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Neurology | Case report

Extensive skull base osteomyelitis, devastating complication of otitis externa: A case report and review of the literature

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Abstract

Skull base osteomyelitis (SBO), also referred to as malignant otitis externa (MOE) in its typical form, is usually a complication of otitis externa and severe uncommon and life-threatening condition requiring early diagnosis and long-term treatment in order to avoid its neurologic sequelae.

We report the case of 69 years old female with a history of uncontrolled type 2 diabetes, who presented refractory and chronic right-sided purulent otorrhea with temporal headaches for 6 months, treated with no improvement by multiple attempts of ambulatory empiric therapy. After the appearance of grade III facial palsy and painful swelling in the right periorbital and zygomatic areas, the patient consulted in our department where a CT scan showed massive cortical and trabecular destruction of the right petrous bone and the mastoid extended to the lateral orbital wall, the zygomatic arch and the greater sphenoid wing realising extensive osteomyelitis of the skull base and the lateral face. The treatment was started immediately based on intravenous broad-spectrum antibiotics. Despite aggressive long-term treatment, the patient passed away, underlying the increased SBO morbidity and mortality secondary to delayed diagnosis.

We present this case to raise awareness of the necessity of early diagnosis and patient's compliance to long-term treatment, close follow-up and late and slow clinical improvement in order to overcome the SBO management challenges and high mortality rate.

Keywords: Skull base osteomyelitis, otitis externa, temporal bone infection, cranial nerve palsy, antibiotics.

Introduction

Skull base osteomyelitis (SBO), also referred to as malignant otitis externa (MOE) in its typical form, is usually a complication of otitis externa and a severe uncommon and life-threatening condition requiring early diagnosis and long-term treatment in order to avoid its neurologic sequelae [1].

We report a case of extensive skull base osteomyelitis treated in our Head and Neck surgery department of the Ibn Rochd University Hospital that supplements and supports the rare literature data concerning the management challenges of SBO and the prognostic value of early diagnosis and patient's compliance to treatment.

Presentation of the case

We report the case of a 69 years old female with normal BMI at 22 and history of hypertension under monotherapy and uncontrolled type 2 diabetes (hemoglobin A1c level at 10,1%) with bilateral blindness secondary to diabetic retinopathy.

She presented refractory and chronic right-sided purulent otorrhea with otalgia, ipsilateral hearing loss and intense and persistent temporal headache for 6 months. She consulted repeatedly at the district hospital where she was treated by multiple attempts of ambulatory empiric therapy based on local and oral antibiotics (amoxicillin, clavulanic acid 3g/day and ciprofloxacin 5 ear drops x2/day for 7 to 10 days) with no clinical improvement or further exploration. After the appearance of facial palsy and painful swelling in the right periorbital and zygomatic areas, the patient consulted in our Otorhinolaryngology department.

The otologic examination revealed dense and purulent discharge in inflammatory and oedematous ear canal with aural polyp and inflammatory tympanic membrane (Figure 1a). No retroauricular collection or abscess was observed. Sensitive swelling in the right periorbital and zygomatic areas was found with preserved ocular movements. Right facial palsy was revealed by positive Bell's sign graded as III on House-Brackmann scale (Figure 1b). No signs of lower cranial nerves lesions were seen and the neurological and vestibular examination was normal.

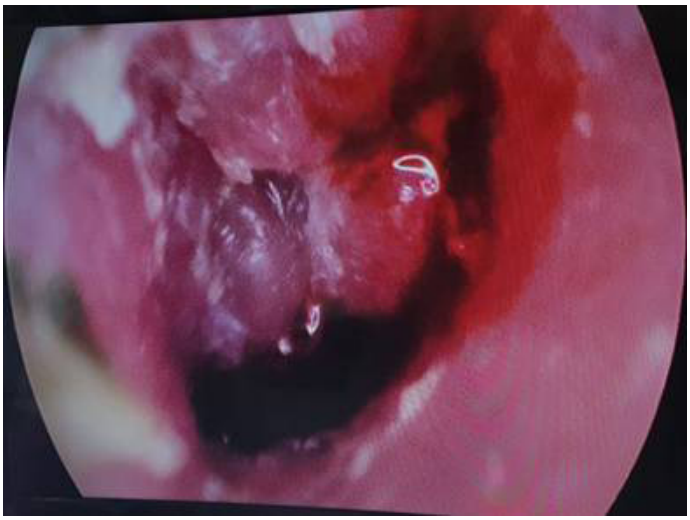

Figure 1a: Otoscopic examination finding inflammatory and oedematous ear canal with purulent discharge, aural polyp and inflammatory tympanic membrane.

