

The Role of Surgical Debridement in Cases of Refractory Malignant Otitis Externa

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Abstract Malignant Otitis externa is a necrotizing condition of external ear involving causing the osteomyelitis of the bone and surrounding soft tissue leading to multiple cranial nerve palsies. Though most patients respond to oral ciprofloxacin but due to emerging resistance cases of refractory malignant otitis externa which are unresponsive to antibiotic therapy for at least 6 weeks are being encountered lately. A study of 20 patients of refractory malignant otitis Externa was conducted at a tertiary care centre in north India; 10 patients were randomly allotted in group A and group B each. Group A was subjected to i/v ceftazidime 1 gm bd with oral ciprofloxacin 750 mg bd and Group B was subjected to surgical debridement with oral ciprofloxacin 750 mg bd. The improvement in symptoms was tabulated and statistical analysis was done using Mann–Whitney *U* test. There was better resolution of nocturnal pain in patients of group B who underwent surgical debridement although existing facial palsy didn't improve in both the groups. The improvement of symptoms in group B was statistically significant with $P \leq 0.05$. We strongly recommend the role of surgical debridement in cases of refractory malignant otitis externa to relieve the patient of nocturnal pain. As the sample size of the study is small we are looking forward to the compilation of a multi

institutional data so that a consensus on definitive protocol in cases unresponsive to oral multidrug therapy can be established.

Keywords Refractory · Malignant otitis externa · Surgical · Role · Debridement

Introduction

Malignant otitis externa is an aggressive, highly morbid and rarely life threatening infection of soft tissue of external ear and surrounding structures, which spread to involve the periosteum and bone of skull base. The infection usually originates from the external auditory canal and progress through stages of cellulitis, chondritis, periostitis, osteitis, and finally osteomyelitis. It is referred to as skull base osteomyelitis once the bone infection is confirmed and also known as necrotising otitis externa due to extensive soft tissue involvement [1].

The term malignant otitis externa is a misnomer as it is not a neoplastic condition, but a rather the disease spreads and deteriorates rapidly like malignancy, involving normal tissue, especially among elderly diabetic individual, hence it is a dreaded condition for any practicing otorhinolaryngologist. The first reported case was published in 1838 by Toulmouche and term malignant otitis externa was first described by Chandler in 1968, because of its high morbidity and mortality [2].

Traditionally in the days of Chandler, therapy was exclusively surgical with high mortality rates of approximately 50% [3]. As medical management of disease with parenteral antibiotics and high glycemic control become standard of care, outcome dramatically improved with surgery reserved for refractory cases. With modern

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treatment paradigms and improved diagnostic measures majority of patients are now expected to achieve high cure. Despite recent success, aggressive and sometimes fatal cases of MOE are still encountered. For this reason successful treatment predictive variables are highly sought after. Unfortunately, the literature is widely heterogeneous on this topic, with little agreement and no standardized protocol [4–8].

To overcome this primary shortcoming of treatment protocols, present study was conducted with hypothesis in mind based on an observation that refractory otitis externa with severe nocturnal pain treated with early surgery under antibiotic cover and aggressive post op care has improved treatment outcome especially in reducing nocturnal pain than with multimodality antibiotic treatment.

Methods and Materials

Present study named The Role of Surgical Debridement in Refractory Cases of Malignant Otitis Externa is a randomised controlled study carried out in department of ENT at a tertiary referral centre of North India from March 2017 to March 2018. For conducting study CONSORT reporting guidelines were followed.

All the necessary ethical clearance was obtained from institutional ethical committee before recruitment of clinical subjects according to principles of Declaration of Helsinki.

Thorough written informed consent was taken from patients in language best understood by them. All necessary measures were taken to maintain patient confidentiality at all the points of study.

Patients of refractory otitis externa were selected based on Levenson criteria. Total of 20 patients were selected randomly following randomisation numbers in two groups.

Levenson Criteria [9, 10]

1. Refractory otitis externa
2. Severe nocturnal pain
3. Purulent otorrhoea
4. Granulation tissue in otitis externa
5. Growth of *Pseudomonas aeruginosa*
6. Presence of diabetes or immunocompromised

Inclusion Criteria

1. All patients of age group 40–80 years of refractory otitis externa

(Who are controlled diabetic or immunocompromised and are on continuous antibiotic therapy for more than 6 weeks

but not responding to antibiotic therapy and have radiological evidence of malignant otitis externa).

