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Malignant Otitis Externa: A Review of Aetiology, Presentation, Investigations and Current Management Strategies

Corresponding Author:
Mr. Oladejo Olaleye,
Specialty Registrar, Otolaryngology - Head & Neck Surgery Department, Russells Hall Hospital - United Kingdom

Submitting Author:
Mr. Oladejo Olaleye,
Specialty Registrar, Otolaryngology - Head & Neck Surgery Department, Russells Hall Hospital - United Kingdom

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Author(s): Illing E , Olaleye O

Review

Background

Malignant otitis externa (MOE), an aggressive infection involving the external auditory canal and temporal bone was first reported in the literature by Toulmouche in 1838. In 1959 Meltzer and Kelemen identified a case of osteomyelitis of the temporal bone due to pseudomonas and malignant otitis externa was described and characterized as a unique clinic entity by Chandler in 1968. This type of otitis externa was termed malignant, due to the high mortality rate, aggressive disease progression and poor response to available treatment.

Aetiology:

Pseudomonas is the commonest cause of MOE1. Resistant strains of pseudomonas have been described following treatment with ciprofloxacin2,3. Staphylococcus aureus has been identified and can be methicillin-resistant staphylococcus aureus4, and rarely staphylococcus epidermidis5.

Fungal MOE is mostly due to aspergillus6 and candida but some unusual organisms have been identified as a cause such as scediosporum apiospermum7, and malassezia sympodialis8. A mixed infection involving both bacterial and fungal infection is possible. Ear swabs are routinely taken and sent to microbiology in an attempt to identify the causative agent.

Presentation:

MOE occurs almost exclusively in diabetics and the elderly. The pathogenesis of this condition is unclear, however a number of factors are thought to contribute; microangiopathy, hypoperfusion and diminished host resistance (impaired phagocytosis, poor leukocytic response, impaired intracellular digestion of bacteria) due to diabetes. Their susceptibility to pseudomonas infection is increased by their ear wax being less acidic and having a lower lysozyme content, more favourable to pseudomonas infection. Hypotheses suggest the external otitis progresses from the external auditory canal to the temporal bone and eventually the skull base via the fissure of Santorini and the osseo-cartilaginous junction. Infection is normally introduced by minor trauma or aural irrigation. Isolated cases have been reported in a small number of non-diabetic patients, particularly in children who are immunocompromised due to malignancy, malnutrition and severe anaemia as well as in patients with HIV9. MOE has also been reported in patients who were not diabetic and not immunocompromised10 and as such a high index of suspicion is required. Malignant otitis externa is more common in males and warm, humid climates.

Presenting symptoms include severe, deep seated otolgia, purulent otorrhea, hearing loss and headaches. Facial nerve palsy, swallowing problems and hoarseness may be present if cranial nerve involvement has occurred. On examination, inflammatory changes and granulations are noted in the external auditory canal, although the tympanic membrane is normal. Pain is often out of proportion to changes seen at otoscopy. In a case series of 37 patients with MOE, 51% had diabetes, 40% had facial nerve palsies and 24% had multiple cranial nerve palsies1.

Skull base osteomyelitis first described in 1959, is a recognised complication of MOE and it has a high morbidity and mortality11. Atypical symptoms and findings of unilateral severe otalgia, unremitting headache, and presence of high ESR, unilateral OME, constitute diagnostic clues of skull base osteomyelitis12. Other complications of MOE include temporoparietal abscess13, multiple lower cranial nerve palsies14, 15, Cerebral abscess16, meningitis15 and involvement of the temporo-mandibular joint17.

Cranial nerve involvement is due to both pseudomonas neurotoxins and inflammation occurring along the skull base as the disease progresses. The facial nerve is classically the most common and first cranial nerve involved in the disease process, at the stylomastoid foramen. Cranial nerves IX, X and XI may become affected as the jugular foramen becomes involved, as may V and VI if the petrous apex is affected. The incidence of cranial nerve palsy is decreasing with early and improved antibiotic therapy. Facial nerve paralysis does not always resolve despite full treatment of the disease and should not be used as an indicator of successful disease treatment. Other cranial nerves have good rates of recovery.

Levenson's criteria can be used to diagnose malignant

otits externa. Criteria include; refractory otitis externa, severe nocturnal otalgia, purulent otorrhoea, the presence of pseudomonas and granulation tissue in the external auditory canal and diabetes or an immunocompromised state.

There are a number of staging classifications for the disease and generally:

Stage 1 – purulent otorrhoea, otalgia (out of proportion), granulation tissue on otoscopy.

Stage 2 – disease extends to soft tissues and skull base. Involvement of CN X1 and X11 occurs.

Stage 3 – intracranial extension.

Intracranial complications include meningitis, brain abscess and dural sinus thrombosis. These are commonly fatal and reflect severe disease progression. Sigmoid sinus thrombosis should be considered if the disease involves the jugular foramen, likewise, cavernous sinus thrombosis should be considered if there is evidence of cranial nerve V or V11 involvement.

Investigations:

Base line blood tests are essential. Biochemical markers give an indication of the underlying renal function and any pre-exisitng renal dysfunction, particularly in the diabetic patient. C Reactive Protein and Erythrocyte sedimentation rate are raised in malignant otitis externa. With appropriate treatment they will start to decrease within 2 weeks and eventually return to normal. White Cell Count is often normal or only mildly raised despite the aggressive nature of this infection. All patients not known to be diabetic should be tested for this condition and the possibility of underlying immunodeficiencies.

