Clinical Profile of Patients with Malignant Otitis Externa in a Tertiary Care Centre

Nandakumar Choorakkattukara Raman[1], Thulaseedharan Sreedharan[2], Ajayan Paithottiyil Varkey[3]

[1, 2, 3] Department of ENT, Government Medical College, Thrissur, Kerala, India.

ABSTRACT

BACKGROUND

Malignant otitis externa (MOE) is a rare disorder occurring in elderly immunocompromised patients mainly in diabetics. Other immunocompromised conditions are myeloid malignancies, iatrogenic suppression secondary to treatment of malignancies, organ transplant patients, and HIV (Human Immunodeficiency Virus) patients. Most common causative organism is *Pseudomonas aeruginosa. Staphylococcus aureus, Staphylococcus epidermidis* also have been reported. *Aspergillus* species is the most common fungal pathogen causing this condition.

METHODS

This is a cross sectional study to find out the clinical profile of patients treated for MOE in the department of ENT of Government Medical College, Thrissur, Kerala. Sample size was 32. Patients were given a self-made questionnaire containing questions on age, gender, clinical history, and history of past illness. After getting the filled form, informed consent was taken. They then underwent general examination as well as ENT evaluation with emphasis on otological examination which included examination of ear and surrounding area. Swab from external auditory canal (EAC) was sent for culture and sensitivity. Granulations were taken from EAC to rule out malignancy. Antibiotics and antifungals depending on the pathogen were given for adequate duration.

RESULTS

Males were more commonly affected (78 %). Mean age of population is 60.97 ± 10.2 years. Diabetes mellitus was seen in 21 patients, of which 16 showed uncontrollable diabetes. Otalgia was present in all the patients. 14 patients showed ear discharge. Facial palsy was present in 8 patients only. Increased ESR was seen in all patients. Culture and sensitivity of all patients showed growth of *Pseudomonas* only. CT (Computed Tomography) revealed soft tissue in external auditory canal of all patients. At the end of the study, complete remission was seen in 18 patients. Follow up was done in 3 months and 6 months. Facial palsy was relieved in 50 % patients.

CONCLUSIONS

MOE predominantly affects elderly immunocompromised patients especially patients with uncontrollable diabetes. Most common organism isolated was *Pseudomonas aeruginosa*. Otalgia which felt more in night (nocturnal otalgia), otorrhoea, granulation in external auditory canal are the important parameters for the diagnosis of this condition. HRCT (High-Resolution Computed Tomography) temporal bone is used to see the extent of disease and also for diagnosis. ESR and CRP levels indicate the prognosis. Complete remission seen in most of the patients and facial palsy[3] was relieved in 50 %. This study can be used to predict the disease progression, and to formulate a treatment plan so that morbidity and mortality associated with it can be avoided as much as possible.

KEYWORDS

Malignant Otitis Externa, Necrotising Otitis Externa, *Pseudomonas aeruginosa*, Nocturnal Otalgia, Immuno Compromised Condition

Corresponding Author:
Dr. Thulaseedharan Sreedharan,
Additional Professor,
Department of ENT,
Government Medical College,
Kollam, Kerala, India.
E-mail: sinuthulasi@gmail.com

DOI: 10.18410/jebmh/2020/617

How to Cite This Article:
Raman NC, Sreedharan T, Varkey AP. Clinical profile of patients with malignant otitis externa in a tertiary care centre. J Evid Based Med Healthc 2020; 7(50), 3022-3026. DOI: 10.18410/jebmh/2020/617

Submission 08-08-2020,
Peer Review 16-08-2020,
Acceptance 21-10-2020,
Published 14-12-2020.