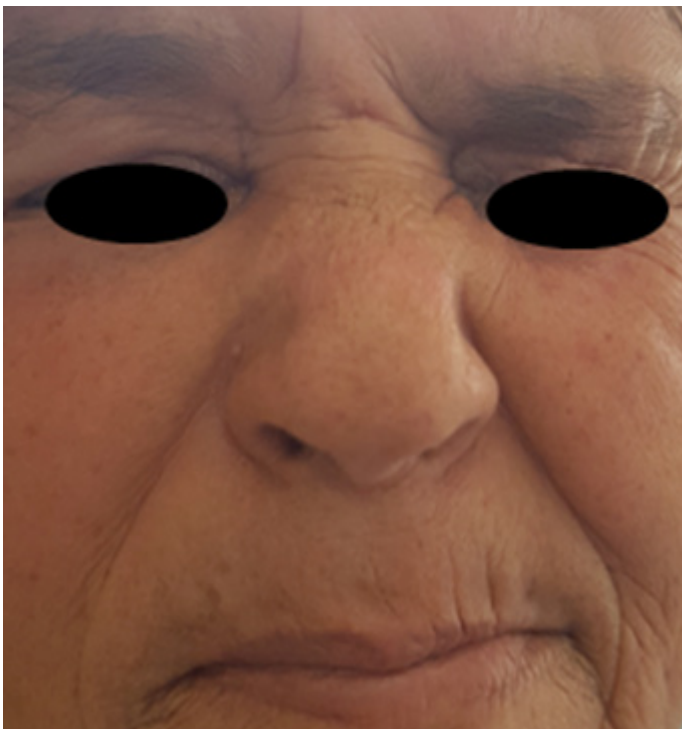

Figure 1b: Right peripheral facial palsy, House-Brackmann grade III.

The temporal bone CT scan showed massive cortical and trabecular destruction of the right petrous bone and the mastoid with thickening and occlusion of the external auditory canal. The middle ear lost its air density but no erosion was observed in the inner ear and ossicular chain (Figure 2). On the complementary face CT scan, the lytic bone destruction was extended to the lateral orbital wall, the zygomatic arch and the greater sphenoid wing realising extensive osteomyelitis of the skull base and the lateral face (Figure 3). The contralateral ear and the brain appeared normal.

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During their follow-up, the patients presented the COVID-19 signs and symptoms. This period takes 8±2 days. In this time, the main clinical and diagnostic presentations were partial shortness of breath, fever, and also nausea and abdominal pain. The patients complained of abdominal pain located on umbilical and epigastric area (Table 2).

A positive RT-PCR result was recorded in all patients. Table 3 shows the laboratorial data of patients during undiagnosed and diagnosed periods. The acquired data was almost different in all items including white blood cell, lymphocytes and neutrophil. Lymphopenia (<1500) was stated in 13 (52%) patients but the lung involvement in chest CT scan was illustrated in 23 (92%) patients.

Of all patients, 7 patients had contact with a suspected subject. There was no history of contact with animal or seafood, wholesale Market or travel to China. However, three of them travel to other cities by public transports. Details of underlying diseases including diabetes, hypertension etc. and another clinical data are shown in Table 1.

