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Case Report

Extensive Skull Base Osteomyelitis Secondary to Malignant Otitis Externa

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Skull base osteomyelitis is a severe complication of malignant otitis externa that affects the marrow of the temporal, sphenoid, and occipital bones. Skull base osteomyelitis is usually diagnosed based on clinical, microbiological, and radiological findings. Here, we present the imaging findings of a 76-year-old man who initially presented with right-sided malignant otitis externa, with the involvement of the otomastoid structures and ipsilateral temporal bone. Over the following 3 years, despite specific extended antibiotic therapy, the skull base osteomyelitis entirely involved the skull base, up to the contralateral petrous portion of the temporal bone, and it affected the cervical vertebral processes. This report describes an exceptional extent of unilateral malignant otitis externa with a severe involvement of the skull base on the contralateral side and the cervical spine.

KEYWORDS: Malignant external otitis, osteomyelitis, skull base

INTRODUCTION

Extensive skull base osteomyelitis is a severe complication of malignant otitis externa (MOE). It is most commonly diagnosed in patients with diabetes and in immunocompromised patients with bacterial and/or fungal infection. The primary infection is often bacterial with fungal superinfection. *Pseudomonas aeruginosa* is the causative pathogen in 50%-90% of cases, although other agents may be isolated [1].

CASE PRESENTATION

A 76-year-old man was referred to our Ear Nose and Throat (ENT) department in 2015 with a 4-month history of worsening right-sided MOE with the involvement of the ipsilateral otomastoid foramen and temporal bone. The patient had been treated empirically with oral ciprofloxacin (Ciprofloxacina; Sandoz S.P.A., Varese, Italy) 500 mg/day for 2 months but showed little clinical improvement. He presented with persistent temporal headache, otalgia, milky otorrhea, right facial palsy (House–Brackmann grade 4), and left hemiparesis as a result of a stroke 16 years earlier. There was no recent history of trauma, but an aural irrigation had been performed a few weeks before the symptom onset. An otologic examination revealed a dense and granulation tissue in an edematous ear canal. Patient's past medical history included nasopharyngeal carcinoma treated with radiotherapy in 1984, hypertension and stroke in 1999, and right carotid surgery in 2005. There was no history of diabetes mellitus, prolonged use of systemic corticosteroids, or immune deficiency.

A swab of the infected right ear was taken for microbiological culture, and it identified the presence of *Corynebacterium Amycolatum*. The acid-fast bacilli staining was negative, and fungal agents were also not isolated. We decided to treat the patient with amoxicillin-clavulanic acid (ABBA, Fidia Farmaceutici S.P.A., Padova, Italy) 1000 mg twice a day, orally, and rifampicin (Rifadin, Sanofi S.P.A. Milano) 600 mg per day, orally; no substantial benefits were seen after 6 months of treatment. Dysphagia appeared for palsy of the IX and X right cranial nerve.

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Computed tomography (CT) revealed occlusion of the right external auditory canal, chronic osteomyelitis of the right temporal bone extending to the right mastoid and tympanic cavity, erosion of the ossicular chain, partial erosion of the inner ear, and preservation of a small portion of the cochlea (Figure 1a). The osteomyelitis extended to the right stylomastoid foramen, jugular foramen, and hypoglossal canal. The patient underwent surgery to obtain biopsies of the cortex of the mastoid bone and tympanic cavity for histopathologic and microbiologic examination. The results confirmed a *Corynebacterium Amycolatum* infection, extensive inflammation, and an absence of fungal organisms, and they were negative for BK. Due to poor response to antibiotic therapy, we decided to shift to fluoroquinolones. In particular, a therapy with moxifloxacin (Moxifloxacina Teva, Teva Italia s.r.l., Milano, Italy) 400 mg per day, orally, was administered for 2 years. In an attempt to improve response to oral antibiotic treatment, we proposed to the patient a mastoidectomy, but he refused. During a follow-up period of over 3 years, the MOE had been persistent and, inexorably, progressive. The patient presented several complications including liquorrhea, caused by a retro-auricular fistula in December 2016, epistaxis and right otorrhagia in May 2017, and in October 2018, he expired. The osteomyelitis had involved the entire skull base up to the contralateral petrous portion of the temporal bone and affected the spinous processes of the cervical vertebrae. The final CT scan of the brain obtained before the patient's death revealed an area of marked bone lysis in the right petrous portion of the temporal bone and the right mastoid, with an aerial component caused by drainage of the infective-inflammatory material through pre- and post-ear fistulas of soft tissue (Figure 1b). The osteomyelitis crossed the midline to involve the contralateral petrous temporal bone and included the bony structures of the right occipital condyle, the lateral masses of C1 and C2, and the posterior arch of the atlas (Figure 2). The fluid-filled space at the cervicomedullary junction was decreased, and the occipito-parietal skull was involved.

