

Bisphosphonate-induced osteonecrosis of the ear canal: our experience and a review of the literature

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Abstract

Background: Oesophageal disorders and osteonecrosis of the jaw are recognised complications of the commonly prescribed medication bisphosphonate. Despite these diagnoses being seen comparatively frequently within the ENT clinic, osteonecrosis of the external ear is a less well reported complication.

Methods: The current literature is reviewed and our experience with six cases of bisphosphonate-related ear canal osteonecrosis is presented.

Results: Six cases were identified as suffering from ear canal osteonecrosis as a result of bisphosphonate treatment. One of our cases suffered bilateral ear canal osteonecrosis after only 20 months of oral alendronic acid treatment. Management ranged from bisphosphonate cessation and topical treatment, to surgical debridement in the operating theatre.

Conclusion: Bisphosphonate-related ear canal osteonecrosis is undoubtedly under-diagnosed. For such a commonly prescribed medication, the risks and side effects of bisphosphonate should be better known and long-term treatment should be avoided if possible.

Key words: Osteonecrosis; Bisphosphonates; Otology; Complication

Introduction

Osteoporosis is a systemic skeletal disorder that reduces bone mineral density, with an associated increase in the risk of fractures. It is a huge social and economic problem. It is estimated that 50 per cent of women and 20 per cent of men aged over 50 years are at risk of osteoporotic fracture. In the UK alone, in 2011, £6 million per day was spent on the treatment and social care of the 230 000 osteoporotic fracture patients.¹

Bisphosphonates are the most commonly prescribed medication for osteoporosis. They are also used in the treatment of multiple myeloma, and in cases of breast cancer and Paget's disease.

By incorporating calcium into bone matrix and reducing osteoclast apoptosis following transcytosis into the cells, bisphosphonates do not alter the physicochemical structure of bone.

There is limited evidence to show the efficacy of bisphosphonates beyond three to five years; therefore, some have advocated a 'drug holiday' with a break in treatment.² Despite this, many patients remain on bisphosphonates for much longer than the five-year period. This duration of treatment may expose them to a higher risk of side effects.³

The recognised side effects, as published in the British National Formulary, include: oesophageal reactions, hypocalcaemia, atypical fractures, atrial fibrillation, musculoskeletal pains, ocular inflammation, renal impairment and bisphosphonate-related osteonecrosis of the jaw. An unrecognised complication of bisphosphonates in the British National Formulary is osteonecrosis of the ear canal. We have recently

treated six patients with bisphosphonate-related ear canal osteonecrosis.

Case reports

We present six patients, five females and one male, with an average age of 80 years (range, 69–89 years), who presented to ENT out-patient clinics. Two of these patients attended with chronic otitis externa refractory to topical treatments in the primary care setting, whilst the rest attended because of the onset or exacerbation of wax impaction.

All six patients were on bisphosphonates for the management of osteoporosis or to reduce the risk of osteoporotic fracture. The duration of treatment ranged from 20 months to over 15 years. None of the patients were diabetic, had previous exposure to radiotherapy or were immunocompromised.

In all cases, initial management involved out-patient microsuction, and the application of steroid and antibacterial ointment. In the two cases presenting with infection, this settled the superficial infective process, but at 12 months follow up only one of these two cases had fully resolved. In the second case, following discussion with the patient's general practitioner, we decided against cessation of bisphosphonate. The exposed areas were bilateral at presentation and have reduced in size, and the patients remain under close clinical follow up.

In the remaining four cases, bisphosphonates were discontinued, and three of the patients responded well to out-patient microsuction and topical therapies. The patients continue to

be followed up, and a year from referral they are all fully healed. The fourth patient in this group had not responded, and underwent a biopsy to rule out malignancy. The biopsy findings were negative. She was subsequently taken to the operating theatre for surgical debridement to healthy bone, and temporalis fascia was used to line the external ear canal. Six weeks following surgery, she was pain free and the affected area was fully healed. The area remains stable at 18 months.

