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Case Report

Bilateral osteonecrosis of the external auditory canal in a patient on bisphosphonates

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Abstract

Introduction: osteonecrosis of the external auditory canal (OEAC) is a rare and poorly recognized skeletal complication of antiresorptive therapy.

Case report: we present the case of a 57-year-old woman with osteoporosis on a 4-year regimen with alendronate. She was referred to an otolaryngologist for the removal of a cerumen plug in her left ear. Otoscopy revealed ulcerated and painless regions on the floor of both external auditory canals, which were consistent with osteonecrosis.

Discussion: although OEAC is an uncommon skeletal complication of antiresorptive use, the development of localized ear symptoms should alert physicians on this rare clinical entity, prompting them to request an otolaryngological evaluation for early diagnosis and treatment.

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Bisphosphonates.
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INTRODUCTION

Osteonecrosis of the jaw (ONJ) is a rare but well-known complication (1/1500-1/100,000 patients per year) in patients on oral bisphosphonates for osteoporosis (1). Its development is associated with oral health status, dental trauma due to dentoalveolar manipulation, and possibly decreased bone turnover and as a consequence of the antiangiogenic effects of bisphosphonates. However, osteonecrosis of the external auditory canal (OEAC) is a similarly rare but less well-known complication of treatment with these drugs (2). Although in 2017, the UK Medicines and Healthcare products Regulatory Agency (MHRA) recognized this disorder as a complication associated with bisphosphonates and denosumab, there is still very little awareness or knowledge surrounding OEAC among health care professionals (3). Therefore, we describe the case of a 57-year-old woman with osteoporosis on a 4-year regimen with alendronate who developed bilateral osteonecrosis of the external auditory canal.

CASE REPORT

A 57-year-old woman was referred to our clinic after experiencing a vertebral fracture from a fall while climbing down the stairs. She smoked around 20 cigarettes a day and drank about 40 g of alcohol daily. Her past medical history included bronchial asthma since childhood, adjustment disorder, early non-surgical menopause at age 42, and traumatic fractures of the right tibial plateau and distal fibula. At that time, she was on duloxetine, mirtazapine, and inhaled bronchodilators (beclomethasone/formoterol/glycopyrronium).

Physical examination revealed a BMI of 17.1 kg/m^2 with slight dorsal kyphosis, but no other significant findings. Complete blood count, ESR, routine biochemistry, including calcium, phosphate, and magnesium levels, proteinogram, TSH, and urinalysis all turned out normal. Levels of 25-hydroxyvitamin D (25[OH]D) were low (5 ng/mL) and PTH was slightly elevated (66 pg/mL; normal range [N]: 15-65 pg/mL), while the N-terminal propeptide of type 1 procollagen (P1NP) was slightly increased (90.3 ng/mL; N: 22-60 ng/ml) and the carboxy-terminal telopeptide of type 1 collagen (CTX) was at the high end of the normal range (0.400 ng/mL; N: 0.132-0.410 ng/mL).

Imaging modalities (dorsolumbar X-ray and lumbar-sacral CT) showed an acute fracture of L3 (height loss of the superior endplate < 25 %) and a chronic fracture of L1 (height loss of 30 %). Bone densitometry revealed values consistent with osteopenia in the lumbar spine (T-2.0) and total hip (T-2.2), femoral neck osteoporosis (T-2.5), and a degraded trabecular bone score (TBS, 1.024). Consequently, treatment with alendronate and calcifediol was initiated and was well tolerated.

Four years later, she was referred by her primary care physician to the Otolaryngology Department for the removal of a cerumen plug in her left ear. After the removal of bilateral cerumen plugs impacted at the floor of the external auditory canal (EAC), otomicroscopy revealed osteonecrosis-consistent ulcerated and painless regions in the floor of both EACs. The computed tomography (CT) of the temporal bones (Fig. 1) revealed the presence of mild soft tissue thickening in the walls of both EACs—particularly in the external and middle thirds—associated with small bone erosions in the anterior wall and floor of both EACs, more evident in the left ear, consistent with the clin-