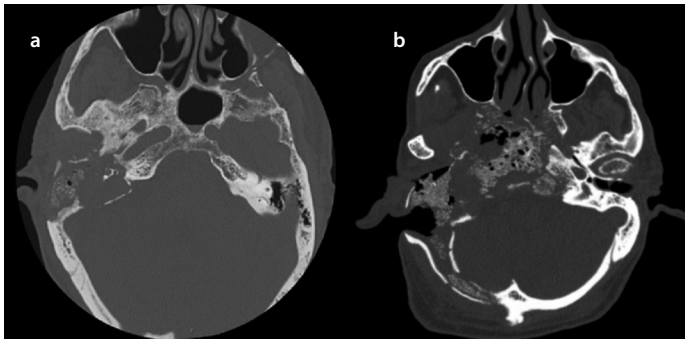

Figure 1. a, b. (a) An axial computed tomography (CT) image of the bone window, at the beginning of the disease, demonstrates erosion of the right mastoid, tympanic cavity, and ossicular chain and subtotal erosion of the inner ear. (b) An axial computed tomography (CT) image of the bone window, in the advanced stage of the disease, demonstrates erosion of the mastoid and sphenoid bone and an area of bone lysis in the right petrous portion of the temporal bone, with a fistula of soft tissue.

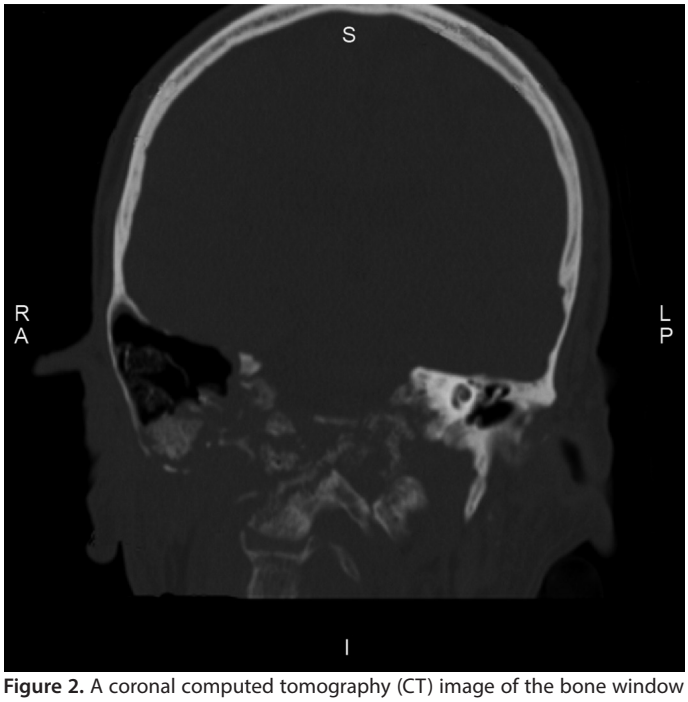

Figure 2. A coronal computed tomography (CT) image of the bone window demonstrates that osteomyelitis has crossed the median line involving the contralateral petrous temporal bone, with upward extension to include the bone structures of the right occipital condyle, lateral masses of C1 and C2, and posterior arch of the atlas.

Informed consent was obtained from the patient during data collection and also from the patient's wife, after his death.

DISCUSSION

Malignant otitis externa is the osteomyelitis of the temporal bone that usually occurs in elderly diabetic or otherwise immunocompromised patients; occasionally, the infection can spread and cause a skull base osteomyelitis [2]. In particular, microangiopathy and impaired blood circulation in patients with diabetes may play a main role in the pathogenesis of the disease [3]. Other causes can favor vascular impairment, such as the radiotherapy or the unhealthy diet [4].

The disease is associated with serious complications with a cranial nerve involvement and high mortality and morbidity rates. MOE is also reported in immunocompromised or diabetic children; however, the incidence is not as common as in elderly diabetic patients [5].

Clinical features of MOE include severe otalgia, purulent otorrhea, aural fullness, and hearing loss [6]. Temporomandibular joint pain, hemifacial pain, headache, and trismus are other common features that can develop from the anterior extension of the disease. Facial nerve palsy can be the presenting feature in some cases [5]. Levenson's criteria can be used for diagnosis. These criteria include refractory otitis externa, severe nocturnal otalgia, purulent otorrhea, the presence of granulation tissue in the external auditory canal, growth of *Pseudomonas* in the culture from ear discharge, and presence of diabetes or immunocompromised state [6].

