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Case Report
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ASPERGILLAR NECROTIZING EXTERNAL OTITIS WITH PRE-PONTIC EMPYEMA: CASE REPORT

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ABSTRACT

Malignant external otitis is a infection of external auditory canal that spreads to bone : temporal and skull base. It is caused commonly by Pseudomonas Aeruginosa but fungal origin should be evoqued in immunocompromised patients with no improvement under anti-pseudomonas antibiotics with large invasive otitis. Fungal otitis externa management still controversial. We report the case of a 60 years old patient with malignant otitis external, which fungal origin was very challenging to diagnose and manage, especially due to involvement of neurological complications.

INTRODUCTION

Necrotizing or malignant external otitis (MEO) also called skull base osteomyelitis is a severe sometimes fatal complication of external auditory canal infection that spreads to the temporal bone and skull base.[1,2,3] It is a rare condition usually seen in elderly diabetic or immunocompromised patients.[4]

Most commonly it is caused by Pseudomonas aeruginosa (>98% of cases). Fungi are rarely involved in MEO, and have been identified particularly in immune-compromised nondiabetic patients, such as patients with AIDS or acute leukemia. Aspergillus fumigates is the most common cause of fungal MEO.[4] The confirmation of fungal infection might be difficult and requires repeated biopsies, especially that the biology and imaging are not specific.

Empyemas are uncommon purulent collections that develop in the subdural or, less frequently, in the epidural space, and they may occur alone or in combination. Otitis are one of the main predisposing conditions.[5]

We report a rare case of cerebral empyema complicating MEO due to Aspergillus in a diabetic patient. The aim here is exposing the difficulty of diagnosis and treatment of fungal complicated MEO.

CASE REPORT

We report a case of a 60 years female patient; she had a medical history of a left sensorineural hearing loss that necessitated the use of a conventional behind the ear hearing aid, type II diabetes under insulin and hypertension. She consulted initially for otalgia and otorrhea, diagnosis of otits externa was made and treated by oral amocicillin and clavulanic acid and otic fluroquinolones topics, oral corticosteroids with no improvement. She was admitted to our hospital two weeks later because of worsening pain and otorrhea. On clinical examination at the admission the left external ear canal was congested filled with purulent secretion and occupied by granulation tissue, the tymanic membrane was not accessible to examination because of the edema. There was no facial palsy or any other sign of neurological complication.

Ear discharge was cultured for bacteria and mycosis, and became negative. Blood examination showed CRP= 5 mg/l, PCT= 0,06 ng/l, WBC= 11200/l. A CT scan of the temporal bone demonstrated a large inflammation of the temporal bone including the meso and hypo tympanum, the external ear canal with erosion of its inferior wall, the ossicular chain and the intern ear were normal(Image I). A technetium-99m bone scan was performed and confirmed the external ear canal erosion.

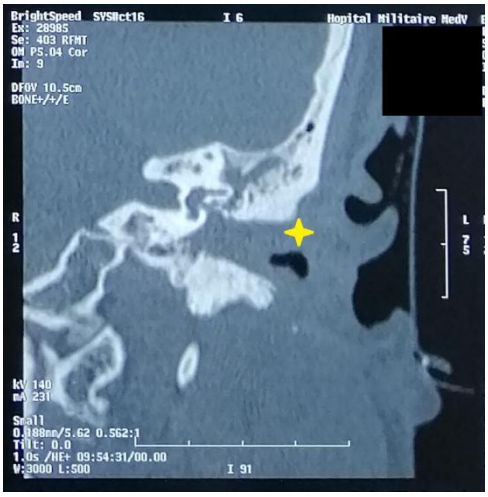

Image I: Coronal CT scans of the temporal bone) show soft tissue (*) filling the left external auditory canal and erosion of the inferior wall of the external auditory canal.

