CASE REPORT

Fungal malignant otitis externa

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SUMMARY

An 89-year-old man presented to the outpatient clinic with a 2-month history of persistent unilateral left-sided otalgia, otorrhoea and reduced hearing despite oral and topical antibiotics. Treatment was protracted, requiring a 4-month hospital admission for intravenous antifungal medication as well as 3 further months of oral antifungal treatment. We describe the clinical presentation, complications and treatment of this potentially fatal condition in the context of an unusual, and easily missed, causative organism.

BACKGROUND

This case report highlights fungal infection as a rare but important cause of malignant otitis externa (MOE). It emphasises the clinical importance of considering fungal infection in refractory MOE and describes the diagnosis and management with reference to the growing literature.

CASE PRESENTATION

An 89-year-old man was referred to the ENT outpatient clinic with a 2-month history of severe unilateral left-sided otalgia and otorrhoea productive of a thin, white discharge. There was no history of recent trauma. Prior to referral to the ENT department, care in the community had comprised of aural irrigation with syringing, and oral and topical antibiotics (amoxicillin/clavulanic acid 625 mg orally three times a day and framycetin/gramicidin/dexamethasone two drops three times a day, respectively). His past medical history comprised hypertension, atrial fibrillation, previous prostate cancer and a transient ischaemic attack 15 years prior. There was no history of diabetes mellitus, prolonged systemic steroid use or HIV infection. Examination revealed an oedematous, collapsed left external auditory canal (EAC) occluded with thick white, blood-stained debris. A large fleshy polyp arising from the medial, posterior-inferior ear canal wall was noted. Examination of the contralateral right ear and cranial nerves examination were normal. The patient was a known bilateral hearing aid wearer and audiometry showed symmetrical moderate to severe presbycusis.

INVESTIGATIONS

The patient was admitted to hospital for further investigation and treatment with intravenous antibiotics, analgesia and aural toileting. Baseline observations showed the patient to be haemodynamically stable and afebrile. Admission blood tests showed an elevated C reactive protein (CRP) of 40 mg/L but were otherwise unremarkable (white cell count $8.0 \times 10^9/L$, platelets $206 \times 10^9/L$, serum glucose

6.7 mmol/L, urea 8.3 mmol/L, creatinine 89 $\mu\text{mol/L}$). A swab of the infected left ear was taken for microbiological culture from which was cultured *Candida albicans*. Acid-fast bacilli staining was negative. A CT scan of the temporal bones showed extensive destructive disease of the middle ear, mastoid cells and surrounding ear canal ring of the temporal bone (see figure 1).

DIFFERENTIAL DIAGNOSIS

Malignant otitis externa.

TREATMENT

The patient was treated with intravenous piperacillin/tazobactam (4.5 g three times a day) and gentamicin (4 mg/kg once daily) on advice from the hospital microbiology department. *C. albicans* was cultured from the ear swab. Oral and topical antifungals were added to the antibiotic treatment (fluconazole and clotrimazole) which was continued due to the strong possibility of concurrent bacterial infection. After a week of treatment, the patient's symptoms still persisted. The aural polyp was excised and a biopsy of the ear canal performed under general anaesthesia. Histology from the aural polyp was consistent with local inflammatory changes and showed no evidence of dysplasia or malignancy.

In the week following surgery, the otalgia resolved. However, 1 week postoperatively, the patient became acutely dysarthric, with examination revealing a left hypoglossal nerve palsy. An urgent MRI scan was performed and revealed osteomyelitis of the left temporal bone extending

Figure 1 CT scan of temporal bones showing destructive middle ear disease surrounding ear canal ring of the left temporal bone.