BACKGROUND

Mostly MOE is seen in patients with diabetes mellitus.[1,2] Recent increasing report of it in HIV[3] patients implicate a compromised immune system as a predisposing factor in this disease. *Pseudomonas aeurugenosa*[4] is nearly always the responsible organism. *Staphylococcus aureus* especially methicillin resistant type, *Staph epidermidis*[5], *Proteus mirabilis, Klebsiella oxytoca* also have been implicated. Only 10 % of malignant otitis externa is caused by fungus in which *Aspergillus niger*[6] and *fumigatus* are the most common pathogens but infection by exotic fungi like *Scedosporium apiospermum, Malassezia sympodialis, Candida albicans, Candida parapsilosis, Candida ciferrii, Pseudallescheria boydii* have also been reported[7]. Widespread use of oral and topical quinolones[8] for the treatment of otitis may cause the isolation of *Pseudomonas*[4] more difficult and has contributed to the emergence of *Pseudomonas* resistant to Ciprofloxacin.[9] Several factors contribute to the development of otitis externa, despite the defence mechanism of auditory canal. Inherent defence mechanisms of ear canal include[1] the tragus and conchal cartilage which partially cover the opening of the ear canal and help to prevent foreign body entrance[9]. Hair follicles and isthmus prevent the entry of contaminants into ear canal.[10]

Toulmouche[11] was the first person to describe a case of progressive osteomyelitis of temporal bone in 1838. It was Chandler[10,4] in 1968 who gave the description of a distinct clinical entity called MOE. He justified the use of the term 'malignant' because of progressively aggressive behaviour of the pathological process once it has spread beyond the confinement of external auditory canal. However, with advent of early radiological imaging and effective antibiotic therapy, the term 'malignant' should be abandoned and a more appropriate description such as "necrotizing" or "osteomyelitis" must be adopted. Now a days, MOE is emerging very much in India,[12] may be due to hot and humid climate which provides a favourable environment for the proliferation of organism and poor immune status of people.

Although rare, MOE has been reported in infants and children with diabetes mellitus[1,2] or other immuno compromised conditions. Grandis JR[1] has observed that 90 % patients of his study population have shown glucose intolerance. Sexual predilection affects men more than women in the age group of 60 years. Due to the significant differences in natural evolution and the treatment, it is essential to differentiate between malignant otitis externa and necrotizing infections of external ear where the structures beyond the soft tissue of EAC are involved.

Skull Base Osteomyelitis (SBO) follows otitis externa, but it can also begin with infection of middle ear. 85 to 95 % of it occurs in elderly but young patients may also be susceptible to it when their immunity is decreased due to any reasons. Microvascular disease aggravated by *Pseudomonas*[4] vasculitis, which further restricts tissue perfusion. Diabetes mellitus[1,2] is also associated with deterioration in the function of polymorphonuclear cells. Higher pH of wax, sensitivity of *Pseudomonas* to a low pH of EAC further restricts the body's defences against infection. Hypo perfusion due to underlying dysfunction and decreased immune status of the patients also contribute to disease. Spread along temporal bone through fissure of Santorini involves stylomastoid foramen containing facial nerve and jugular foramen containing 9th, 10th, and 11th nerves. It also involves foramen lacerum and clivus. Sub temporal extension starts at osseocartilaginous junction near the fissure of Santorini and spreads to retro condylar fat, parapharyngeal fat, TM (Temporo-Mandibular) joint and masticator space.

CT shows bone erosion and demineralization in multiple planes. Early lesion shows soft tissue swelling with thinning of fat plane but does not show bone destruction always. In fungal causes, it occurs even later. Subtle changes can be seen by comparing the affected side with contralateral side although bilateral SBO is possible. MRI shows replacement of normal fatty bone marrow of skull base and temporal bone by inflammatory tissue which results in decreased signal intensity of T1 image without fat suppression. Affected soft tissue and muscle are thickened and demonstrate more hypo intense signal on T1 image. Affected area as suspected on T1 image is hypo intense on T2 image in contradiction with most infectious process where T2 images show hyper intense signal because of hyperaemia and oedema. Diffusion Weighted Imaging (DWI) can be used to differentiate from lymphoma, and malignancy nasopharynx. Apparent Diffusion Coefficient (ADC) decreased in malignancy. Increase in signal on DWI with low ADC indicates abscess in SBO.