The patient was treated for MEO with aural calibration and ear drops (association of cyclin, polymyxin B, nystatin and dexamethason), parenteral antibiotherapy Ciprofloxacin 500mgx2 Ceftriaxone 2g x2 and control of her diabetes. When two weeks later there was no amelioration when still on treatment and the repeated ear swabs were still negative and other Tc-99m bone scan was ordered showing an increasing of the bone erosion. A meatoplasty with tympanomastoidoplasty to remove necrotic tissue was performed and the samples sent to pathology and revealded non specific chronic inflammation bacteriology and mycology were still negative.

The medical treatment was continued, and the patient was discharged two weeks later after regression of her symptoms. The patient was controlled weekly, and the medical examinations showed a regression of the inflammation of her left external ear canal, the tympanic membrane was normal. CT scans were thrown monthly showing stationary lesions. Five months later, the patient presented otalgia with imbalance tremor and fever. Medical examination found granulations of the external ear canal with purulent otorrhea, a biopsy was done.

We ordered a cerebral MRI (Image II) that showed an extension of the infection and a pre-pontic empyema. A TEP-scan showed a hyper a left petrous and pre-pontic metabolism (Image III).

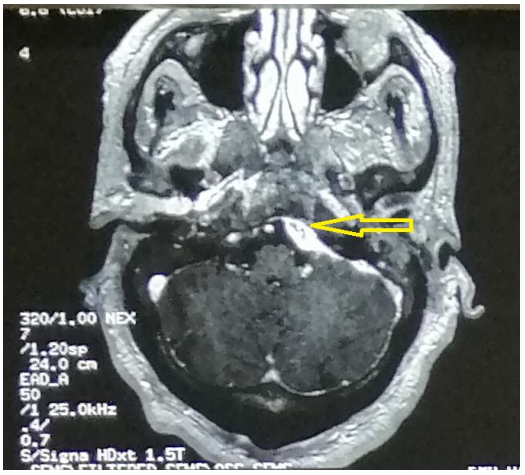

Image II: MRI Contrast-enhanced, axial image revealing a left pre-pontic empyema (arrow head).

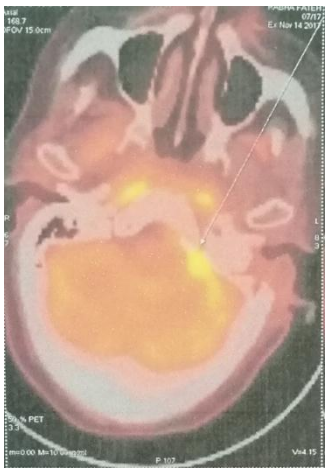

Image III: PET-scan axial image showing petrous and pre-pontic hypermetabolism

A lumbar puncture was performed and found a lymphocytary meningitis with negative cultures.

A parenteral probabilistic antibiotherapy was administrated to our patient (fluroquinolones 500mgX2) while waiting for the pathology results.

The biopsy revealed chronic inflammation and fungal hyphae with necrotic granulation, the culture yielded A.niger. Tuberculosis tests were ran and became negative.

A body scan was performed in order to look for other locations of invasive aspergillosis and found nothing but the initial location with an extension of the osseous erosions to the petrous apex with a pre-pontic empyema.

A vestibular examination using videonystagmography (VNG) and vieo head impulse test (VHIT) found a central vestibular syndrome.

The therapeutical decision was taken a multidisciplinary team involving neurosurgery neurology and pathology specialists. The patient was put under voriconazole

200mg orally and antipnseudomonas intravenous antibiotics (ciprofloxacin) and local treatment (association of cyclin, polymyxin B, nystatin and dexamethason). Because of the deep location of empyema surgery was not indicated. She showed an improvement of her otitis and reduction of volume of the empyema by half on CT scan and MRI after two weeks of treatment (Image IV).

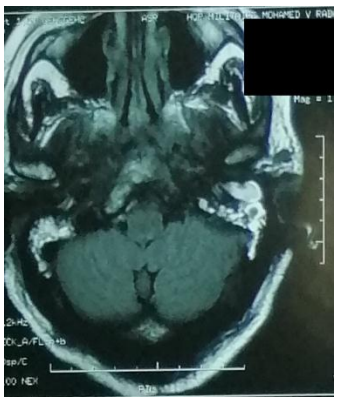

Image IV: MRI axial image showing a regression of the pre-pontic collection.

