

Malignant Otitis Externa-A Review

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Abstract

Objective: To review the literature about Malignant Otitis Externa.

Methodology: A comprehensive review of existing knowledge that is available in literature has been summarised in this article.

Results: There is a rising incidence of Malignant Otitis Externa in the developing countries, predominantly seen in elderly diabetics. The common organism isolated is *Pseudomonas aeruginosa* though other microbials have been described as a causative agent. Radioimaging such as Technitium 99m MDP Scintigraphy, Gallium 67 Single Photon Emission CT and Tc99m Sulesomab scan has been recently used to assess and monitor therapy. The treatment protocol involves initial management with intravenous antimicrobials, regular aural toileting with adjunctive Hyperbaric Oxygen therapy. Unresponsive patients require either a trial with antifungals or a tissue diagnosis to rule out other differentials. Surgery is no longer found to be a first line treatment of MOE.

Conclusion: Malignant Otitis Externa is a highly fatal, necrotizing condition of the external auditory canal and temporal bone which is seen in elderly immunocompromised individuals. It is a highly aggressive skull base infection that is associated with high morbidity/mortality and cranial nerve complications. Although a variety of organisms such as *Proteus mirabilis*, *Staphylococci*, *Klebsiella* species and *Aspergillus fumigatus* have been implicated in the pathogenesis of MOE, *Pseudomonas aeruginosa* has been a predominant organism closely associated with MOE. With the advent of present day radiological imaging and effective antimicrobials coupled with a high index of suspicion, the mortality rate has been reduced from an alarming 50% to 20% over the past few decades.

Keywords: Malignant Otitis Externa; Elderly diabetic; Necrotizing Otitis Externa; *Pseudomonas aeruginosa*

Introduction

Toumouche was the first physician to have described a case of progressive osteomyelitis of temporal bone in 1838 [1]. Later Meltzer et al. in the year 1959, reported a case of Pyocyanus Osteomyelitis of Temporal bone, Zygoma and Mandible [2]. It was in 1968, Chandler in a historical case report had discussed in detail the various clinical features and identified it as a distinct clinical entity termed 'Malignant Otitis Extern' [3]. He had justified the usage of the term "malignant" due to the progressively aggressive behaviour of the disease process once it had spread outside the confinement of the external auditory canal [3].

Malignant Otitis Externa is a potentially life-threatening, invasive condition involving the skull base. The condition is "malignant" in that the disease spreads aggressively from the external auditory canal to the middle ear or skull base, with high mortality and morbidity. However, with the advent of both early radiological imaging and effective antibiotic therapy in the treatment of MOE, the term "malignant" should be abandoned and a more appropriate description like "Necrotizing Otitis Externa" or "Skull Base Osteomyelitis" should be adopted.

Incidence

Malignant Otitis Externa is an emerging disease in developing nations like India [4,5], where warm humid climate provides a favourable environment for the organisms to proliferate and infect those with an already compromised immune status especially the elderly group and those with Diabetes Mellitus. Though rare, MOE has been reported to occur among infants and children with Diabetes Mellitus or other immunocompromised states [6-10]. Apart from the main demographic presentation in elderly diabetics [3], this condition has also been reported among other immunocompromised individuals and those suffering from malnutrition [11] and AIDS [12,13]. Sex predilection is more towards males than females and the elderly age group above 60 years of age [5].

The incidence rate has improved over the decade in India, greatly due to better clinical awareness, availability of better diagnostic modalities and better health awareness and care among geriatric population [5].

Etiopathogenesis

MOE begins as a soft tissue infection originating at the junction of the cartilaginous and bony part of external auditory canal, which later rapidly spreads to deeper surrounding structures. It progresses from a stage of Pre-auricular Cellulitis to Chondritis, Petrositis, Temporal osteitis and osteomyelitis via the Fissures of Santorini and

tympantomastoid sutures, eventually ending with multiple cranial nerve palsies. The inciting factor has been attributed to trivial trauma following aural irrigation for cerumen disimpaction or ear picking in elderly diabetics [14]. Hence occurrence of clinical picture of MOE in an otherwise healthy individual should prompt for evaluation of an immunocompromised state.

