Malignant Otitis Externa and Atypical Skull Base Osteomyelitis

https://doi.org/10.47210/bjohns.2024.v32i3.204

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ABSTRACT

Introduction

Malignant otitis externa/ Skull base osteomyelitis is a common yet challenging disease to establish a diagnosis and manage efficiently to achieve a complete cure. We aimed to study the clinicopathological and radiological profile of Malignant Otitis Externa and atypical skull base osteomyelitis in the COVID-19 era.

Materials and Methods

Ours is a descriptive observational study conducted in an ambispective manner. It includes 11 patients diagnosed with either malignant otitis externa or atypical skull base osteomyelitis from 2015 to 2023. The clinicopathological, radiological, and management details of these patients were collected from their respective case sheets. The patients were followed up to learn their current status.

Results

Among the 11 patients, 4 were from the pre-COVID period, and the remaining 7 were from the post-COVID period. 10 patients had malignant otitis externa or lateral SBO, and 1 had atypical/Central skull base osteomyelitis. All the cases were associated with type II diabetes mellitus, with 64% relying on insulin. Otalgia (100%), otorrhea (82%), aural fullness (73%), vertigo (27%), and facial nerve palsy (18%) were the symptoms on presentation, and the external auditory canal granulation was seen in 82% on clinical examination. 82% of patients had an elevated erythrocyte sedimentation rate. Microbiology of the ear swabs revealed the growth of Pseudomonas aeruginosa in 36% of cases. 64% of patients had involvement mastoid seen in radiological imaging of the temporal bone. All the patients were treated as inpatients with long-term antibiotics and surgical debridement when needed, and the average duration of hospitalisation was 18 days.

Conclusion

Malignant otitis externa or skull base osteomyelitis can be diagnosed and managed adequately only when there is a high index of clinical suspicion in elderly diabetic patients with deep-seated earache. Meticulous clinical examination, serial documentation of clinical examination, ear swabs for culture and sensitivity, and imaging studies will help in staging the disease. The appropriate management includes histopathological examination of the EAC granulation tissue, followed by culture-sensitive antibiotics. Treatment must be monitored with regular Erythrocyte Sedimentation Rate levels and serial imaging of the temporal bone. Our study noted an apparent increase in Malignant otitis externa during the COVID-19 pandemic.

Keywords

Necrotizing Otitis Externa; Malignant Otitis Externa; Skull-Base Osteomyelitis; Diabetes Mellitus

Malignant otitis externa (MOE), synonymous with necrotizing otitis externa, invasive otitis externa or skull base osteomyelitis (SBO), is a common yet clinically challenging disease. MOE mainly affects the elderly diabetic population and the immunocompromised. It starts as an infection that initially involves the external auditory canal (EAC), which later spreads to the other regions of the temporal bone.[1]

Although there has been an attempt to understand the various clinical patterns of MOE, the literature is limited around the globe and also in India in regards to its incidence, risk factors, especially diabetes mellitus, clinical profile and lack of unified consensus on its management.

MOE was first reported by Toulmouche in 1838, after which Cohen and Friedman defined the diagnostic criteria and Carney provided a clinicopathological staging

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system.[1] The most common organisms causing MOE are Pseudomonas aeruginosa, Methicillin-resistant Staphylococcus aureus (MRSA), Klebsiella pneumoniae, Proteus mirabilis and also Aspergillus and Candida species.[2] The main line of treatment is culture-sensitive antibiotics for a prolonged period.[3] The role of surgery in this clinical entity is limited and is reserved for removal of sequestrum, drainage of abscess and the decompression of the facial nerve.[4]

MOE is classified as typical or classic lateral SBO and atypical or central SBO.[5] The atypical or central SBO is a relatively newer clinical entity that mainly involves the clivus or occipital bone and does not have the classical presentation of granulations in the EAC or temporal bone involvement, hence, the diagnosis may be delayed till radiological evaluation is done, as the tissue biopsy is often inaccessible.[6]

During the COVID-19 pandemic, there were quite a lot of changes in the treatment-seeking behaviour of patients, especially diabetics and their control of sugars. Our hospital, with limited infrastructure, had also noticed an increase in the number of cases of MOE and a case of atypical SBO in the post-pandemic period as noted by several other authors around the world.[7, 8]

We studied the clinicopathological and radiological profile of the MOE patients, the treatment protocols and their outcomes. We also tried to understand the factors that could have caused an apparent increase in the number of cases that were reported after the COVID-19 pandemic.