A second lumbar puncture was done and found normal. Hepatic enzymes were controlled weekly. The patient showed clinical and biological tolerance to treatment. She was discharged tree weeks later and was seen on regular basis in consultation. She took Voriconzole for a total duration of 6 months and showed a good clinical a biological outcome, although there was persistent but stable lesions at the follow up imaging.

The patient was also treated for her imbalance with vestibular rehabilitation exercises weekly during 3 months, and showed amelioration of her imbalance.

DISCUSSION

Necrotising otitis externa or malignant external otitis (MEO) is an insidious and aggressive infection, that can be lethal if not diagnosed and treated properly.

The infection penetrates through the osteocartilaginous junction in the floor of the external auditory canal and invades the connective tissues, cartilage, bone, nerves and blood vessels in the temporal bone and its surroundings (base of skull, masseter and pterygoid fossa).[6]

Most cases of necrotising otitis externa occur in elderly diabetics due to macroangiopathy (atherosclerosis) and microangiopathy, which result in poor local blood supply, compromising systemic antibiotic uptake.

The diabetic immune response is compromised by poor migration, reduced chemotaxis and defective phagocytosis of polymorphonuclear leucocytes; this decreases the host response to pseudomonas. In addition, the cerumen of diabetic patients has a higher pH, which makes for a hospitable environment for bacterial growth.[6]

Causative pathogen has been Pseudomonas aeruginosa (>98% of cases) it is frequently a saprophyte in the external auditory meatus and sometimes other associated bacteria or fungi can have an important or predominant role in the aetiology of MEO, particularly in immunocompromised patients.[7] such as Fungi who are rarely involved in MEO and also have been identified particularly in immune-compromised non diabetic patients.[4]

The diagnostic criteria for necrotising otitis externa are divided into obligatory (major) which are present in 100% of cases and occasional (minor) criteria according to D.Cohen & al.[8] (Table 1).

Table 1: The Diagnostic Criteria Of Malignant External Otitis.[8]

Major (obligatory) signs:	Minor (occasional) signs:
Pain	Pseudomonas in culture
Exudate	Positive radiograph
Edema	Diabetes Mellitus
Granulations	Cranial nerve involvement.
Microabscess—when surgery is done.	Debilitating condition
Positive Tc99 scan *or* failure of local treatment after more than 1 week.	Old age

All of the obligatory criteria must be present in order to establish the diagnosis. The presence of occasional criteria alone does not establish it.

Patients usually present with extreme otalgia and otorrhoea. The pain is classically worse at night.[6]

Our patient gathered all the major and minor signs except from cranial nerve involvement and Pseudomonas.

Although fungal infections are generally more invasive than bacterial disease, all the other clinical and radiological features, including survival, are similar. Thus, even the isolation of *Pseudomonas* from aural

discharge may be not sufficient or specific enough to distinguish between the two forms.[7] Also aspergillus is frequently isolated in the external canal smears, so the diagnosis of fungal MEO should be based on histopathologic confirmation or from blood culture of fistula exudates.[7,9]

In a study about fungal malignant external otitis directed by Y.Hamzani & al.[4] of 9 patients diagnosed with fungal MEO over an 18-year period, found that fungal culture at the time of admission was negative. Findings converted to positive only in later samples. Also, the fact that patients had received antibiotics before referral might contribute to negative cultures.

The aspergillus found in our case was first negative then later positive on pathology on a repeated deep biopsy of the external ear canal. It shows the importance of doing repeated bacterial and fungal cultures and deep biopsies in MEO, because it stays the only way to confirm the diagnosis.

Blood tests are generally non-specific except for a constant elevation of inflammatory indices (CRP ESR) Conversely, leukocytosis is rare. ESR and CRP are also indicators of disease activity and are useful for monitoring the course of therapy and effectiveness of antibiotic treatment.

