

Malignant Otitis Externa: a review

Abstract: Malignant otitis externa is a rare but potentially fatal disease of the external auditory canal seen mostly among elderly, diabetic or immunocompromised patients. The causative organism is mainly *Pseudomonas aeruginosa*. The disease spreads rapidly, invading surrounding soft tissues, cartilage and bones causing their necrosis and even spreading to the cranial nerves. The disease can be fatal if treatment is not aggressive and timely, especially if it spreads outside the auditory canal with involvement of the cranial nerves. Treatment is mainly medical with antipseudomonal drugs like the third generation cephalosporin and the fluoroquinolones and local debridement. With aggressive treatment the mortality rate from this disease, which used to be 50% in the past has now been reduced to 10-20%. The pathophysiology of the disease, clinical presentation, diagnosis, treatment and the outcome has been discussed and reviewed.

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Introduction

Malignant Otitis Externa (MOE) also known as invasive/granulomatous/necrotising otitis media is an unusual but potentially fatal infective condition of the external auditory canal. Toulmouche first reported it as early as 1838. Meltzer in 1959 reported a case of pseudomonal osteomyelitis of the temporal bone. However first complete report on 13 cases with this infection was published in 1968, of whom 7 patients died subsequently. Chandler, in 1977 was the first person to refer this condition as "malignant" because he observed an aggressive behavior, poor treatment outcome and high mortality if the disease process spreads outside the external auditory canal.

Pathophysiology

Malignant Otitis Externa is an invasive granulomatous infection that invariably originates at the junction of cartilaginous and bony part of the external auditory canal. It commonly affects elderly (>50 years) patients who are

diabetic or immunocompromised. The organism responsible is mainly *Pseudomonas aeruginosa* though multiple bacteria may be cultured. Recent studies have shown strains 2, 6 and 11 to be associated with more aggressive disease.¹ Other organisms seen are *Staph aureus*, *Proteus* species and *Klebsilla*. Diabetics, for unknown reason are more susceptible to this condition irrespective of the type (insulin dependent or non-insulin dependent, well or poorly controlled).² Theories proposed include deficient cell-mediated immunity and tissue hypoperfusion secondary to diabetic microangiopathy.^{3,4} Studies have also shown that cerumen of diabetic patients has a higher pH and reduced concentration of lysozyme, which could impair local antibacterial activity.⁵

The condition may also originate following syringing of the ears in both diabetic as well as non-diabetic patients.^{3,6}

As many as 50% of cases have been reported to be preceded by traumatic aural irrigation in diabetic patients. Some reports have shown the condition to be arisen from acute otitis media as seen in six out of 15 cases reported by Meyerhoff,

Gates and Montaibo in 1977 or also associated with active chronic otitis media as seen in 4 out of 11 patients reported by Doroghazi et al. in 1981.^{7,8}

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The term "necrotizing" and "invasive" is used because in most the infection invades the adjacent deep periauricular tissues into the cartilage and bones resulting in necrosis and osteomyelitis of the temporal bone and base of the skull. Spread of the disease outside the external auditory canal occurs rapidly and progressively through the fissures of Santorini and the osseo-cartilagenous junction into the temporal bone and mastoid. The facial nerve lies in close proximity here as it exits through the stylomastoid foramen and can be affected easily. Facial Nerve is the most commonly affected nerve; a 32% incidence has been reported in Chandler's series.¹⁰ With the recent introduction of more aggressive medical therapy, the incidence of facial palsy has decreased and it does not signify worse prognosis of the

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disease. From here the infection may spread further toward the skull base, involving the jugular foramen as well as glossopharyngeal, vagal and spinal accessory nerve. The petrous apex may be involved where the abducens and trigeminal nerves may be affected. Although as compared to facial nerve other cranial nerves are involved less frequently, they carry grave prognosis with mortality rate as high as 80-100%.

Parotid gland and the paranasal sinuses can also be involved by the aggressively spreading infection and also cause venous thrombosis of the jugular vein, leading to cavernous sinus thrombosis. Meningitis is another fatal complication of this disease.