Materials and Methods

This is a single-centre ambispective observational descriptive study done in a tertiary care hospital from 2015 to 2023.

All the patients diagnosed and managed with MOE during this period were included. The details of 10 patients with MOE and 1 patient with atypical SBO were studied from their medical case records after obtaining appropriate permission from the hospital administration. The patients were followed up by contacting them over the telephone to know their current status.

The information regarding demographics, co-morbidities, signs and symptoms, COVID-19 vaccination history, examination findings done under otomicroscope (Fig.1), biochemical and microbiological tests, histopathology, imaging, management and follow-up were recorded.

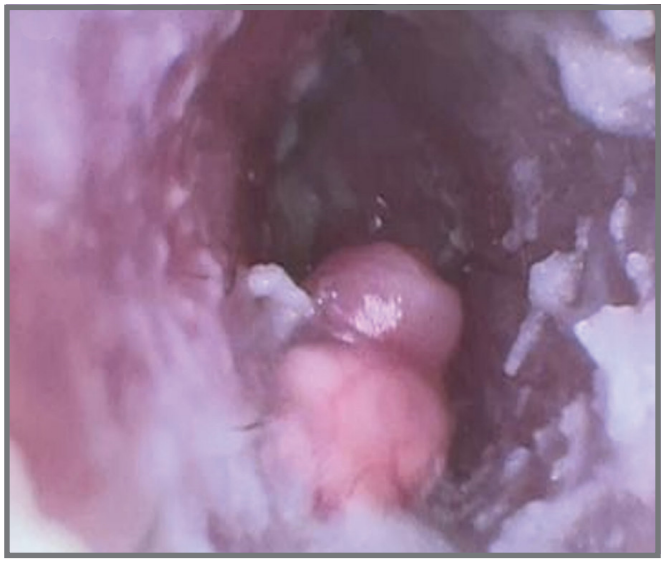

Fig. 1. Granulation tissue seen along the floor of the External auditory canal with the surrounding area of congestion.

Biochemical parameters like ESR, renal and sugar profile were studied. Histopathological examination of the granulation tissue taken from the EAC demonstrated polymorphonuclear infiltration with inflammation with or without sequestrum (Fig. 2).

Given limited resources, nuclear imaging was not done, and all the patients underwent high-resolution computed tomography (HRCT) of the temporal bone and magnetic resonance imaging of the same (MRI) to understand the extent of the disease.

The severity of the disease was stratified as per Stevens et al protocol in which severe MOE exhibits either the presence of the facial nerve palsy or two or more clinical variables (other than facial nerve palsy) or two or more radiographic variables or 1 or more clinical variable

(other than facial nerve palsy) and 1 radiographic variable at the time of presentation.[9]

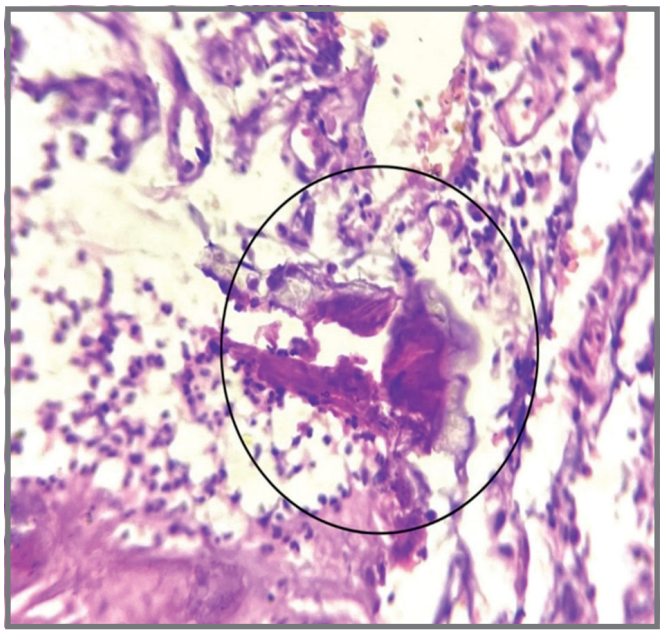

Fig. 2. Histopathological examination revealing sequestrum (within the circle) surrounded by dense infiltration of polymorphonuclear cells, lymphocytes and macrophages