Discussion

Osteonecrosis of the ear canal secondary to bisphosphonate treatment has been reported in a handful of case reports and papers. In the first case report, published in 2006, a patient receiving intravenous bisphosphonates for the treatment of multiple myeloma, developed bilateral exostoses with superimposed infection.⁴ The left ear was operated on. Six months later, a painless ulcerated area at the site of surgery in the left ear canal was identified. Necrotic bone was exposed, extending beyond the ulceration. There was no clinical or radiological evidence of myeloma deposition or infection, and so the changes were deemed to be secondary to bisphosphonate. The condition improved with cessation of the bisphosphonate and local debridement. The proposed theory is that bones demonstrate a reduced ability to respond to physiological demands in the presence of a bisphosphonate-induced reduction of osseous remodelling and blood flow.

The first case series presented three patients with bisphosphonate-related osteonecrosis, two with unilateral symptoms and one with bilateral symptoms.⁵ The patients had received intravenous bisphosphonate for the management of multiple myeloma or breast cancer. Successful resolution was achieved with bisphosphonate discontinuation and surgical debridement.

There was an epidemic of bisphosphonate-related osteonecrosis of the jaw, many years before the development of bisphosphonate medications. Yellow phosphorous was used in the match-making industry in the nineteenth century and, when inhaled, bisphosphonates were created. With continued exposure, many factory workers developed a debilitating disease known as ‘phossy jaw’. The office workers, shielded from exposure, escaped the disease. The reported mortality was 20 per cent.⁶

- **Bisphosphonates are commonly used for treatment of osteoporosis and other conditions**
- **Concerns have been raised regarding the implications and risks of long-term treatment**
- **We have treated six cases of the rarely reported bisphosphonate-related ear canal osteonecrosis**
- **Most patients respond to bisphosphonate cessation and topical treatment**
- **The risks and side effects of such a commonly prescribed medication should be better known in the clinical community**

There is an abundance of literature on bisphosphonate complications linked to bisphosphonate-related osteonecrosis of the jaw. Many of the conclusions drawn may be transferred to the otology setting. Whilst initially reported with the administration of intravenous bisphosphonate, oral

bisphosphonates have also been reported to cause osteonecrosis of the ear canal.⁷

We have presented six further patients, one of whom developed complications after only a year and a half of oral bisphosphonate treatment. Interestingly, a large study into bisphosphonate-related osteonecrosis of the jaw, found that the incidence within the UK is highest in Liverpool and Northern Ireland. It is unclear what environmental factors may play a role. That study calculated the risk of bisphosphonate-related osteonecrosis of the jaw as between 1:1000 and 1:10000.⁸ More research is required to provide an accurate figure for bisphosphonate-related osteonecrosis of the ear canal.

Pertinent to otolaryngologists are the oesophageal problems encountered with bisphosphonates. In fact, these medications are contraindicated in any patients with an oesophageal abnormality. Oesophageal problems range from simple inflammation to ulceration, strictures and perforation. There is an ongoing debate regarding the increased risk of oesophageal malignancy attributed to bisphosphonates. Evidence is conflicting, but recent meta-analyses have found no increased risk.^{9,10}

The risks and side effects associated with bisphosphonates are numerous. These medications are used on such a massive scale that we will all invariably deal with patients who have suffered some of these ill effects. As otolaryngologists, we should be vigilant in taking good drug histories, and piecing together any ear, oral or oesophageal symptoms that are likely to be due to these medications.

Admittedly a rare disease, bisphosphonate-related osteonecrosis of the ear canal carries significant morbidity for the patient, and as such is of clinical importance. As we become more astute with making the diagnosis and bisphosphonates continue to be prescribed across our ever-ageing population, we will undoubtedly encounter it more frequently.

Bisphosphonate-related osteonecrosis of the ear canal needs to be recognised in the medication literature, and the specialties prescribing the drugs should be aware of the effects. A review of a patient’s prescription is also encouraged, so as to avoid continued exposure beyond three to five years, if possible.

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