Exclusion Criteria

1. Newly diagnosed patient who have not completed 6 weeks of antibiotic therapy
2. Uncontrolled diabetes mellitus

Patients were randomly allocated in two groups Group A was given multidrug therapy (intravenous ceftazidime with ciprofloxacin) with aural toileting and group B was offered monotherapy of antibiotic with surgical intervention with aural toileting

After careful selection of patient based on clinical history and examination, all patients were subjected to examination under microscope with culture sensitivity of ear discharge, puretone audiometry, impedance audiometry. After audiological examination all patients underwent HRCT temporal bone and technetium 99 and those patients who had evidence of cranial palsies were further subjected to MRI temporal bone and skull base

Following parameters were studied on HRCT temporal bone

Spreading pattern; Soft Tissue and Bone involvement; Anterior Retrocondylar fat; Temporal fossa; Masticator space; TM joint Parotid; styloid foramen; Posterior Mastoid process; Medial Para Pharyngeal fat; Sphenoid; Nasopharyngeal fat; Clivus; Gpn nerv; Petrous Apex; Vagus nerve; Juglar foramen; Accessory nerve. Intracranially Sigmoid sinus; Jugular fossa; Jugular vein; petroclival area; ICA and Dura were accessed.

After thorough radiological work up for the patient, GROUP A patients were offered intravenous ceftazidime with oral ciprofloxacin 750 mg twice daily and with acetic acid wash three times a day

Group B patients were started on oral ciprofloxacin 750 mg bd with surgical intervention and regular post op care.

Aim of surgical treatment was

1. Local debridement of necrotic tissue
2. Abscess drainage and creation of drainage route
3. Control of complication

Patients in both groups were followed by questionnaire in improvement of symptoms and pain and further by Gallium 67 scan to monitor active inflammatory response by disease process. Data was collected and tabulated by SPSS system and statistical analysis was done by Mann–Whitney test for null hypothesis.

Results

Out of total patients 6 patients were in age group 40–60 years and 14 patients were in age group 60–80 years (Fig. 1). All patients were immunocompromised. 17 patients were diabetic and 3 patients were post radiotherapy. There were 14 males and 6 females. The clinical features as per levenson criteria are enumerated (Table 1; Fig. 2) Nocturnal pain was present in all 20 patients. The clinical signs are tabulated and also shown in pie chart (Table 2; Fig. 3). The organisms isolated were Pseudomonas; Kleibsella and MRSA in 16; 15 and 3 patients respectively. 4 patients showed no growth (Fig. 4). The treatment response in both groups was tabulated (Table 3) and then statistically analysed using mann–whitney test.

Discussion

In the Modern era, MOE has been treated effectively with antibiotics with activity against Pseudomonas sp., but a subset of these patients does not respond well with medical line of treatment and merits special attention and treatment, in order to figure out best treatment strategy for refractory MOE patients, Present study named ‘The role of surgical debridement in refractory cases of malignant otitis externa’ was undertaken with aim to answer these questions.

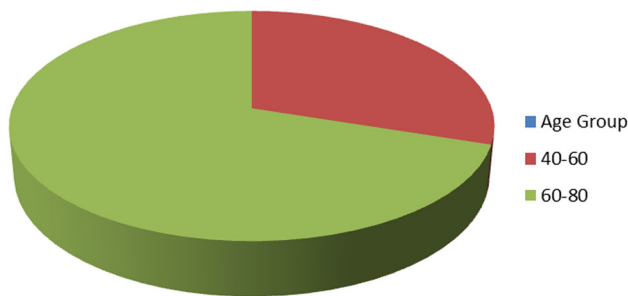


Fig. 1 Age distribution of patients enrolled in the study

Table 1 Incidence of symptoms in total number of patients

Symptoms	Number of patients
Nocturnal pain	9
Ear discharge	7
Hearing loss	5
TM joint pain	6
Facial nerve palsy	10
Pre existing CSOM	8

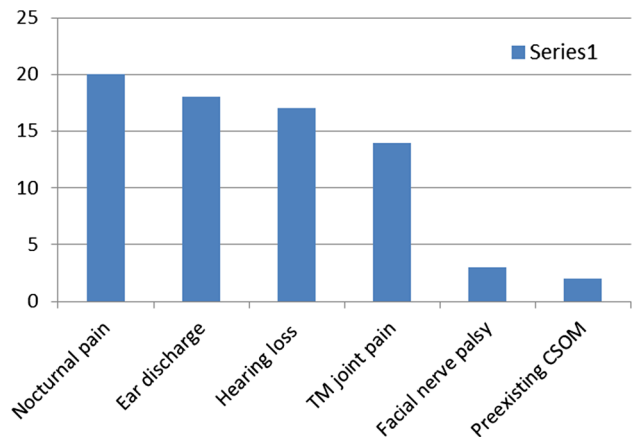


Fig. 2 Clinical features

Table 2 Clinical signs in total number of patients

Signs	Patients
EAC oedema	9
EAC oedema + granulation	10
EAC oedema + granulation + polyp	1