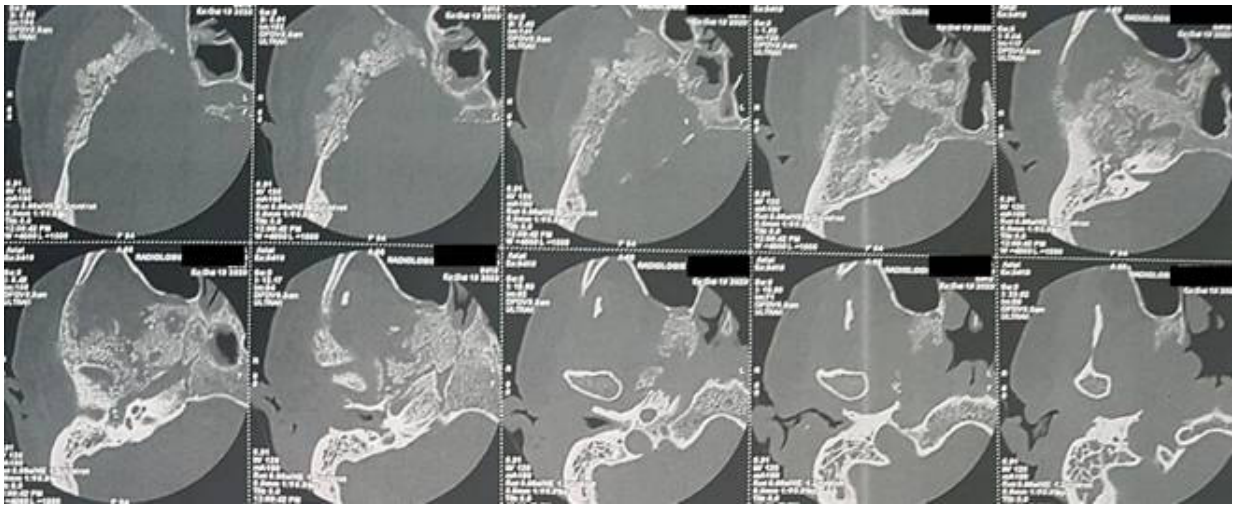

Figure 2: Temporal bone CT scan, axial sections: Massive petrous and mastoid bone destruction with preserved ossicular chain (red arrow) extended to the sphenoid bone and the zygomatic arch.

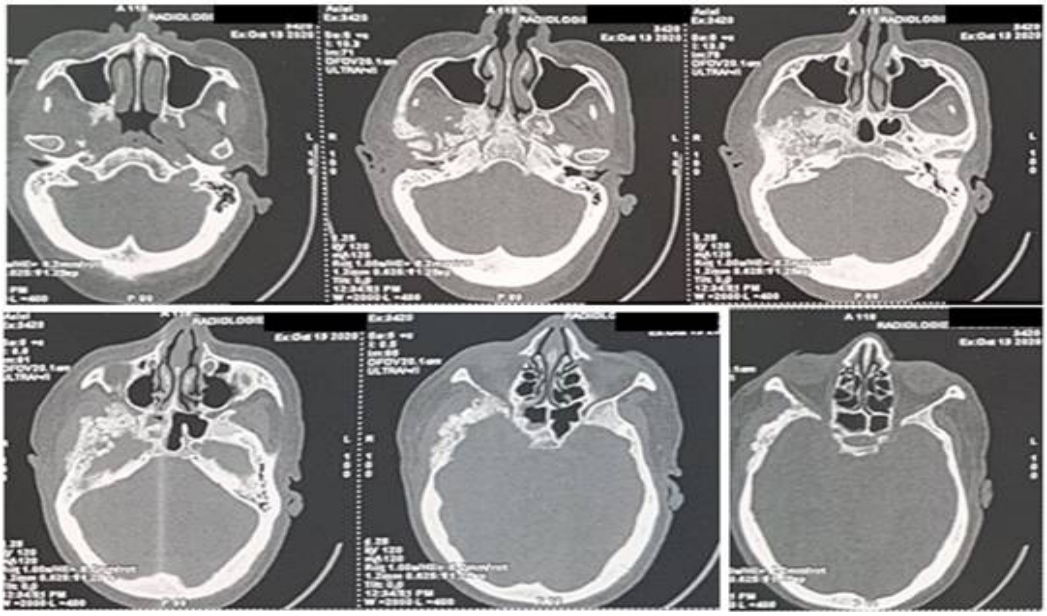

Figure 3: Face CT scan, axial sections: Extension of the osteomyelitis to the lateral orbital wall, the zygomatic arch and the greater sphenoid wing.