Tc99m bone scan, which is a gamma emitting tracer is positive early in SBO. It is cheap and easily available but changes lag behind the clinical improvement, so cannot be adequately used for follow-up of treatment. Technetium labelled leucocyte is more expensive and more laborious so also not used. Gallium – 67 is also a gamma tracer and binds to actively dividing cells like leucocytes in infectious process and it accumulates in soft tissues. Adequately treated infectious lesions lose the ability to concentrate so used in the treatment response monitoring. Demerits are high cost, time consumption and high radiation dose.

SPECT (Single-Photon Emission Computed Tomography) -CT combines 3 D tracer imaging with higher resolution of CT gives better anatomical correction compared to above gamma emitters. FDG (Fludeoxyglucose), which is a beta emitting tracer is not a specific infection tracer, but its widespread availability, good spatial resolution and decreased radiation compared to gallium make it the nuclear diagnostic tracer of first choice. Abnormal MRI signal may get 6- 12 months after the treatment, and this makes MRI unreliable for distinguishing resolved from ongoing SBO. PET (Positron Emission Tomography) - MRI and separate CT if not available, FDG PET CT and either MRI or CT can then also be used for follow-up. Most effective treatment is the debridement of necrotic tissue or surgical management with prolonged course of antibiotic and control of diabetes.[1]

We wanted to study the clinical profile of patients with malignant otitis externa in a tertiary care centre.

METHODS

It is a cross sectional study conducted among patients with clinical and radiological features of malignant otitis externa attending the Department of ENT, Government Medical College, Thrissur, Kerala. Study done over a period of 1 year from January 1st, 2017 to December 31st, of 2017.

Sample Size and Method

No reliable statistical data are available in any of previous studies on profile of patients with malignant otitis externa. Hence, in our study, we included all the patients who attended the OPD (Out-Patient Department) of ENT department with clinical and radiological features of malignant otitis externa. Total 32 patients were enrolled in the study. Universal sampling method was used. Patients aged above 18 years with clinical and radiological features of malignant otitis externa were included in the study.

Exclusion Criteria

1. Patients with debilitating illness.
2. Patients having severe neurological abnormalities.

After taking informed written consent, patients presenting with history and clinical features suggestive of malignant otitis externa were examined generally and ENT area wise. Swab was taken from external auditory canal for culture and sensitivity. Granulation from external auditory canal was taken only to rule out malignancy. HRCT[8] of temporal bone were taken to assess the extent of disease. CRP (c-Reactive Protein) and ESR (Erythrocyte Sedimentation Rate)[3] used for prognosis.

Study Tools

Self-made questionnaire containing name, age, gender, clinical history, past history of illness.

Statistical Analysis

EPI info version 7 was used relevantly to analyse statistical variables wherever required. Mean score and standard deviation was assessed and prevalence was expressed in proportions.

Ethical Considerations

Informed consent was taken from all patients or their legally valid relatives. There are no major ethical issues involved as no invasive procedures are done on patients as part of study.

RESULTS

The results of study are discussed under following headings: Age and Gender Distribution. Gender distribution showed that males were the majority constituting 78 % of the population[10,4] and the age group included 56 to 65 years and 66 to 75 years (9 numbers in each). Females were in the age group of 46 to 65 years and 66 to 75 years (3 in each). Lowest number of males and females were seen in the age group of 35 to 55 (6 in male and 4 in female). Mean age[13] of the study population is 60.97 ± 10.2 years, in that males were having higher mean age of 61 ± 7 9.8 years when compared to 58.8 ± 11.6 years for females.