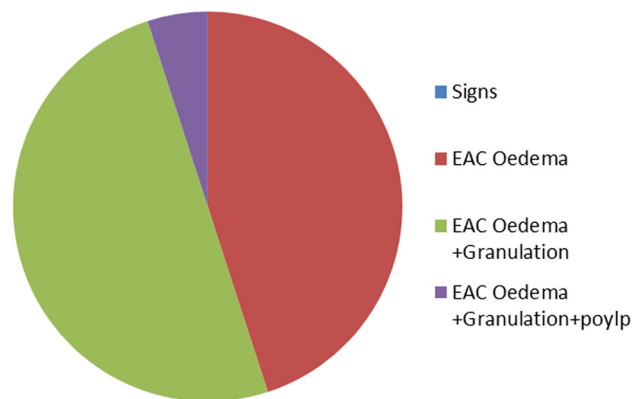


Fig. 3 Clinical signs present in patients

It was found that majority of patients who were enrolled were diabetic with 85% incidence and most common age group was 60–80 years (Fig. 1). Male outnumbered females.

Nocturnal pain was most common presenting feature (100%) which was out of proportion to clinical feature, followed by ear discharge (90%), hearing loss (85%), and TM joint pain (70%) (Table 1; Fig. 2).

EAC oedema with granulation were most common otoscopic findings (50%), followed by only EAC oedema (45%) and aural polyp in one patient (Table 2; Fig. 3).

Pseudomonas was most common organism isolated from ear discharge (80%) followed by Kleibsella (75%) (Fig. 4).

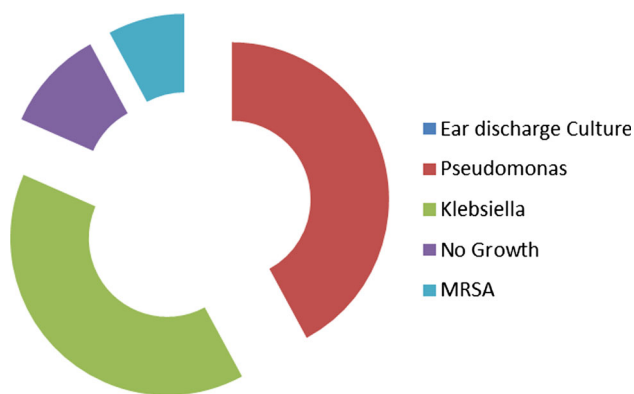


Fig. 4 Organisms obtained from the culture swab of the patients

Treatment response was studied in both groups by studying effect of treatment on resolution of following symptoms (Table 3).

1. Complete resolution of oedema and granulation
2. Resolution of pain (Nocturnal Pain)
3. Hearing loss resolution
4. No disease on post treatment gallium scan
5. Resolution of ear discharge
6. TM joint pain resolution

Mann–whitney *U* test was applied and *U* stat value for group A was 2 and *U* stat value for group B was 34

U critical value was found out to be 5

Since *U* stat for group A $2 < 5$ (critical value) @ $p < 0.05$

Null hypothesis that there was no difference in two treatment groups were rejected and alternate hypothesis that group B treatment was more effective treatment in refractory MOE was accepted.

Major limitation of present study was small sample size, short follow up, normalcy of data cannot be achieved because of small sample size, which can be a reason for non generatability of results in future studies, however all the efforts were made to remove all confounding factors and also to keep errors due to comorbid conditions to minimum.

Randomization, well designed study plan in terms of criteria for selection of patients, investigation and criteria for treatment response along with thorough review of literature before commencing study were major strengths of present study

Teams for both the groups for reporting and treating were kept same for each group to reduce any error.

Malignant otitis externa progressing to skull base osteomyelitis is an aggressive infection of temporal bone and skull base associated with possible involvement of the facial nerve, carotid artery, jugular vein and mastoid. It was termed malignant, due to the high mortality rate and poor response rate to treatment [11, 12].

Levenson Criteria Can be Used for Diagnosis

Criteria Include

1. Refractory otitis externa
2. Severe nocturnal pain
3. Purulent otorrhea
4. Pseudomonas infection
5. Granulation tissue in an immunocompromised patient

Patient with malignant otitis externa typically present with severe nocturnal otalgia accompanied by otorrhea that has been unresponsive to treatment, pain tend to be severe and often extends to TM joint [13].

In present study nocturnal pain was most common presenting features followed by ear discharge, hearing loss and tm joint pain, and incidence and sequence of these features correlated in a similar fashion in study.

Conducted by Shamanna et al. [14]: Changing Trends in the management of Malignant otitis externa.