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Figure 2 MRI with contrast showing disease involvement of the left hypoglossal canal.

to the skull base involving the hypoglossal canal (figure 2) and soft tissue thickening of the left nasopharyngeal wall. There was no evidence of acute stroke. The patient underwent another surgery during which the cortical mastoid bone was debrided and a tympanostomy tube inserted. Biopsies of the EAC, temporomandibular joint (TMJ) capsule and nasopharynx were taken for histopathology and microbiology but the results showed only extensive inflammation. Fungal and microbiological cultures of the specimens were negative.

On advice from microbiology, antifungal treatment was changed to intravenous anidulafungin (100 mg OD) which was continued until his discharge from hospital 9 weeks later. Over the following week, the patient's hypoglossal nerve palsy resolved and inflammatory markers fell (CRP from 40 mg/L to 9 mg/L and erythrocyte sedimentation rate (ESR) from 52 mm/hour to 28 mm/hour). Radiological imaging performed 6 weeks later confirmed regression of the osteomyelitis.

OUTCOME AND FOLLOW-UP

The patient was discharged following 3.5 months in hospital, on oral voriconazole with weekly review in the outpatient setting. Six months following discharge from hospital, the patient remains under outpatient review. His condition is stable, with no evidence of residual or recurrent disease.

DISCUSSION

MOE is an uncommon, but potentially fatal, complication of otitis externa affecting immunocompromised and elderly patients, particularly those with diabetes.¹ Patients present with severe otalgia, hearing loss and purulent otorrhoea with infection spreading from the ear canal to the temporal bone via the fissures of Santorini.² There may be associated TMJ pain, oedema of the external ear canal, coexisting chronic suppurative otitis media and/or aural polyp.³ In severe cases, associated cranial neuropathy may occur. The facial nerve is most often affected, commonly at the stylomastoid foramen.^{1 2} The glossopharyngeal, vagus and spinal accessory nerves may be affected at the level of the jugular foramen, as may the hypoglossal nerve as it passes through the hypoglossal canal. Rarely, petrous apex infection may result in involvement of the trigeminal and

abducens nerves.¹ While the pathophysiology is not completely understood, factors which are thought to contribute include diminished host resistance (eg, diabetes mellitus, HIV infection), microangiopathy and local hypoperfusion.⁴ Aural water exposure (such as irrigation for cerumen impaction) has also been reported as a potential iatrogenic factor.⁴ In the case we report, aural irrigation received in the community may have caused minor trauma in the already inflamed external ear canal, leading to fungal infection over the pre-existing bacterial infection.

The most commonly associated causative micro-organism is *Pseudomonas aeruginosa*, although cases of *Staphylococcus epidermidis*, *Proteus mirabilis* and *Klebsiella oxytoca* have also been reported.⁵ Fungal infection is increasingly recognised as a cause of MOE with *C. albicans* and *Aspergillus* species the most commonly implicated micro-organisms.^{5 6} Fungal and bacterial culture may be negative at initial presentation^{3 5} with positive culture arising only later in the treatment process. It has been suggested that fungal pathogens result as an opportunistic infection, due to prolonged intravenous antibiotic treatment of a primary bacterial MOE.⁵ A case series of 60 patients with MOE found a more invasive disease process in the fungal, compared

Patient's perspective

When I began to experience deafness and pain in my left ear my general practitioner began a treatment of wax removal (with syringing) and antibiotics but to no avail and I was referred to the ENT department. After further tests, the consultant diagnosed a fungal condition, malignant otitis, and said I must be hospitalised at once. I began a range of tests, and biopsy investigations, into and behind my left ear and nose. Various daily antibiotic treatments were begun, also proving to no avail. These upset me and I began to feel quite unwell. Good news came from the biopsies—no malignancy had been found. Less happy was that treatments so far were only making me more unwell. Having always had good health, after some 6 weeks in hospital, I had lost 3 stones in weight and became so weak that I could hardly get out of bed unaided. Although trying to keep my own spirits up, even my sons began to think that I was losing the battle for life. Sadly, nor did I much care if it were so. Embarrassingly, the intravenous antibiotics were affecting my bowels, and repeated replacement of cannulas in my arms was causing much bruising and anxiety. A peripherally inserted central catheter (PICC) line was put in and the microbiologist and consultant team produced a daily potion with antifungal treatment as well as the antibiotics, infused for 2+ hours a day. This lasted over 2 months but was for me a turning point as I slowly began to recapture some of my former stamina and resolve. The infusion had no upsetting effect, and allowed my bowels to begin getting back in control. I had daily blood chemistry tests to check that the aggressive treatment was working and that my major organs were coping with extra strain.