Drugs	Dosage	Comments
Ciprofloxacin	(400 mg) IV / 12 hrly (750 mg) orally / 12 hrly	Fluroquinolone
Ticarcillin-Clavulanate (Timent in)	(3 gm) IV / 4 hrly	Anti Pseudomonal Penicillin
Piperacillin – Tazobactam (Zosyn)	(4 - 6 gm) IV / 4 - 6 hrly	Anti-Pseudomonal Penicillin, Aminoglycoside can be Combined
Ceftazidime (Fortum)	(2 gm) IV / 8 hrly	3rd generation cephalosporin
Cefepime (Maxipime)	(2 gm) IV / 12 hrly	4th generation cephalosporin
Tobramycin (Nebcin)	1-1.6 mg / Kg / IV / IM / 8 hrly	Aminoglycoside, can be combined with penicillin
Gentamycin	1-1.6 mg / Kg / IV / IM / 8 hrly	Aminoglycoside, can be combined with penicillin

Table 1. Systemic Antibiotics Used for the Treatment of MOE

Age Group (Year)	Males (%)	Females (%)	Total (%)
35 - 55	2 (8)	1 (14.28)	3 (9.37)
46 - 55	4 (16)	3 (42.85)	7 (21.87)
56 - 65	9 (36)	1 (14.28)	10 (31.25)
66 - 75	10 (40)	2 (28.57)	12 (37.5)
Total	**25 (100)**	**7 (100)**	**32 (100)**

Table 2. Age and Gender Distribution

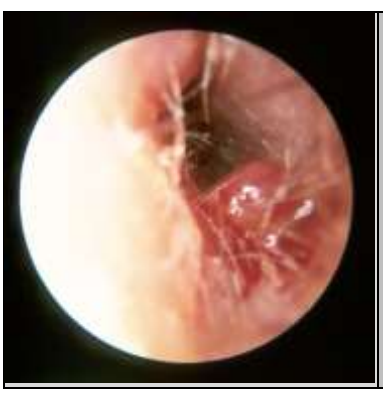

Figure 1. Granulation Tissue in the Floor of EAC

Addictions

75 % patients didn't have any addiction, alcohol was used by one patient, smoking by 5 and both by 2 patients.

Co-Morbidities

Diabetes mellitus[7] was present in 21 patients of which 17 showed uncontrollable diabetes. Those who have HbA1c > 6.5 % were considered to be uncontrolled diabetes and remaining 4 patients showed HbA1c < 6.5 %. HbA1c indicates glucose level of last three months only and not the present condition. Hypertension was seen in 9 patients.

Symptomatic Presentations

Otalgia[14] was present in all 32 patients and it was deep and severe in 22 patients. Ear discharge was seen in 14 patients,

and fever in 8 patients. Hearing impairment was shown by 19 patients in whom 13 were having conductive hearing loss and rest 6 with mixed hearing loss.

Complaints	N (%)
Co-morbidities	
Diabetes mellitus	21 (65.6)
Hb-A1C > 6.5 %	17 (53.1)
Hypertension	9 (28.1)
symptoms	
Otalgia	32 (100)
Discharge	14 (43.8)
Hearing impairment	19 (59.4)
Conductive hearing loss	13 (40.6)
Mixed hearing loss	6 (18.8)
Tinnitus	6 (18.8)
Ear fullness	19 (59.4)
Facial palsy	8 (25)
Fever	8 (25)
Addictions	
Alcohol use	1 (3.12)
Smoking	5 (15.6)
Both	2 (6.2)

Table 3. Co-Morbidities, Symptoms and Addictions

Only 6 patients showed tinnitus. 8 patients presented with facial nerve palsy. Ear fullness and pressure were reported by 19 patients. All patients showed increased ESR but CRP elevated in 30 patients only. The culture and sensitivity showed *Pseudomonas aeruginosa* growth in all 14 patients having discharge. Before getting the culture report, all patients were started on injection ciprofloxacin 400 mg IV / 12th hourly and gentamicin 1 mg / kg / IV / 8th hourly. Since culture reports showed *Pseudomonas* sensitive to ciprofloxacin and gentamicin, we continued the same for 2 weeks. When the pain, ESR and CRP decreased, patients were discharged with oral ciprofloxacin 750 mg twice a day plus ciprofloxacin and vinegar (acetic acid) ear drops in 1:1 ratio for 4 more weeks.