In a large retrospective review conducted from 2004 to 2014 by Shawn et al. where systematic review of literature of senior authors from 1968 to 2014 was done and it was found that severe MOE was most commonly found elderly diabetic (type 2) males and most frequently associated

Table 3 Treatment response in both groups

Symptom resolved	Treatment response in group A Number of patients	Treatment response in group B Number of patients
Complete resolution of oedema and granulation	3	9
Resolution of Nocturnal Pain	4	7
Resolution of Hearing Loss	2	5
Disease resolved on post treatment gallium scan	2	6
Resolution of ear discharge	6	10
TM joint pain resolution	5	8

organisms were *Pseudomonas aeruginosa*, methicillin resistant staph aureus and *E. Coli* [15].

Finding of above study correlated with present study in terms gender incidence, underlying comorbid condition, and most commonly organism isolated from ear discharge of MOE patient, however instead of MRSA and *E. coli*; Klebsiella was the second most common organism found, reason for such difference can be a small size of sample, and selection of patients.

Clinicopathological classification system has divided the MOE disease process in 4 stages [1].

- | | |
|---------|---|
| Stage 1 | Clinical evidence of malignant otitis externa with infection of soft tissue of external auditory canal, but negative Tc 99 scan |
| Stage 2 | Soft tissue infection beyond external auditory canal with positive Tc -99 bone scan |
| Stage 3 | As above but with cranial nerve palsy |
| | 3A Single cranial nerve palsy |
| | 3B Multiple cranial nerve palsy |
| Stage 4 | Meningitis, empyema, sinus thrombosis or Brain abscess |

EAC oedema with granulation had almost similar incidence EAC oedema on otoscopy. One patient had aural polyp along with granulation and EAC oedema.

This was in contrast to study conducted by Karthik et al. [14] whereby EAC oedema and granulation were most common otoscopic finding outnumbering other two otoscopic findings that can be due random sample and small sample size.

Treatment of otitis externa and skull base osteomyelitis is a long process.

There is consensus for medical treatment with long term antipseudomonal medication with strict glycemic control and meticulous treatment for early and responsive MOE. However when question comes to treatment of refractory malignant otitis externa there is little consensus for treatment protocol, thus question can be raised whether medical intervention alone can be sufficient for this group.

We tried to compare two treatment arms (Long Multidrug treatment with antipseudomonal activity versus Early surgical intervention in refractory malignant otitis externa).

Systemic antipseudomonal are the primary therapy for malignant otitis externa, in last 15 years oral quinolones esp ciprofloxacin have revolutionised the treatment, ciprofloxacin 750 mg bd seems to be antibiotic of choice however comparative trials have not been done [16], more ever emergence of fluoroquinolone resistant Pseudomonal stainplays significant role in poor outcome and refractory cases [17].

Therefore we decided to treat patient with refractory malignant otitis externa not responding to oral

ciprofloxacin with intravenous multidrug therapy in one treatment arm.

Although literature on the modern era role of surgery in treatment of MOE is lacking, but there does seem to be a growing international movement towards use of operative intervention for refractory cases [18, 19].

In present study following treatment protocol was followed in treatment arm B.

Refractory MOE: No clinical improvement after 6 weeks of conventional treatment, patient evaluated for

1. Radical Debridement of necrotic tissue
2. Abscess drainage and creation of drainage routes
3. Control of complication

Treatment response was studied in both arms by following below responses in both groups

1. Complete resolution of oedema and granulation
2. Resolution of pain (Nocturnal Pain)
3. Hearing loss resolution
4. No disease on post rx gallium scan
5. Resolution of ear discharge
6. TM joint pain resolution

Treatment response in Surgical intervention arm clearly shows that there is definite statistical advantage in resolution of all above mentioned parameters if Refractory MOE are offered relevant surgical intervention.

Shawn et al. stated that With high mortality rate and poor treatment response, the risk benefit balance in severe MOE cases actually favour early surgical intervention as a treatment option (D4) which further supported our hypothesis that early surgical intervention is better treatment option in refractory otitis externa.

Conclusion

Refractory MOE is a serious invasive disease affecting mainly elderly diabetic patients and other immune compromised patients. The most common presentation is severe nocturnal otalgia with otorrhoea followed by hearing loss. Although strict glycemic is mandatory for success of any treatment of MOE, there is definitive role of early surgical intervention in treatment of refractory MOE. However we still believe that because of rarity of disease, large prospective cohort is difficult for effective protocol model and large multi-institutional study be undertaken.

Compliance with Ethical Standards

Conflict of interest The author declares that they have no conflict of interest

Informed Consent Before starting the study Ethical Clearance was taken from the institutional ETHICAL Committee as per DECLARATION OF HELSINKI

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