The patients were treated with empirical third-generation cephalosporins for 6 weeks, which were later modified based on the culture sensitivity. The patients on follow-up were treated with oral fluoroquinolones, tablet Ciprofloxacin 750 mg twice daily for a period of 6 to 8 weeks. Supportive care included the management of otalgia according to the WHO step ladder pattern of pain management,[10] keeping the renal parameters of the patient as a concern and also good diabetic control that needed insulin administration in all 11 patients.

Furthermore, the impact of COVID-19 on the incidence, clinical profile and outcome of MOE patients was studied.

Results

Background and clinical characteristics (Table I)

Out of the 11 patients, 4 were from 2015 to 2019 (pre-COVID) and 7 from 2020 to 2023 (post-COVID) period. The sample had 8 male and 3 female patients, and their mean age at presentation was 58 years (range 40-72 years).

Clinical presentation

The right ear was more commonly affected (64%) than the left ear (36%), and none of our patients had bilateral involvement. 82% had deep-seated otalgia and purulent otorrhea, which were among the commonest symptoms, followed by aural fullness (73%), vertigo (27%), facial nerve palsy (18%) and other cranial nerve involvement (18%). Examination of the ear under otomicroscope revealed granulation tissue in the EAC in 82% of patients.

Comorbidities

All 11 patients had uncontrolled type II diabetes mellitus, with a mean duration of the disease being 14.18 years (range 3-30 years), for which 64% were dependent on insulin at the time of presentation. The mean blood sugar value was 251mg/dl at the time of admission and all 11 patients needed insulin during the hospital stay for adequate blood sugar control. The other co-morbidities seen in our patients were systemic hypertension (55%), chronic kidney disease (18%), dyslipidaemia (9%) and anaemia (9%). None of the patients were on immunosuppressants or had positive retroviral serology.

Laboratory tests

At the time of admission, a high ESR was seen among 82% pf patients with a mean of 54 mm/hr (range 10 - 110). 18.1% had a deranged renal profile and 9% had iron deficiency anaemia.

Microbiology

Ear swab was sent for culture and sensitivity from all 11 patients, and 36% had Pseudomonas aeruginosa, followed by Klebsiella pneumonia, Candida species and Methicillin-Resistant Staphylococcus Aureus (MRSA) seen in 9% each. 36% of the patients had no growth from the ear swab culture.

Table I: Clinico-pathological and radiological profile of MOE patients

Case No.	Age/Sex	Lat	Comorbidities	VX	Clinical findings	EAC finding	ESR (mm/hr)	HRCT/MRI	Organism	Antibiotics	DOH
1	46/M	R	DM, HTN, Dyslipidaemia	NA	Otalgia, otorrhoea	G	24	No significant involvement	P. aeuroginosa	CTX,AK	9
2	70/M	L	DM, Diabetic foot	NA	Otalgia, otorrhoea	–	26	No significant involvement	Candida albicans	CTX,MET	7
3	55/M	R	DM,HTN	NA	Otalgia, otorrhoea, hearing loss	G	100	No significant involvement	P. aeuroginosa	CTX,MET,CIP	14
4	71/M	R	DM,HTN	NA	Otalgia, otorrhoea, hearing loss, cranial nerve palsy (9,10,12)	G	110	Soft tissue density noted in the mastoid air cells	No growth	CTX,MET,CIP	22
5	59/M	L	DM,HTN	NA	Otalgia, hearing loss	G	55	Soft tissue density noted in the mastoid air cells	P. aeuroginosa	CTX,MET,PTZ	17
6	56/M	R	DM	Y	Otalgia, otorrhoea, hearing loss, Vertigo, Facial nerve palsy	G	10	Soft tissue density noted in the mastoid air cells with TMJ and ITF involvement	No growth	CTX,MET,PTZ	26
7	36/F	R	DM, IDA	Y	Otalgia, Vertigo, cranial nerve palsy (9,10,12)	–	40	No significant involvement	MRSA	CFT,LZ,GEN	6
8	65/F	L	DM,HTN	NA	Otalgia, otorrhoea, hearing loss	G	20	Soft tissue density noted in the mastoid air cells with TMJ and ITF involvement	No growth	CTX,CIP	25
9	55/F	L	DM,HTN, CKD	Y	Otalgia, otorrhoea, hearing loss, Vertigo	G	28	Soft tissue density noted in the mastoid air cells with ITF involvement	P. aeuroginosa	CTX,MET,CIP	23
10	58/M	R	DM	Y	Otalgia, otorrhoea, hearing loss, Vertigo, Facial nerve palsy	G	79	Soft tissue density noted in the mastoid air cells with TMJ and ITF involvement	K.pneumoniae	PTZ,MET	14
11	65/M	R	DM,CKD	Y	Otalgia, hearing loss	-	110	Soft tissue density seen in the retropharyngeal area with extension into the tegmen and nasopharynx	No growth	PTZ,MET,CIP	21