The action of vinegar is to change the pH of EAC which prevents the growth of *Pseudomonas*. Those who had not having much change in pain, ESR and CRP were put on 'Piperacillin-Tazobactam' injections 4 gm / IV / 6 hourly for 2 weeks and responded well. Every 3rd day, we did RFT which were normal, so no dose adjustment was needed. If the patient is having CKD (Chronic Kidney Disease), RFT (Renal Function Test) will be done on alternate day but there were no CKD patients. HRCT[15] temporal bone revealed soft tissue density of EAC in all patients.

Treatment end point was 'pain relief' only because facial palsy was not relieved in 100 % patients and there was no granulation because whatever remaining granulation present after taking biopsy had disappeared when p ciprofloxacin, steroid ointment pack was given for a few days. No surgical procedures were carried out except for biopsy of granulations. Opacification of mastoid cells without bony destruction was seen in 22 patients.

Follow up was done after 3 months and 6 months which showed complete remission in 56.25 % i.e., 18 patients out of 32 patients. Recurrence was noted in 8 patients after 6 months. Facial palsy was relieved in 50 % patients only. Bony erosion was identified in 22 patients.

DISCUSSION

In our study population, majority of patients were males i.e. 78 % which is similar to those studies conducted by Chandler.[10,4] Study by Lambor DV[13] shows 63.59 years as mean age group and our study also showed similar results. High incidence of MOE in diabetes mellitus [1,2] has been well documented. In our study, 21 patients showed diabetes, in which 16 had uncontrollable diabetes[1,2] as revealed by glycosylated haemoglobin level (HbA1c). There are a few people without diabetes and with malignant otitis externa. The exact cause of MOE in non-diabetics is not known, but it could be age related small vessel disease and altered immune status. MOE typically presents with as otalgia, otorrhoea[14] and granulations in external auditory canal. Otalgia is described as deep boring, lancinating and throbbing type and felt more in the night and is called "nocturnal otalgia" and it is resistant to analgesics. In our study, otalgia was present in all patients but otorrhoea only in 14 patients. This is similar to studies by Cohen D.[14] Our study showed hearing impairment in 19 patients, among whom 13 had conductive type and 6 had mixed hearing loss. Conductive hearing loss may be due to external auditory canal obstruction by granulation or oedema, while sensory neural hearing loss can be due to ageing or diabetes mellitus. The studies of Chandler showed similar results.[10,4] Facial nerve palsy was shown by 40 % patients i.e. 8 patients out of 32 patients.[10] Facial nerve is the most common nerve involved because of its proximity to external auditory canal. But the study of Chandler[10] revealed facial palsy in 20 % only. Culture and sensitivity showed *Pseudomonas*[4] growth. HRCT[15] temporal bone revealed soft tissue density of external auditory canal in all patients, but opacification of mastoid air cells without bony destruction was shown by 22 patients, whereas destruction of tympanic portion of temporal bone was seen in 3 patients.

Study of Naghbi M[2] shows elevated ESR, WBC and CRP. Our study also shows similar results. Lee[16] in his 12 patients found the mean ESR and CPR level as 34.8 mm / 1st hr and 5.33 mg / dl respectively. But our study showed, mean ESR and CRP levels as 52.76 ± 32.49 mm / 1st hr and 2.54 ± 1.90 mg / dl respectively. Both studies indicate that, ESR and CRP may be used as laboratory markers for screening MOE. In our study, 100 % patients showed *Pseudomonas aeuroginosa*[4] growth whereas study by Berenholz[10] showed *Pseudomonas* only in 44 %. We identified *Staph aureus*[5] in 3 patients and *Aspergillus flavus*[6] in 2 patients. But the Study of Berenholz,[9] showed *Staph aureus* in 7 patients. The outcome of our study showed complete remission in 56.3 %. Follow up was done after 3 months and 6 months. Bone erosion was seen in three quarters of patients and 50 % patients showed improvement in facial palsy. There was no death in our study, but disease related morbidity is higher