I cannot think that I could have received better care and effort by the ENT team and other clinicians in their persistence to find a course that tackled the fungal symptom. Some effects of the infection still remain. My balance is not good, although there is no infection or pain. My taste/smell remains greatly impaired. I remain under review of by the ENT consultant and his team in the clinic until they are satisfied that reactivation of the skull base osteomyelitis will not arise.

Learning points

- ▶ Fungal infection should be considered in cases of intractable malignant otitis externa (MOE).
- ▶ The pathophysiology of MOE remains incompletely understood. Factors such as microangiopathy, hypoperfusion and diminished host resistance are thought to contribute. Infection, which may be introduced by minor trauma or aural irrigation, spreads to the skull base through fissures of Santorini.
- ▶ More invasive disease processes may signify fungal infection. Osteomyelitis of the ear canal wall may spread to the temporal bone and skull base, with cranial nerve involvement a sign of advanced disease.
- ▶ Fungal pathogens may result as an opportunistic infection, due to prolonged intravenous antibiotic treatment of primary bacterial MOE
- ▶ Formal diagnosis of fungal MOE is difficult. Tissue biopsy is recommended but may not yield diagnostic proof, with diagnosis based on clinical history and microbiological culture from ear swabs.
- ▶ Management is with intravenous antifungal medication and may require long-term oral antifungal treatment and outpatient follow-up.

with the non-fungal, group characterised by higher rates of facial nerve palsy, a younger mean age and lower 5-year survival rate.⁵ Nasopharyngeal soft tissue involvement, as was the case in our patient, has been shown to be prognostic of aggressive or persistent disease.⁷

Treatment of MOE is largely medical with combined prolonged systemic and local antibiotic and/or antifungal treatment lasting 6 weeks to several months in intractable cases. Strict control of diabetes and regular aural lavage is also required. Radiological imaging performed at presentation confirms the diagnosis and serves as a baseline from which to monitor treatment response. CT scanning is the preferred modality while technetium-99 m bone scanning is more sensitive for MOE but lacks specificity. Gallium-67 scanning shows positive uptake during the active disease process, returning to normal once the infection has resolved and is therefore beneficial in monitoring treatment response.³ ESR may be elevated and although not

diagnostic, is a useful prognostic marker.³ Hyperbaric oxygen therapy has been used in persistent cases, although its limited availability and evidence base mean that it is not currently common practice.^{5 8} Some reports advocate debridement of infected tissue, while others recommend that surgery is reserved for removal of granulation tissue and histopathological purposes.^{3 5} Treatment of fungal MOE requires the addition of antifungal therapy, with antibiotic medication continued initially due to the likelihood of underlying primary bacterial infection. Itraconazole, fluconazole and amphotericin B have been the preferred treatments, with voriconazole playing an increasingly important role since it became available in 2002, particularly in cases of invasive *Aspergillus* or resistant *Candida* spp.^{5 6} Anidulafungin is effective in cases of invasive candida infection. Monitoring of liver and renal function is required due the hepato-toxic effects of many antifungal medications. Treatment may be protracted. In some cases, patients without cure may require lifelong treatment with oral antifungal medication.⁵

Contributors PFB, VP and ES made substantial contributions to the conception or design of the work, or the acquisition, analysis or interpretation of data. All authors drafted and revised the work including critical appraisal for important intellectual content. They approved final version to be published. PFB, VP and ES agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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