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The positive diagnosis was based on clinical and radiological findings and the patient was admitted immediately. Complete blood count showed normal white blood cells (WBC) count (9990/mm^3) with negative CRP. Blood sugar level was high up to 2.26 g/l. Blood culture was negative. In order to rule out secondary meningitis, a lumbar puncture was performed. Spinal fluid samples were clear, with elevated protein level at 1.10 g/l, normal glucose level at 0.95 g/l, less than 3 WBC/mm^3 and negative microscopic examination and culture. Intravenous empiric broad spectrum antibiotic therapy was started based on Ceftazidime 1gx2 per day, Metronidazole 500mgx3 per day and Ciprofloxacin 400mgx2 per day, in addition to local antibiotics (topical ciprofloxacin 5 dropsx2 per day) and daily debridement and cleaning of the ear canal. Biopsy was postponed not to delay medical treatment and a swab of the infected right ear was taken for microbiological analysis. It identified on microscopic examination the presence of Gram-positive bacilli but the culture was negative.

Since poor glycemic control favors acute infectious exacerbations, the patient followed close insulin regimen based on basal and rapid acting insulin with correction doses decreasing blood sugar level to 1.86 g/l and hemoglobin A1c level to 8.5%.

The treatment was switched to long-course oral antibiotics after four weeks (Metronidazole 500mgx3 per day and Ciprofloxacin 500mgx2 per day). The 3 months close follow-up showed decreased pain and better controlled diabetes. However, no improvement was reported on the grade III facial palsy and the otorrhea persisted. Also, no complication has arisen, such as lesions of lower cranial nerves, cerebral abscess or cellulitis. Surgery was scheduled for tissue debridement and taking biopsies of the mastoid bone cortex and tympanic cavity for histopathologic and microbiologic examination. However, regarding the COVID-19 pandemic situation and the consequent travel restrictions, the patient was lost to follow-up unable to reach our hospital. Her daughter then, announced that the patient was deceased.

Informed consent was obtained from the patient and her family. This case was reported in line with the SCARE 2020 criteria [2].

Discussion

Osteomyelitis can be defined as an inflammatory process of the bone starting as an infection of the medullary cavity, rapidly involving the haversian systems progressing and impairing the flow, and extending to the periosteum of the affected area resulting in necrotic bone forming sequestra. It can affect any bone of the body but usually occurs in long bones such as tibia and fibula. The temporal bone is then, a rare location [3, 4].

The first description of progressive osteomyelitis in the temporal bone was reported by Toulmouche in 1838 [5]. In 1959, Meltzer and Keleman described a case of extensive temporal bone osteomyelitis secondary to *Pseudomonas aeruginosa* otitis externa in a patient with severe diabetes which will become the most typical form of SBO [6].

The most common causes of SBO are otitis externa and infections arising from the mastoid, paranasal sinuses, the mandible or maxilla due to odontic caries, direct head injuries and temporal bone fractures, postoperative craniotomy and scalp infections [3, 4]. During otitis externa, inflammation and infection disseminate from the external auditory canal (EAC) to the cartilages and the skull base through the fissures of Santorini, the tympanomastoid suture and osseocartilaginous junction of the EAC due to the lack of subcutaneous tissue [3, 7]. Then, infection continues to spread further rapidly through the combination of air cells and Haversian nutrient channels [7]. Anterior dissemination involves the parotid gland, the temporomandibular joint or cranial nerve VII at the exit of the stylomastoid foramen. Posteriorly, the sigmoid sinus, the mastoid or the vertical portion of cranial nerve VII may be affected. The inferomedial spread leads to the participation of the carotid artery, the jugular bulb and the sigmoid sinus. When the skull base foramina are involved, cranial nerves palsies can occur. The facial nerve paralysis results typically from the affection of the styloid and mastoid foramen while lower cranial nerves IX, X, or XI palsies can occur when the jugular foramen becomes involved. The infection can also spread to the contralateral side and involve the cervical spine [3, 4].

Patients with conditions decreasing the vascularity of the bone such as radiation, malignancy, osteoporosis, osteopetrosis, and Paget disease are prone the develop SBO [4]. Also, systemic diseases and personal conditions altering the host defense mechanisms like age older than 65 years, immune-compromised state, acquired immunodeficiency syndrome, diabetes mellitus, renal or hepatic failure, chronic hypoxia, severe anemia and malnutrition are predisposing factors influencing the course and the evolution of SBO [3, 4, 7].