Ear swabs are essential to guide the choice of antimicrobial therapy and should ideally be taken prior to commencing antibiotics, either topical or systemic. They should be sent for culture and sensitivity. Imaging to establish the extent of disease is routine nowadays. A CT scan defines the anatomical extent of the disease and remains the initial investigation of choice. Subtle changes in bone density can be picked up, along with swelling in the nasopharynx and parapharyngeal space. Serial CT scanning helps identify the extent of soft tissue swelling, however it is not useful for monitoring resolution of skull base osteomyelitis; significant bone re-mineralization requires time.

MRI scanning is useful for assessing the initial severity of the disease and is excellent at delineating the extent of soft tissue disease present and intracranial complications28. There have been some reports of serial MRI scans being used for follow up.

Radioisotope scans (technetium 99 / gallium 67) have an increasing role in assessing malignant otitis externa. Gallium 67 is a very sensitive but non-specific test, detecting and binding to any cells actively dividing. A base line gallium scan is obtained for comparison followed by serial scans to monitor treatment response. Scanning the affected side and comparing to the non-affected side often improves interpretation of the scan. Gallium scans are useful for comparing radiological improvement to clinical improvement and guiding the length of antibiotic treatment required. Single Photon Emission Tomogrophy (SPET) technology has improved poor spatial resolution, an initial concern with this scan.

Radioactive labelled white cell scans have a role in assessing the presence and degree of osteomyelitis. A study on the various radiological and radionuclide investigations for malignant otitis externa concluded that CT and/or MRI should be supported by routine SPECT bone imaging for initial diagnosis of malignant otitis externa. Routine SPECT bone imaging further supplemented by gallium scintigraphy should be the investigation of choice in the follow up for assessing response to treatment and disease recurrence4, 18, 19.

Dual In-WBC/Tc-99m MDP bone SPECT scintigraphy provides an accurate imaging modality for diagnosis and follow-up of temporal and facial osteomyelitis when existing clinical or postoperative bone changes make it difficult to detect active osteomyelitis by computed tomographic scan31

Treatment:

Treatment for malignant otitis externa may take several months before complete resolution is achieved. Meticulous aural toilet of the affected ear, antibiotics both topically and systemically and strict glucose control in diabetic patients is absolutely vital for success. Analgesia is also required for the severe otalgia associated with this condition.

Classically, first line treatment is with antibiotics, normally, oral ciprofloxacin (a fluoroquinolone with high soft tissue and bone penetration when used orally) in the outpatient setting. However, due to the increased use of ciprofloxacin for both simple ear infections and upper respiratory tract infections there is concern pseudomonas malignant otitis externa infections are increasingly resistant to ciprofloxacin3. These patients require alternative parenteral antibiotics, but do not have an increase in mortality.

If there is no resolution despite oral ciprofloxacin, intravenous antibiotics are used. Antibiotic choice depends upon hospital policy and discussion with microbiology. A number of different regimes have been documented in the literature including prolonged courses of; Meropenem, Tazocin, Ceftazidime and Gentamicin. The length of antibiotics required is

determined by improvement seen on repeat imaging and clinical examination and may be continued even when imaging returns to normal.

Hyperbaric oxygen has been used successfully, in conjunction with antibiotics for cases where intracranial spread has been identified or the disease appears refractory to antibiotics or is recurrent. This treatment involves placing the patient in a compression chamber and increasing the environmental pressure whilst providing 100% oxygen. This increases the oxygen supply to avascular tissue, allowing improved leukocyte function essential for infection resolution. Typical treatment courses involve 15-30sessions of about 1 – 2 hours. A Cochrane review of hyperbaric oxygen was conducted which concluded not enough data was available on suitable patient selection and oxygen dose to provide recommendations.

A Cochrane Review found no clear evidence exists to demonstrate the efficacy of hyperbaric oxygen therapy when compared to treatment with antibiotics and/or surgery20. There were no randomised controlled trials identified on the use of hyperbaric oxygen in the management of MOE. No data were found to compare rates of complication between the different treatment modalities20.

There are however studies that suggest hyperbaric oxygen may be useful in the treatment of MOE21. A large case series of 17 patients with MOE treated with hyperbaric oxygen concluded that although hyperbaric oxygen therapy confers minimal morbidity, its role in the management of these patients is uncertain22. Of the 17 patients, 12 were considered cured of their disease, 3 died from the disease and 2 patients had recurrent disease (with a good outcome after a second cycle of treatment) 22.

Immunomodulators, such as topical tacrolimus to the affected ear have also been reported in the literature as being effective when used in combination with other treatments23, 24.

Surgery in cases of MOE remains controversial. Although initially recommended by Chandler in his original report, the benefit of surgical resection is not well documented. Mastoidectomy can be performed25 but consensus is growing that this may be pointless due to its lack of efficacy against an already extensive process especially with the advent of quinolone antibiotics26. Removal of diseased bone is not recommended due to spread of the disease through fascial and vascular planes. Biopsies can be obtained and drainage of any abscess is recommended. In the presence of facial nerve palsy, decompression is not indicated. The identification and treatment of any underlying immunological deficiency is also very important.

Conclusion

Despite advances in the treatment of malignant otitis externa, multiple complications can ensue including parotiditis, mastoiditis, meningitis, cerebral abscess and jugular vein thrombosis27. There is the emergence of resistant strains of causative organisms to the fluoroquinolones that have improved treatment of these cases. Morbidity and mortality from this condition is still high especially with skull base osteomyelitis and cranial nerve involvement.

Several investigative modalities are currently available and include MRI28, CT Scans, and gallium 67 SPET29, 30. Therapies being used with varying success include immunomodulators and hyperbaric oxygen. The central management principles remain meticulous aural toileting, long-term antibiotics and ensuring adequate glycaemic control.

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