In our case the CRP was normal at the admission. It could be related to her prior antibiotic and corticosteroid treatment.

Recently, two different markers, galactomannan and β-glucan have demonstrated their value in diagnosis and monitoring the course of invasive invasive aspergillosis during therapy. Unfortunately, false positivity may be related to antibiotic treatment, while false negativity may be observed in immunocompromised patients.[7] Unfortunately these test were not available in our structure.

Concerning imaging, numerous imaging modalities have been used to assess patients with necrotising otitis externa. High resolution CT is the preferred modality for defining the anatomical extension of the osteomyelitic process. The value of CT scans is limited due to the inability of this technique to detect bone erosions in the early stages of disease. Computed tomography scans can only detect the disease when at least 30–50 per cent of bone erosion has already occurred.

Magnetic resonance imaging is sufficiently sensitive to evaluate intracranial extension of the disease.

It also plays a significant role in early diagnosis and successful outcome or empyemas. Several authors have emphasized the failure of CT to visualize small, crescentic extra-axial collections of fluid, especially when they are located superficially near the inner table of the skull MRI has become the imaging modality of choice for detecting and defining the extent of subdural empyemas.[11]

Radionuclide scanning techniques, such as those using technetium-99m methylene diphosphonate or gallium-67 citrate, are useful in detecting the lesions of early disease. The radionuclide accumulates at the site of osteoblastic activity, and the bone scan can detect a minimum of 10 per cent osteogenic activity.[6]

For bacterial MEO, antipseudomonas antibiotherapy is recommended especially fluoroquinolones. Several studies recommend oral ciprofloxacin for maintenance therapy in a dose of 0.5–1.0 gram 12-hourly for 8–10 weeks,[6,12,13,14] in addition to local therapy,]but it should be considered that the incidence of mycotic forms has significantly risen since the end of 1990s, when the use of quinolone ear drops became common clinical practice.[7]

Antifungal therapy is warranted because MOE can be caused by fungal organisms or a mixed bacterial and fungal infection.[10] According to the literature review, treatment of *Aspergillus* MEO requires long-term antifungal therapy in association with appropriate management of the underlying condition, mostly diabetes mellitus.

Voriconazole is currently considered the first-line therapeutic option for invasive aspergillosis, based on its high intrinsic anti-*Aspergillus* activity and its superiority against intravenous amphotericin B in a large randomized trial. In addition, this broad-spectrum azole is distributed throughout the body, including soft tissues and bone. This antifungal agent is well tolerated despite prolonged treatment and available intravenously and orally.

There may be renal side effects of voriconazole, and the renal function should thus be closely monitored.[10]

Our patient is one of the very few reported cases of fungal MEO treated witch Voriconazole.

In addition, as in the management of *Aspergillus* osteomyelitis, prompt surgical debridement consisting of radical mastoidectomy is required in the majority of cases.[10,15] However, other authors stress the fact that extensive surgery may be even counterproductive because of the risk of exposing healthy bone to infection. Unfortunately, there are neither guidelines nor definite recommendations with regard to the surgical treatment of the different forms of MEO.[7]

The efficacy of hyperbaric oxygen therapy has not been demonstrated when compared with treatment with antibiotics and/or surgery.[10]

CONCLUSION

The course of MEO is initially subtle, and the disease may have poor prognosis if not properly treated, especially in elderly diabetic or immunocompromised patients, who should be initially treated as potential forms of bacterial MEO and samples should be sent for both bacterial fungal research.

Nevertheless, no diagnostic conclusions can be drawn from single positive cultures from the external auditory canal. In fact, colonization with *Pseudomonas*, both in chronic otitis media and in superficial external otitis is probably common, and thus mycosis should be suspected whenever clinical signs of infection do not improve despite adequate anti-*Pseudomonas* treatment due to the potential risk of complication of fungal otitis :extensive skull base osteomyelitis, with multiple cranial nerve palsies and sometimes a fatal outcome. In these cases, deep tissue biopsy or isolation from blood cultures is required for histopathological confirmation.[7]

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