CONCLUSIONS

1. In the present study, necrotising otitis externa predominantly affected elderly men with

uncontrollable diabetes mellitus.
2. The most common organism isolated was *Pseudomonas aeruginosa*. Otorrhoea, nocturnal otalgia, granulations in EAC are the most important clinical parameters for the diagnosis.
3. As the disease progresses along the skull base, cranial nerves become involved and facial nerve is the most common nerve involved in the disease.
4. ESR and CRP levels indicate the prognosis.
5. Radiological investigations like HRCT temporal bone, MRI, Tc99m, Ga67 and SPECT can be used for the diagnosis, and to know the extent of disease.
6. This study can be used to predict the disease progression and to formulate a treatment plan so that morbidity and mortality associated with it can be avoided.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Grandis JR, Branstetter BF 4th, Yu VL. The changing face of malignant (necrotising) external otitis: clinical, radiological and anatomic correlations. Lancet Infectious Disease 2004;4(1):34-39.
[2] Naghibi M, Smith RP, Baltch AL, et al. The effect of diabetes on chemotactic and bactericidal activity of polymorphonuclear leucocytosis. Diabetes Res Clin Pract 1987;4(1):27-35.
[3] Hern JD, Almedya J, Thomas DM, et al. Malignant otitis externa in HIV and AIDS. J Laryngol Otol 1996;110(8):770-775.
[4] Chandler JR. Malignant external otitis. Laryngoscope 1968;78(8):1257-1294.
[5] Keay DG, Murray JA. Malignant otitis externa due to Staphylococcus infection. J Laryngol Otol 1988;102(10):926-927.
[6] Philips P, Bryce G, Shepherd J, et al. Invasive otitis externa caused by Aspergillus. Rev Infect Dis 1990;12(2):277-281.
[7] Yao M, Messner AH. Fungal malignant otitis externa due to Scedosporium angiospermum. Ann Otolrhinollaryngol 2001;110(4):377-380.
[8] Morrison GA, Bailey CM. Relapsing malignant otitis externa successfully treated with ciprofloxacin. J Laryngol Otol 1988;102(10):872-876.
[9] Berenholz L, Katzenell U, Harell M. Evolving resistant *Pseudomonas* to ciprofloxacin in malignant otitis externa. Laryngoscope 2002;122(9):1619-1622.
[10] Chandler JR. Pathogenesis and treatment of facial paralysis due to malignant external otitis. Ann Otol Rhinol Laryngol 1972;81(5):648-658.
[11] Toulmouche MA. Obervations otorrheecerebrale: survis des reflexion. Gaz Med Paris 1838;6:422-426.
[12] Prasannakumar S, Ravikumar A, Somu L. Malignant otitis externa: an emerging scourge. J Clin Gerontol Geriatr 2013;4(4):12-31.
[13] Lambor DV, Goel HC, Tiwari M. Necrotising external otitis: clinical profile and management protocol. J Laryngol Otol 2013;127(11):1071-1077.
[14] Cohen D, Friedman P. The diagnostic criteria of malignant external otitis. J Laryngol Otol 1987;101(3):216-221.
[15] Sudhoff H, Rajagopal S, Mani N. Usefulness of CT scan in malignant external otitis: effective tool for the diagnosis, but of limited value in predicting outcome. Eur Arch Otorhinolaryngology 2008;265(1):53-56.
[16] Lee H, Kim J, Nguyen V. Ear infections: otitis externa and otitis media. Primary Care: Clinics in Office Practice 2013;40(3):671-686.