MOE : malignant otitis externa; M : Male; F : Female; Lat : Laterality; R : Right side; L : Left side; DM : Diabetes mellitus; HTN : Hypertension; CKD : Chronic kidney disease; VX : Vaccination for COVID-19; Y : Yes; NA : Not available; EAC : External auditory canal; G : Granulations; TMJ : Temporomandibular joint; ITF : Infratemporal fossa; ESR : Erythrocyte sedimentation rate; CTX : Cefotaxim; CFT : Ceftriaxone; PTZ : Piptaz; AK : Amikacin; MET : Metronidazole; LZ : Linezolid; CIP : Ciprofloxacin; GEN : Gentamycin; DOHS : Days of hospitalisation; $: Atypical skull base-osteomyelitis

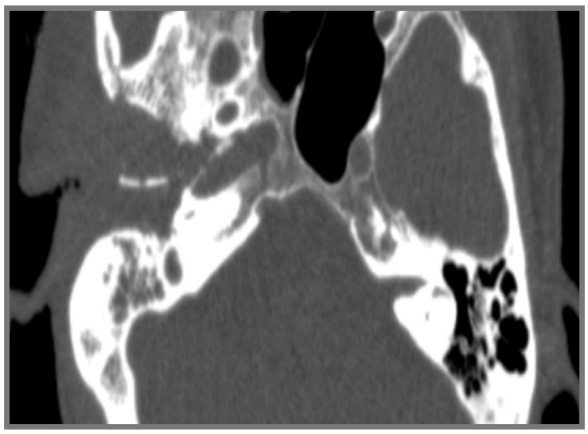

Fig. 3a. HRCT temporal bone showing erosion of the anterior canal wall extending into the TMJ, mastoid air cells

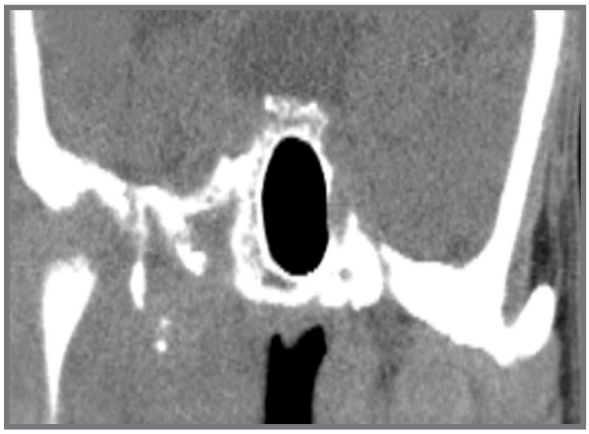

Fig. 3b. HRCT temporal bone showing erosion of the carotid canal.

