diagnosis.

✉ Conclusions

In the case of facial palsy and acute otological symptoms, the diagnosis of systemic diseases can be challenging. Therefore, besides the usual clinical and radiological examinations, the histopathological examination is essential for accurate diagnosis.

Conflict of interests

The authors declare that they have no conflict of interests.

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