The typical form of SBO related to otitis externa or mastoiditis presents with severe otalgia, pain in the involved temporal, parietal, post-auricular and retro-orbital areas, aural fullness and purulent otorrhea with fever. The clinical examination may find induration of pinna, mastoid cutaneous fistula or preauricular cellulitis with fibrotic granulation tissue or a polyp in the EAC particularly at the level of bony-cartilaginous junction [3, 4, 7, 8]. The atypical form can be revealed by unremitting headaches but the absence of localized and evident infection poses diagnosis challenges [3, 8]. Indeed, on Singh *et al.* [9] study about 10 patients treated for atypical SBO, the main clinical symptom was a vague dull

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headache with one or more cranial nerve palsy(s) while the radiological examination showed clival involvement in all the cases, concluding that the suspicion of atypical SBO should be raised in front of non-specific symptoms of headaches with cranial nerve palsy even with no evident signs of otological or rhinological infections especially in immune-compromised patients.

The progression of SBO can lead to cranial neuropathies [8]. The facial nerve is the most common and first cranial nerve involved when the infection spreads sub-temporally at the stylomastoid foramen [3] with a rate reported by Chandler *et al.* [10] at 46%, presented by facial palsy or facial twitching suggestive of facial canal dehiscence [4]. Lower cranial nerves (IX, X, and XI) may be affected with jugular foramen involvement while V and VI nerves are affected when the petrous apex is involved. After complete treatment, cranial nerves deficits have good rates of recovery while the facial nerve does not always recover and should not be considered as a factor of clinical improvement [3].

Untreated SBO may lead to central complications such as meningitis, brain parenchymal involvement, abscess formation (intracranial empyema), and venous sinus thrombosis [3]. Involvement of the cavernous sinuses has been described with sphenoid sinus infection while the thrombosis of the transverse and sigmoid sinuses have been described with otogenic infections due to spread of infection through the mastoid emissary veins [11]. Weitzman *et al.* [12] reported a case of SBO complicated by petrous internal carotid artery blow out revealed by fulminant epistaxis recommending consideration of this etiology in front of epistaxis in that context.

Only early diagnosis can prevent central nervous system complications but it can be difficult and is then, often delayed [3, 8]. It is based on clinical, radiological and laboratory findings but the absence of infectious symptoms and normal blood tests is not uncommon in immune-compromised patients [1]. Repeated swab and biopsy with both histopathology and microbiology analysis help to rule out malignant disease and give positive diagnosis [3].

To establish the location and extension of infection, the imaging modalities include computed tomography (CT) and magnetic resonance imaging (MRI) for anatomical imaging and gallium-67 scintigraphy, Indium-111 (In-111) white blood cell (WBC) scan, and Tc99 m MDP bone single-photon emission CT (SPECT) scintigraphy exposing in the functional process [1, 3].

CT scan best demonstrates cortical and trabecular bone erosion or periosteal remodelling which is relatively a late phenomenon, soft tissue swelling with thinning of the fat planes and the extent of disease even if the demineralization in only seen if ≥ 30% [1,4, 8]. But it is insufficient to represent intracranial extension, bone marrow involvement, and to measure treatment response measured by bone remineralization because it rarely returns to normal [1, 3, 4]. MRI has superior soft tissue discrimination allowing better assessment of dural enhancement, extent of the disease, involvement of marrow space, extraosseous soft tissue and intracranial complications [4, 8]. SBO usually appears as T1 hypointensity since the fatty bone marrow of the skull base and temporal bone is replaced by inflammatory tissue and T2 hyperintensity because of hyperaemia and oedema usually replaced by T2 hypointesity secondary to compromised vascular state and diffuse enhancement after Gadolinium admission [1, 4]. Also, retrospective analysis of Razek *et al.* [13] showed that apparent diffusion coefficient is a non-invasive imaging parameter useful for predicting SBO with a sensitivity >80%. However, abnormal bone marrow signal can still be present for 6–12 months after successful treatment, making MRI unreliable for distinguishing resolved from ongoing SBO of the bone marrow [1].