Pseudomonas aeruginosa [2,3,15,16] has been the main microorganism commonly implicated with the occurrence of this disease. Other bacterial organisms that have also been associated are *Staphylococcus aureus* [17,18], especially MRSA, *Staphylococci epidermidis* [19], *Proteus mirabilis* and *Klebsiella oxytoca* [20,21]. *Pseudomonas aeruginosa* is an obligate gram negative aerobe that tends to colonize in a moist external auditory canal especially in individuals with impaired immunity; whereas *Staphylococci*, *Proteus* and *Klebsiella* are not true pathogens but commensals. *Pseudomonas* has been a pathogen in the absence of an effective host immune defence largely due to the presence of mucoid layer that is resistant to phagocytosis, along with the production of various lytic enzymes that incite a necrotizing vasculitis and endarteritis, invading the surrounding tissue [21]. Since high moisture content in the canal predisposes to *Pseudomonas* colonization, topical Acetic Acid 2% otic solutions has been found of use following water exposure in such patients.

Fungal infections have only comprised 10% in incidence of MOE, amongst which *Aspergillus Niger* [22], *Aspergillus Fumigatus* [23-25], *Scedosporium apiospermum* [26] *Malassezia sympodialis* [26] and *Candida species* [16] have been the most common. The role of fungi in the pathogenesis or outcome in management of MOE is not clear but isolation of fungi in the absence of bacterial pathogenesis will warrant treatment with antifungal drugs.

Even though MOE has been reported for centuries now, little is known about its pathophysiology. Diabetics are predisposed to developing MOE due to occurrence of microangiopathy and hypoperfusion [27]. The normal host immune defences are altered in immunocompromised individuals like Diabetics. Unlike the normal inflammatory response of local vasodilation, vasoconstriction is seen in diabetics due to underlying endothelial dysfunction. These factors coupled with defective chemotaxis, adherence, phagocytosis, and intracellular killing result in a prolongation of the disease process [27-29]. Another contributing factor reported has been reduction in effectiveness of cerumen produced by Diabetics as an antimicrobial agent due to increased pH of the cerumen and reduced lysozyme content [30].

Diagnosis

The typical presenting symptoms of individuals suffering from MOE are deep seated, unremitting, throbbing otalgia and purulent otorrhoea unresponsive to local therapy [31]. Pain has been often found radiating to the Temporomandibular joint, worsening at night and associated with hearing impairment. The presenting symptom is out of proportion to the otoscopic finding of granulation tissue at the junction of the osseo-cartilage junction with an intact tympanic membrane, in the absence of systematic symptoms such as fever.

It is essential to accurately diagnose MOE from other differential of severe otitis externa, external auditory canal carcinoma, or granulomatous conditions. A tissue diagnosis becomes essential to rule out occult malignancy in patients unresponsive to antimicrobial and antifungal therapy [31].

Cranial nerve palsy has been a common complication found during to the course of the disease, with facial nerve palsy being the most common and occurring in the early phase of disease process [32]. The occurrence of lower cranial nerve palsy involving nerves VII, IX, X, XI, and XII has been a reliable indicator of disease progression, involvement of skull base and poor prognosis.

At present there is no universally acceptable diagnostic criterion for MOE [33]. In 1989 a diagnostic criteria had been devised by Babiatski and Sade, however till date, clinical presentation, isolation of *Pseudomonas aeruginosa* and a positive bone scan with/without the presence of microabscess at surgery has been the mode of diagnosis [34].

Sterile ear swab culture analysis for aerobic, anaerobic, fungus and antibiotic sensitivity is essential in diagnosis.

Radiological Imaging Studies have been found helpful in further corroborating the diagnosis and defining the extent of the disease. High resolution CT Imaging (HRCT) and Magnetic resonance imaging (MRI) have been found useful in defining the anatomical extent of soft tissue involvement, bony erosion, and intracranial complications. HRCT has been the initial imaging of choice as it is more accurate in delineating bony involvement apart from being economically feasible. MRI has been effective in identifying soft tissue involvement and intracranial extension particularly dural enhancement [35,36]. However, it remains to be inferior to CT in terms of identifying bone involvement. Both HRCT and MRI have been found to be unreliable in monitoring resolution of osteomyelitis as bone re-mineralization takes at least a year to be detected by these imaging modalities [35,36].