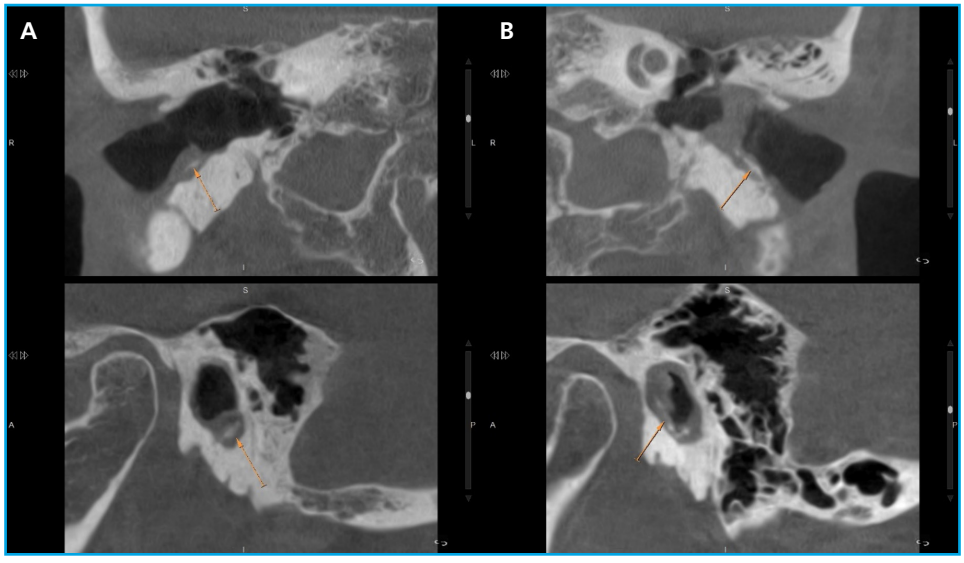

Figure 1. Cone beam computed tomography (CBCT). Coronal and sagittal reconstructions of both external auditory canals (EACs). Moderate stenosis of both external auditory canals (A: right; B: left) due to circumferential soft tissue (likely necrotic skin) and within this, fragmentation and bone sequestra (orange arrows) of the bony cortex. Findings are more prominent on the left side.

ical suspicion of external auditory canal osteonecrosis. The patient had no previous history of treatment with systemic corticosteroids or local radiotherapy, nor any history of malignancy or diabetes. Routine biochemical data were normal. The concentration of 25(OH)D had increased (28 ng/mL) and the markers of bone remodeling had decreased significantly (P1NP: 43.8 ng/mL; CTX: 0.198 ng/mL). Alendronate was discontinued and treatment with teriparatide was initiated. Lesions did not progress at the 2-year follow-up, and the recurrent formation of wax plugs in the necrotic area persisted without complete healing but with clear improvement.

DISCUSSION

Osteonecrosis of the EAC (OEAC) is a rare skeletal complication associated with the use of antiresorptive drugs (2,3). It was first described in 2006 by Polizzotto et al. (4) in a patient with multiple myeloma treated with intravenous bisphosphonates. Since then, around 40 cases have been reported in the literature (3). It is characterized by the appearance of a circumscribed, painless ulcerated area, mainly on the floor of the EAC (2). Some patients may present with otorrhea, otalgia, or recurrent infections, and in advanced stages, facial paresis, hearing loss, and possible involvement of the mastoid and temporomandibular joint. OEAC is a poorly recognized clinical diagnosis among specialists, even otolaryngologists. Additionally, it can be confused with other conditions, such as EAC cholesteatoma or malignant external otitis (2). Similar clinical findings have been made with other antiresorptives, such as denosumab, and with other drugs, such as sorafenib, sunitinib, or bevacizumab, leading some authors to prefer the term drug-related EAC osteonecrosis to describe this condition (3). As with ONJ, OEAC is typically defined as the presence of exposed bone in the EAC for more than 8 weeks in the absence of prior local radiotherapy and after excluding the presence of cholesteatoma or metastasis (5).

According to the literature, the published cases predominantly involve patients diagnosed with osteoporosis (65 %) and, less frequently, patients with malignant neoplasms (35 %) who had undergone prior chemotherapy (3). In the systematic review published by López-Simón et al. (2), the most common presentation was an overinfected ulcer with unilateral bone exposure. Bilateral involvement occurred in about one-third of cases, as in our patient. The initial site of onset was the floor of the auditory canal. Regarding accompanying symptoms, slightly more than one-third of the patients sought medical attention for the onset or exacerbation of a wax plug, while the remaining patients reported chronic otalgia and otorrhea. In some cases, the patient may be asymptomatic or may more easily form wax plugs, as it happened in our case, where the lesion was detected after cerumen removal.

Although the etiopathogenesis of the disease is not fully understood, it is thought that, as it happens with ONJ, local inflammation and infection phenomena, and the inhibition of bone remodeling and angiogenesis, are involved (3,4). In addition to antiresorptive and antiangiogenic therapy, corticosteroids, chemotherapy, minor trauma caused by cotton swabs or fingers, and wax plugs with the formation of wounds in the EAC can be considered risk factors for osteonecrosis. Most cases occurred in patients who had been treated for more than 2 years, and, at least, one-quarter of the patients also had ONJ (3,6).

Imaging modalities are not initially essential to establish the diagnosis. CT of the temporal bone is useful to determine the extent of the lesion, exclude the presence of underlying myeloma, and rule out bone metastases. Technetium-99 bone scintigraphy may be helpful as it can detect subclinical osteonecrosis, confirm the diagnosis of osteomyelitis, and distinguish it from the presence of malignant lesions (2). In cases in which biopsies of the lesions were performed, necrotic and local inflammatory bone changes were observed (7).

As with ONJ, initial treatment is usually conservative and based on the potential discontinuation of the risk drug and treatment with topical corticosteroids and topical or systemic antibiotics. The outcomes have been varied and poorly defined: some cases respond well to conservative therapy, while others require more extensive treatment, such as IV antibiotics, debridement, or surgical resection of the necrotic bone and subsequent reconstruction. However, cases of recurrence after surgical treatment have been reported, so debridement is usually limited to the removal of bone sequestra and sharp edges that may cause repeated direct trauma to the EAC (2,3,7).

In conclusion, OEAC is a very rare and poorly recognized complication of antiresorptive therapy. The development of otorrhea, otalgia, or hearing loss during antiresorptive treatment should alert physicians to this rare clinical entity so that an otolaryngological evaluation can be requested to facilitate early diagnosis and treatment of this condition, preventing the progression of the lesions.

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