The treatment should start as early as possible to prevent further spread and complications. In the literature, the average delay between diagnosis and therapy is up to 70 days [1]. The main treatment for SBO includes culture-guided long-term intravenous broad-spectrum antibiotic therapy [3]. Often, the culture is negative and the treatment is carried out empirically like 71-43% of the cases in Sokołowski *et al.* study [7] and in our case. Three general protocols are used: Aminoglycoside and a β-lactamase antibiotic, a third-generation cephalosporin (Ceftazidime), or an oral quinolone (ciprofloxacin) for duration of 4 to 6 months [4, 7]. For fungal SBO, the use of high-dose Amphotericin B is recommended as well as liposomal Amphotericin B, a new lipid formulation with lower toxicity, and equal efficacy [3]. Topical antimicrobial agents are controversial since they can affect the culture results but, acidifying agent and daily debridement of the EAC are helpful [4]. In another hand, hyperbaric oxygen therapy (HBO), 100% oxygen given for 90 minutes at 2.5 ATA absolute pressure 5 days a week, 20 times, is indicated, next to antibiotics and surgery, in chronic, refractory SBO. Also, management of SBO also requires control of underlying comorbid factors with strict diabetic control and improvements in immune status of immunocompromised patients [3, 4].

Nowadays, the role of surgery is often limited to biopsy to discern infection from malignancy and drainage of associated abscesses. It is usually indicated in cases of widespread soft-tissue involvement, severe pain, complications or refractory cases [1, 3, 4]. Next to biopsy, surgical procedures involve removal of infectious sequestra, debridement of necrotic tissue particularly in fungal SBO, antromastoidectomy, radical mastoid surgery,

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drainage of the skull base or dural plasty [1, 3, 4]. When the EAC is affected and stenotic, extensive meatoplasty can be required [3]. Facial nerve decompression should be considered in front of persistent facial palsy [7]. With early and adapted treatment, SBO can take several months before a complete resolution is achieved [3].

SBO was almost universally fatal before the era of antibiotics [13]. Prognostic factors are not all clear yet due to the rarity of the affection. Precocious diagnosis for early aggressive and adapted long-term intravenous broad-spectrum antibiotic treatment decrease the rate of complications. In cases of widespread soft tissue involvement, early aggressive surgical removal of infectious sequestra with preferentially HBO therapy is associated with better prognosis and less mortality rate; in addition to strict glycemic control in diabetic patients and improvements in the immune status of immunocompromised patients [3].

The overall mortality of SBO reported by Abdel Razek *et al.* [13] reaches a rate of 33%, extended to 80% if cranial nerves are involved while Khan *et al.* [3] described a rate of 10% with 31% of long-term neurologic sequelae despite aggressive treatment. All in all, with awareness spread and early and prolonged treatment, the mortality rate improved considerably from 50 to 0-15% [1]. More specifically, regarding associated comorbidities, the survival for elderly patients is lower than younger patients with higher morbidity rate than expected for the elderly with a significant age-related decline in survival. Patients above 70 year of age have a 5-year survival of 44%, in contrast to patients under 70 years with a 5-year survival rate of 75% [14].

Conclusion

Typical or atypical SBO is devastating and life-threatening condition with considerable diagnosis and management challenges. We reported this case to highlight the importance of prevention of SBO by adequate treatment of every infection arising from the ear, the mastoid or the paranasal sinuses, in addition to strict diabetes control. Also, early diagnosis is an important prognostic factor. Then, family doctors and general practitioners should be aware of the signs and symptoms of SBO since they are the first medical line the patient refers to. Positive diagnosis should be based on clinical findings, both CT scan and MRI imaging whereas the results of biopsy and culture, even if useful to rule out malignancy and select adapted antibiotic therapy, should not delay the treatment. The treatment is based on early aggressive and adapted long-term broad-spectrum antibiotics completed by surgery and HBO in some indications and good control of the predisposing factors. Finally, the patient should be aware and compliant with the need of long-term treatment, close follow-up and late and slow clinical improvement.

The patient and family gave informed consent for publication.

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