Imaging

All the patients underwent HRCT of the temporal bone, and 64% of patients had soft tissue density and bony erosions involving the mastoid, followed by temporomandibular joint (TMJ) involvement in 36% and infratemporal fossa involvement in 27% (Fig. 3a & 3b). None of our patients had involvement of the petrous apex. HRCT imaging of the patient with atypical SBO showed fullness of the nasopharynx superior to the eustachian tube opening, along with irregularity of the bone in the inferior clival margin. The Contrast MRI of this patient revealed bone marrow changes involving the clivus (Fig. 4).

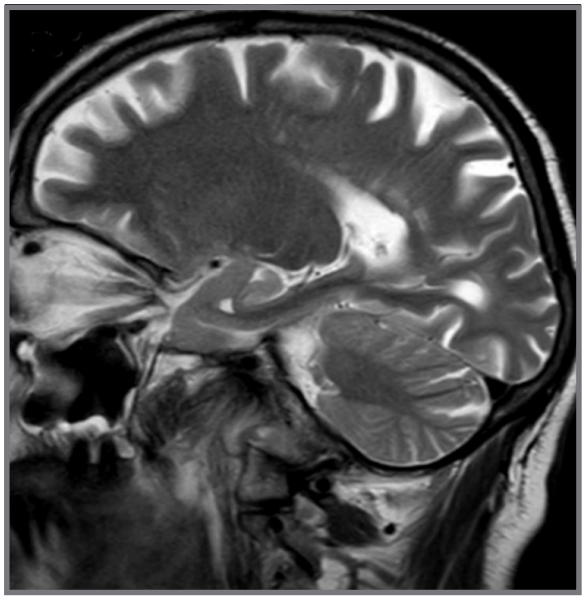

Fig. 4. Central or atypical skull base osteomyelitis MR image showing erosion noted in clivus and basi-occiput**.**

Treatment

All the patients were empirically started on intravenous cefotaxime followed by culture-specific antibiotics that included ciprofloxacin (45%), piperacillin-tazobactam (36%), amikacin (9%), linezolid (9%) and meropenem (9%). Topically they were given antibiotic ear drops like ciprofloxacin and gentamycin or dilute acetic acid ear drops as per the culture sensitivity pattern. The average duration of the treatment was 17.6 days.

Surgical management was reserved for cases that needed debulking of the granulation (40%) and facial nerve decompression (20%), done along with the drainage of micro-abscesses and the debridement of the diseased bone.

Outcome

All our study patients were clinically followed up for a period of 1 to 2 years of duration until they were symptom-free and clinically did not show granulations in the EAC. Of the total 11 patients, 5 had a severe MOE at the time

Table II : Severity and outcome of the disease

CASE NO	SEVERITY	DISEASE OUTCOME	FOLLOW-UP PERIOD
1	Non severe	Stable	Alive to date
2	Non severe	Stable	Alive to date
3	Non severe	Stable	Alive to date
4	Non severe	Expired	-
5	Non severe	Stable	Alive to date
6	Severe	Recalcitrant	Referred to the higher center
7	Non severe	Stable	Alive to date
8	Severe	Lost to follow up	-
9	Severe	Recalcitrant	Referred to the higher center
10	Severe	Stable	Alive to date
11	Severe	Expired	-

of admission (Table II). Post-treatment, 6 patients showed complete control of their MOE status and are alive to date, while 2 had a recalcitrant disease requiring referral to higher centres, 2 patients suffered mortality, and 1 patient was lost to follow-up.

Discussion

Chandler coined the term "Malignant" otitis externa because of its high mortality and morbidity during the pre-antibiotic era. The disease starts in the EAC and extends to the soft tissue and the periosteum, involving the skull base.[1]

The age of presentation, gender predilection and the laterality of the disease in our study were the 5th to 6th decade of life, with male preponderance and right-ear involvement, respectively which were similar to other studies.[11, 12] Uncontrolled type II diabetes mellitus followed by systemic hypertension were the commonly associated comorbid conditions, as in other studies done by Marina et al.[13, 14] Increasing age, along with uncontrolled sugars, is proposed to be a risk factor for MOE as it impairs phagocytosis and chemotaxis, leading to amplified virulence and the adherence of microorganisms to the cells. The lytic enzymes produced by the bacteria cause necrotizing endarteritis, which further leads to coagulation necrosis, granulation and microabscess formation, resulting in osteomyelitis, especially in patients with preexisting microangiopathy, as in cases with uncontrolled diabetes mellitus.[15, 16]