Pseudomonas aeruginosa is the most commonly isolated microbiological agent for this disease [7]. Other bacteria such as *Staphylococcus aureus*, *S. epidermidis*, *Proteus mirabilis*, *Klebsiella oxytoca*, and *P. cepacia* have been isolated in MOE [5]. Moreover, a mycotic super infection can complicate the disease. *Aspergillus fumigatus* is the most common fungal organism causing MOE. Bacterial culturing provides the basis for antibiotic selection. If culture results are negative, ciproflox-

acin (with or without rifampin), new generation fluoroquinolones, or third-generation cephalosporin are commonly used [8]. Antifungal therapy is warranted because MOE can be caused by fungal organisms or a mixed bacterial and fungal infection.

An imaging study is mandatory when patients present with complications, such as facial palsy or temporomandibular joint pain. A high-resolution CT scan of the temporal bone is commonly used to evaluate the presence of bony erosion [6]. Magnetic resonance imaging (MRI) offers a better resolution in the evaluation of soft tissue, especially the parotid gland, meninges, and cranial nerves. In particular diffusion-weighted MRI provides better anatomical resolution when compared to standard MRI sequences [9]. However, the use of both CT and MRI allows diagnostic imaging to be more sensitive, and the use of diffusion-weighted MRI aids to assess disease progression [9].

Unlike most of the affected subjects, the patient from this report was neither diabetic nor immunocompromised. He was previously treated, 20 years before the presentation of MOE, with radiotherapy in the head and neck region. Radiotherapy is considered ototoxic from the moment that it can cause early and late reactions in the external ear, middle ear, and inner ear. In the external ear, the late reaction appears as acute otitis externa, chronic otitis externa, skin ulcer, and osteo/cartilaginous necrosis after several months of radiotherapy [10]. Only one other case is reported in literature, and the infection was diagnosed 4 months after radiotherapy [4]. In our patient, radiotherapy may have induced a very slow process of necrosis in the bone, and after many years, a bacterial infection could have invaded the necrotic tissue of the temporal bone.

The pathogen isolated from the mastoid biopsy was *Corynebacterium Amycolatum*. The spectrum of human infections with *Corynebacterium* is broad ranging from community-acquired infections such as conjunctivitis, pharyngitis, genitourinary tract infections, prostatitis, skin and soft-tissue infections, and breast abscess to nosocomial-acquired infections such as cerebrospinal fluid infections, pneumonia, intravenous catheter-related bloodstream infections, endocarditis, post-surgical infections, urinary tract infections, and peritoneal dialysis-related peritonitis [11]. *Corynebacterium* is a cause of otitis and osteomyelitis, and the infection is associated with prior otologic procedures and treatments [12]. The association of previous radiotherapy with the surgical procedure may have caused the development of this rare infection.

The patient was treated exclusively with antibiotic therapy. He underwent surgery only to obtain biopsies of the mastoid cortex and tympanic cavity for histopathologic and microbiologic examination. The introduction over the years of newer, more effective, and less toxic antibiotics has reduced the role of surgery. Moreover, according to us, an extensive surgical procedure in this particular patient could have caused spreading of the infection and increased morbidity and complications.

In our case, clinically there was a marked progression of unilateral MOE with a severe involvement of the skull base, the contralateral side, and the cervical spine inferiorly. Bilateral skull base osteomyelitis is very rare, and there are no reports of bilateral involvement of the skull base from extension of unilateral disease. However, cases of bilateral skull base osteomyelitis concomitant with or following bilateral MOE have been described [13]. In some cases of bilateral skull base osteomyelitis, there is no evidence of an obvious active source of infection, making it impossible to identify MOE as the source. Furthermore, the spread of the infection to the cervical spine in patients with skull base osteomyelitis is extremely rare, with only two such cases being described in the literature [13].

CONCLUSION

Unilateral MOE complicated by extensive skull base osteomyelitis in a non-diabetic and immunocompetent patient is uncommon. An extensive skull base osteomyelitis extending up to the contralateral petrous temporal bone and cervical vertebra is exceedingly rare. This case presented multiple concurrent factors: prior radiotherapy treatment, an extensive otitis externa, a rare bacterial infection; perhaps, the sum of these conditions could have caused the extraordinary extension of the infection to the skull base. We recommend early detection of such cases in non-diabetic and immunocompetent patients.

Informed Consent: Informed consent was obtained from the patient during data collection and also from the patient's wife, after his death.

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