Incidence

The disease is more common in humid and warm climates. Perhaps this is attributed to the fact that more individuals go swimming in hot weather and, if the skin defense mechanism is already compromised, the combination of getting their ears wet and perhaps irritated by the chemicals in the pool water or contaminated water causes the condition to erupt. It affects elderly, diabetic (> 90%) and, immunocompromised patients as mentioned earlier. In immunocompromised and AIDS patients, younger age group people may be affected. Males are more affected by MOE than females

Diagnosis

History of diabetes mellitus or immunocompression may be elicited from most of the patients. The chief complaint will be severe, unrelenting, deep-seated otalgia. There may be other signs and symptoms like otorrhea, temporal headache as well as neurological involvement in some cases. Examination will reveal inflammatory changes in the external auditory canal and periauricular soft tissue. The pain may mimic diffuse otitis externa or furunculosis but it is out of proportion to the clinical findings. There may be referred pain of the temporomandibular joint present Presence of granulation tissue at the osseo-cartilagenous junction at the floor of the external auditory canal is virtually pathognomic of MOE. Necrosis of the cartilage and bony exposure may be seen in some. The tympanic membrane if visualized is usually intact. Fever is however uncommon unless associated with intracranial complication.

Investigations reveal normal or moderately high leukocytes count, elevated ESR, with average values of 88mm/hour.¹¹ The level of ESR starts decreasing usually after 2 weeks of medical therapy and may normalize over several months. This may support clinical diagnosis, as it is uncommon with

malignancy or acute otitis externa. Known diabetics need an evaluation of the serum chemistry to determine if the infection is affecting their baseline glucose intolerance. Those with no previous history of diabetes should still be tested for glucose intolerance. Depending upon the general condition of the patient and the systemic complications of diabetes other biochemistry findings may vary.

Culture and sensitivities from the external auditory canal will identify *Pseudomonas aeruginosa* as the predominant causative organism (95%). This is a gram-negative rod, which has mucoid coating that deters phagocytosis. It also releases powerful exotoxins, namely exotoxin A, collagenase and elastase that can cause tissue necrosis. Certain strains produce a neurotoxin that may be responsible to some extent for cranial neuropathies

Imaging studies are important adjunct for determining the presence of disease, its extent as well as to determine the modality and response to therapy. Plain radiographic studies have limited role in the diagnosis. CT scan and MRI are helpful in evaluating the anatomical extent of soft tissue, bone erosions, abscess formations and intracranial complications. However, CT scan may not detect early osteomyelitis, as 30-50% of bone

destruction may be required for CT to detect osteomyelitis. MRI on the other hand provides a poor bone resolution. Bone changes will remain persistently abnormal on CT scan for at least one year. Therefore although both tests are advocated for initial evaluation for all cases and both are equally sensitive in detecting the soft tissue extent, neither of the tests can be used to determine osteomyelitis resolution. Technetium -99 bone scan and gallium-67 scan are more sensitive but not specific as it is based on binding to osteoblasts and binding to dividing cells including osteoblasts respectively. Indium -111 has same sensitivity as gallium -67 scan but more specific in cases of inflammatory processes, therefore has role in establishing the correct timing of disease resolution.^{12,13,14}

Biopsy may help to rule out malignancy or other pathologies. Nadol described histopathology of two temporal bones affected by MOE and determined that the infection did not spread through the pneumatized air tracts of the temporal bone. Rather, the infection spread along the vascular and fascial planes on exiting the temporal bone through the external auditory canal osseo-cartilagenous junction or fissures of Santorini. The otic capsule being a tough bone appeared to be resistant to the disease process.¹⁵

In patients with AIDS the presentation may differ in that they are generally younger, not necessarily diabetic. Granu-

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lation tissue may not be seen and the organism responsible may not be predominantly *Pseudomonas*. These patients have worse prognosis than the diabetic patients.¹⁶

The condition can at times be misdiagnosed as acute otitis externa or otitis media with complications. Other differential diagnosis includes squamous cell carcinoma, glomus jugulare, Wegener's granulomatosis, Han Schuller-Christian disease, eosinophilic granuloma, chordoma of the clivus and meningeal carcinoma.