The clinical presentation of the patients in our study was similar to the studies around the globe, with deep-seated otalgia and purulent otorrhea being the most common symptoms, followed by aural fullness, facial nerve palsy and EAC granulations.[17, 18]

Although a non-specific inflammatory marker, ESR was elevated in 82% of patients and correlated well with the treatment response, as is also observed in studies by Rajasekar et al and Hasibi et al.[17, 18]

Pseudomonas aeruginosa was the most common organism seen in the ear swab culture study, and the other organisms found were Klebsiella pneumoniae, MRSA, Candida and Aspergillus species. However, there was no growth was noted in 36 %. These findings from ear swab culture were similar to the studies done by Loh et al and Vinayakumar et.al.[19, 20]

The mainstay of treatment for MOE is medical management with third-generation cephalosporins, fluoroquinolones, and carbapenems.[21] In our study, we tailored the use of antibiotics based on the antibiogram and in cases of no growth on the culture of the ear swab, an empirical treatment showed good results. Surgery was reserved for limited cases, similar to other studies such as biopsy of the granulation tissue in the EAC, removal of the sequestrum, drainage of the abscess, mastoidectomy and decompression of the facial nerve.[22, 23]

Although there is no unified protocol for the management of MOE, we recommend third-generation cephalosporins for a duration of 4 to 6 weeks and then follow up with oral fluoroquinolones like ciprofloxacin 750 mg twice daily for 8 to 10 weeks. This is also the recommendation as given by Lambor D et al.[25] We also recommend local therapy, such as topical ear drops that are culture-specific and dilute acetic acid ear wash. Surgical management is reserved only for biopsy, removal of sequestrum, to obtain core biopsy and microbiological samples, drainage of abscess or decompression of the facial nerve

While 55.5% had good treatment outcomes, around 36 % had relapsed and required readmission both for the disease and diabetic control, which was comparable to the study done by Glikson et al.[24] The mean duration of hospital stay was 18.2 days, akin to Lambor D et al.[25] We saw a mortality rate of 18% similar to Bhandary S et al,[26] although the mortality rate depends on various factors such as the patient factor, treatment factor and stage of the disease.

In our study, we observed certain patient factors that can be the cause for the poor outcomes such as older age, poor glycaemic control, multiple co-morbidities, multiple cranial nerve palsies and clivus involvement. These factors were similarly seen in the study by Lee et.al.[27]

The incidence rate of MOE was about 2.24 per million person-years of observation as per the study done by Yang et al and overall, the incidence of MOE is very less.[28] The COVID-19 era seems to have faced an apparent increase in the incidence of MOE as reported by Eweiss et al and many more are still being reported.[29,30] This can be because the pandemic had a great impact on patients with type II diabetes mellitus, and their glycaemic control, to the extent of causing immunosuppression as well. Although the clinicopathological and the radiological profile did not vary from the pre-covid MOE, the apparent increase in the number of cases should alert the surgeons, towards early clinical diagnosis, good control of sugars and appropriate treatment which is the cornerstone of management for this clinical entity.

Limitations

This is a single-center descriptive observational study with a small sample size, therefore, additional research in terms of a larger sample size and a multicentric study will help in a better understanding of the etiopathogenesis, disease activity, management protocols, treatment response and prognosis in MOE as well as in atypical SBO. However, while our sample size is small, the findings may reflect a national trend, and it may be an epiphany to this association between the post-COVID-19 pandemic and MOE.

Conclusion

Despite recent advances in diagnostic workup and treatment, MOE remains an obscure, highly unpredictable, serious and potentially fatal clinical condition. In our study, we observed poor outcomes in MOE patients of older age, poor glycaemic control, multiple co-morbidities, multiple cranial nerve palsies and clivus involvement. We advocate organism-specific antibiotics based on the ear swab culture. ESR and HRCT of the temporal bone, though non-specific, can guide us during treatment and follow-up. In our study, there was an apparent increase in the number of cases of MOE that were reported during the pandemic.

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