Osteonecrosis of the temporal bone secondary to bisphosphonates: a potentially life threatening complication.

N Amiraraghi, MMC Yaniza, Y Husami, A Iyer, NHS Lanarkshire, Scotland.

ABSTRACT

Background
Osteonecrosis of the mandible related to bisphosphonates is well described in the literature. Bisphosphonate-related osteonecrosis of the external ear canal has been reported but temporal bone involvement is extremely rare. We describe two cases of this rare but important complication.

Methods
Case study.

Results
A 53 year old lady with limited attic cholesteatoma was listed for mastoidectomy. She had received intravenous bisphosphonate therapy for osteoporosis and was concerned about the risk of osteonecrosis. Consultation with Rheumatology confirmed that previously reported cases were restricted to the jaw in patients with poor dental hygiene who received high dose intravenous bisphosphonates for cancer and rarely reported in oral or intravenous treatment for osteoporosis. Intra-operatively the whole of the tegmen was noted to be brittle. A large piece of tegmen was found detached from the surrounding bone but was not affected by cholesteatoma. The tegmen defect was repaired with conchal cartilage with no complications detected during follow-up.

A 57 year old lady on bisphosphonates, presented with a left sided lower motor neuron (LMN) facial palsy and otalgia. She had extensive comorbidities, including osteonecrosis of the jaw. The left ear canal had an area of exposed bone in the posterior-superior canal with overlying debris. CT scan demonstrated bone erosion involving the descending facial nerve, floor and anterior wall of external ear canal. Unfortunately extensive comorbidities have prevented surgical management in this patient’s case. Although repeat CT scans are promising, the facial palsy has not resolved.

Conclusions
Bisphosphonates can cause osteonecrosis of the temporal bone in patients with localised infection at doses used to treat osteoporosis. The otolaryngologist should be aware that complications such as tegmen erosion and facial palsy may occur in patients on bisphosphonates.

INTRODUCTION

Osteonecrosis is a common condition that affects approximately 10 million people in the USA (1) and 3 million people in the UK approximately and causes over a quarter of a million fractures per year (2). Bisphosphonates are a common treatment for osteoporosis and work by maintaining bone density by suppressing osteoclastic activity. Bisphosphonates are also used in oncology patients for complications associated with malignant bone metastasis. A known complication of bisphosphonate treatment is osteonecrosis of the jaw however osteonecrosis of the temporal bone is incredibly rare and only eleven cases have been reported in the literature. We describe two further cases with severe and important clinical presentations. Firstly in a patient with concomitant cholesteatoma and secondly a patient presenting with facial palsy. Both of these patients were on bisphosphonates for the treatment of osteoporosis. In each of there was history of infection which may have triggered the bisphosphonate related osteonecrosis.

CASE STUDIES

A 53 year old lady with limited attic cholesteatoma was listed for mastoidectomy in March 2012. She had received annual intravenous Zolendronic acid therapy for osteoporosis since 2010 and was concerned about the risk of osteonecrosis. She had received two infusions and was due to have a third and final infusion 6 months after the mastoidectomy. Rheumatology opinion deemed her at low risk for osteonecrosis as the literature described the complication in patients receiving high dose intravenous bisphosphonates for oncological indications and was usually seen in patients with poor dental hygiene. Osteonecrosis was rarely reported in lower, oral or intravenous doses used in the treatment of osteoporosis. Given this reassurance the patient elected to proceed with surgery. Examination of the ear under anaesthetic had demonstrated a small attic retraction pocket. Pre-operative CT scanning had demonstrated limited cholesteatoma (Fig 1) Intra-operatively there was cholesteatoma lateral to the head of the malleus, long process of incus and around the incudostapedial joint. The cholesteatoma was found to abut the tegmen but there was no involvement of the tegmen. However during the exploration of the middle ear, 3cm of the tegmen was brittle and was found to be detached from the surrounding bone. The tegmen defect and small cavity was obliterated with conchal cartilage. The patient is doing very well on review with hearing thresholds of 15-20dBHL bilaterally.

Fig 1. Axial CT of mastoids demonstrating soft tissue density opacification lateral to malleus in the right ear. Tegmen appears intact.

A 57 year old lady on monthly alendronate for osteoporosis presented with left sided otalgia and left facial nerve palsy. Her past medical history included seven episodes of deep vein thrombosis, four episodes of pulmonary emboli, Crohns disease with colostomy, left below knee amputation and a recent admission to the Intensive Care Unit (ICU) with pneumonia. During the ICU admission she had a myocardial infarction and developed osteonecrosis of the mandible secondary to bisphosphonates. She was not previously known to the Ear, Nose and Throat (ENT) department but history revealed relapsing and remitting episodes of otitis externa over the preceding three years that was managed in Primary Care with topical antibiotic ear drops. On presentation to the ENT department she had a left sided House-Brackmann Grade 6 lower motor neuron facial nerve palsy. Examination of the left ear demonstrated findings in keeping with otitis externa with an oedematous ear canal which was filled with mucopus and debris. The tympanic membrane was intact and microsuction revealed exposed bone. The tegmen defect and small cavity was obliterated with conchal cartilage. The patient is doing very well on review with hearing thresholds of 15-20dBHL bilaterally.

Fig 2. Sagittal images: Red arrows demonstrate facial nerve and blue arrows bony erosion.

DISCUSSION

Bisphosphonate related osteonecrosis of the jaw (BRONJ) has an incidence of approximately 1 in 10,000 (3) and was first described in the literature in 2003. The number of patients treated with intravenous and higher doses of bisphosphonates. Further risk factors include longer duration of treatment and poor oral hygiene. The exact aetiology is unknown however it is believed to be due to the inhibition of bone turnover (4). Other factors can include poor vascular supply, local infection or surgical procedures.

The Otologist may be aware of BRONJ of the external auditory canal, as 11 cases have been reported since 2005, 10 of which have occurred in patients with multiple myeloma on high intravenous doses of bisphosphonates causing facial nerve palsy (5). Importantly our patients were on standard low doses for osteoporosis but still experienced side effects.

The chemical structure of bisphosphonate is similar to pyrophosphate. Pyrophosphate is a compound formed by the hydrolysis of ATP to AMP in cells and prevents ‘calcification’ of the blood. Bisphosphonates inhibit bone metabolism as it helps control the rate of calcification in the normal skeleton. (11) Bisphosphonates are an analogue of pyrophosphate thus have an affinity for hydroxyapatite in bone. Once absorbed, bisphosphonates deposited in bone can remain for many years. Bisphosphonates also inhibit osteoclastic (thus resorptive) activity. Bisphosphonates which contain a nitrogen group have a greater affinity for hydroxyapatite and thus greater inhibition of bone resorption. (12) Inhibition of bone remodelling over longer periods of time is felt to be a likely cause for osteonecrosis of the temporal bone, as gingivitis and tooth decay is to BRONJ.

CONCLUSION

As Otolaryngologists we should be aware of the possibility of osteonecrosis of temporal bone with bisphosphonates. This should involve counselling our patients with chronic ear infections of the risks of taking bisphosphonate medications. In addition an accurate and thorough drug history, as these medications are often taken on a weekly, monthly or annual basis, will ensure this condition is included in our differential with those patients presenting with chronic ear infection or cranial nerve palsy.

Reference