Nuclear imaging has been the mainstay of monitoring disease progression. Technitium 99m MDP Scintigraphy and Gallium 67 Single Photon Emission CT have both been found highly sensitive, but not specific. The radiotracer binds to actively dividing cells; hence serial imaging done over a period of time could be used for determining the duration of antibiotic therapy and for monitoring the treatment response [37]. Since the above nuclear imaging techniques reflect an on-going bone repair process, their reliability for prolonged treatment monitoring is ineffective. Technitium 99m Sulesomab scan has been identified as an effective alternative in monitoring disease progression and treatment response. It uses radionuclide labelled with murine monoclonal antibody with a faster execution time and comparatively low radiation exposure when compare to Gallium 67 SPECT scan [38]. Tc99m Sulesomab binds to neutrophils and leukocytes present at the site of inflammation with a sensitivity of 80-90% [39].

Gallium 67 SPECT scan in particular, as reported by Stokkel et al., has been found reliable in early detection and monitoring of treatment response [37].

Treatment

Management methods have been evolving slowly with recently advanced effective antimicrobial medications and a multi-disciplinary approach in treatment. Strict glycaemic control, correction of electrolyte imbalance, improvement in immunocompetence, aural toileting, hyperbaric oxygen therapy and prolonged systemic and ototoxic antimicrobial therapy (3-6 weeks) has become crucial in effective treatment of MOE [14,27].

Antimicrobial therapy is started initially following clinical diagnosis of the disease, after having sent discharge for a bacterial and fungal smear and culture/sensitivity. Initial antibiotic of choice are anti-pseudomonal Penicillins like Piperacillin with Tazobactam and Fluoroquinolones like Ciprofloxacin [27].

Piperacillin with Tazobactam is given as a monotherapy or along with an Aminoglycoside, intravenously 6th or 8th hourly at a dose of 4.5 grams in adults. With such combinations, monitoring of ototoxicity and nephrotoxicity is required, especially in Diabetics already prone to impaired renal function. Piperacillin with Tazobactam has been more effective than other anti-pseudomonal Penicillins like Ampicillin with Sulbactam or Ticarcillin with Clavulanate due to its broader spectrum of action against anaerobes [40].

However, oral Fluoroquinolones like Ciprofloxacin have far superior antipseudomonal action, replacing the need for intravenous antimicrobials, along with excellent penetration into bones, making them the drugs of choice for MOE [41-43]. Another advantage offered by Quinolones has been safe administration in elderly diabetics with an already deranged renal functionality. Their low toxicity negates the need to monitor renal parameters and dose adjustment. Patients are usually discharged with an oral Ciprofloxacin along with appropriate antifungal if fungal smears are positive. The widespread use of oral fluoroquinolones along with incomplete treatment course for MOE, has led to increase in reports of resistance [43].

Use of third generation Cephalosporins with antipseudomonal activity like Cefaperazone has become an alternative in cases of Ciprofloxacin resistance [43]. Combination therapy of Cefaperazone with Sulbactam has been found to be synergistic and effective as Cefaperazone provides a broad gram positive and gram negative coverage, and Sulbactam provides protection from beta-lactamase [41].

With advancement in antimicrobial therapy, surgical intervention is no longer required in initial stages and is employed only in case of biopsy and culture to differentiate from malignancy or surgical drainage of abscesses or debridement of deep invasive lesions.

As highlighted in a case series by Galletti et al with regards to treatment protocol and follow up, following a clinical diagnosis aided by radiological assessment, regular aural toileting and every 2 week follow up is essential. A tissue diagnosis is required for further assessment in a unresponsive patient. Thereafter radiological follow up can be done following 2 months and every 6 months thereafter [38].

Use of Hyperbaric Oxygen Therapy has been only used as an adjunct to microbial therapy [44]. A review by Phillips and Jones proved that there is no clear cut advantage of hyperbaric oxygen therapy over antimicrobial therapy and hence its usage has been only as an adjunctive treatment [45].

Prophylaxis

Since majority individuals developing MOE are diabetics with self-inflicted or iatrogenic trauma to the ear as an inciting event, susceptible individuals should be cautioned regarding the same. A strict glycemic control in known diabetics, and appropriate treatment of eczematous conditions of the auditory canal that may lead to inadvertent injury of the epithelial lining of external auditory canal by scratching should be advised. Aural irrigation for cerumen

disimpaction should be done by a medical staff with caution, avoiding injury to the skin [14].

Conclusion

This article has reviewed in depth the management of MOE and the patient demographic to concentrate on. Early detection is crucial in management and reduction of morbidity and mortality. Prolonged appropriate antimicrobial treatment has replaced the need of surgical debridement as the initial mode of treatment. This has been aided by early identification using various radiological imaging with a background of raised clinical suspicion.

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