MOE in children

In children no true pathognomonic features of MOE are demonstrated. Rubin reported 15 cases of MOE in 1988 of which the predominant risk factor was immune dysfunction and not diabetes. They may present with sudden onset of severe earache, ear discharge and hearing loss. Tympanic membrane unlike adults was commonly involved and so was the presence of bacteremia. Facial nerve palsy is more common in children probably due to anatomic variation.⁴

Levenson, Corey, Benecke, and Davis have all proposed staging system for MOE based on soft tissue and bony involvement or neurological involvement. However these staging systems are not widely accepted or adopted.

Treatment

The guidelines of treatment are as follows

1. Control of blood sugar level and improve the general condition of the patient including nutrition, immunity and other co-morbidity.
2. Aural toilet and local debridement of granulation tissue and external auditory canal.
3. Aggressive treatment with suitable antimicrobial agent (topical and systemic).

Choice of antibiotic

In the past the standard regime used to be anti-pseudomonal penicillin such as piperacillin, ticarcillin, mezlocillin or azlocillin and aminoglycosides. In the recent past the new drugs like the third generation cephalosporin and fluoroquinolones that attain high soft tissue and bone levels even with oral doses have replaced the older antimicrobials. Several studies have shown effective control with systemic ceftazidime (Fortaz), cefotaxim (Claforan) or moxalactam (Moxam).^{11,21,22} Oral ciprofloxacin (Cipro) has also been proven successful given with or without ri-

fampicin. This drug in turn has added value of being cost effective, bactericidal as well as less ototoxic side effect as compared with the aminoglycosides.^{17,18-20} More studies with oral ciprofloxacin in the management of MOE are being carried out.

Duration of therapy, according to the protocol determined by Benecke for 13 patients ranges from 4-17 weeks with the average of 8.8 weeks. He recommended that, besides clinical improvement, treatment response should be evaluated with a gallium-67 scan every 4-6 weeks during treatment and should be ended one week after the scan returns to normal. Conforming this with a repeat gallium-67 scan a month later treatment can be stopped.²³ Initially high doses of systemic antibiotics is recommended for a period of minimum of 6-8 weeks which may be replaced by oral

ciprofloxacin depending upon the response. Although there are no established treatment guidelines, limited cases series and anecdotal experience suggest that initial outpatient therapy with oral ciprofloxacin is efficacious for patients without any other cranial nerve, intracranial or other complications requiring admission

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Hyperbaric oxygen may be used, as an adjunct to antimicrobial therapy but is not to be used alone.²⁴

Surgery is reserved for local debridement and bony sequestrum removal or drainage of abscess. Chandler's report showed poor outcome with a 50% mortality rate with surgical removal of the lesion when antimicrobials were not available.^{9,10,25} This is due to the fact that large portions of temporal bone required resection and also that knowing the histopathology of MOE, removal of contiguous areas of bone may not be sufficient due to the spread of infection through vascular and facial planes. Similarly, facial nerve decompression in those with facial paralysis has also been discouraged.²⁶

Prognosis and outcome

With adequate and aggressive antibiotic use the cure rates have improved from 55 % in 1968 to 74-91% in 1985 to 1989.¹¹ Chandler had initially reported mortality of 50%, which has been decreased, now decreased to 20% due to improved imaging studies, early intervention with antibiotics. Most recent studies report a mortality rate of less than 10% except for those patients with cranial nerve involvement other than facial nerve and those with intracranial complications. Disease recurrence rate is reported in 9-27% of the cases and usually seen with inadequate length of therapy. It can recur as long as one year after the completion of therapy and usually manifests as recurrent otalgia,

headache and not as otorrhea. The ESR level starts to rise again and findings can be confirmed by imaging.

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There's no art
To find the mind's construction in the face
William Shakespeare. Macbeth Act 1, Scene 4