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CLINICAL STUDY

A Study to Estimate the Variations in Management of Malignant Otitis Externa at Two Different Socio-Economic Hospitals - A Clinical Dilemma

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ABSTRACT
Introduction: Malignant otitis externa is an aggressive and potentially fatal infection of ear and skull base. Few studies have attempted to frame a protocol for management of this condition. However, the applicability of protocols involving radionuclide investigations in rural areas with restricted access is a challenge. Also, treatment with oral quinolones has since been threatened as their use has become widespread and indiscriminate. Objective: Owing to a lack of standardized diagnostic criterion and treatment regimes, and growing concerns regarding quinolone resistance, we reviewed cases of malignant otitis externa treated across two different socio-economic centres to identify diagnostic and management difficulties.
Methods: A retrospective data analysis of patients with malignant otitis externa managed in a tertiary and primary care hospital was done between December 2017 and November 2018. All relevant data were retrieved for assessment.
Results: 43 patients were identified, out of these 19 were at the private institute and 24 at the charitable institute. Otalgia was the predominant symptom among all. Pseudomonas aeruginosa was the most commonly isolated organism (81% of patients). Ciprofloxacin resistance reported was 38%. The tertiary care institute used CT and Gallium scans for diagnosis, whereas primary centre employed clinical parameters and CT only. Treatment included Meropenem, Ceftazidime, Amikacin at the tertiary centre and Ciprofloxacin and Streptomycin at the primary centre.
Conclusions: Incidence of Ciprofloxacin resistance was high in our study confirming the growing concern documented in other studies. Access to higher antibiotics was restricted in rural areas where Streptomycin was used in combination with other drugs with promising results.

KEYWORDS: Malignant Otitis Externa, Pseudomonas Aeruginosa, Ciprofloxacin.

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INTRODUCTION

Malignant otitis externa (MOE) is an invasive infection of the external auditory canal leading to osteomyelitis of the base of the skull, which typically occurs in elderly patients with diabetes mellitus [1-3]. Pseudomonas aeruginosa is nearly always the responsible organism. The diagnosis of this entity is often delayed and a strong degree of suspicion is necessary to avoid delays in treatment. Moreover, the management of this rare but severe infection is not currently standardized. The diagnostic criteria especially laboratory and radiographic tests vary across centres depending on their availability and affordability. In the absence of widely applicable criterion, the diagnosis of is often reached on the basis of a constellation of clinical, laboratory, and

radiographic findings. Antipseudomonal antimicrobials provide the mainstay therapy for MOE; surgery and topical antibiotics have no role to play in the treatment [1]. Culture-directed therapy for 6–8 weeks is generally recommended, as indicated for osteomyelitis [1,3]. A wide variety of antibiotic regimens and durations of treatment have been reported in the literature, and choosing the best antibiotic therapy is therefore difficult. Owing to lack of standardized diagnostic criterion which may not be widely applicable in especially in regions of developing countries with limited resources, as well as treatment regimens which mainly involve higher antibiotics, and growing concerns regarding quinolone resistance, we reviewed cases of malignant otitis externa treated across two different socio-economic centres to identify diagnostic and management difficulties.

METHODS

A retrospective review of medical records was done across two different hospitals, centre one being private tertiary care institute and centre two being a charitable/ funded primary care hospital. The records of all patients admitted during one year (December 2017 to November 2018) with diagnosis of malignant otitis externa were accessed after institutional permission and institutional ethical committee clearance. Patient characteristics noted were symptoms, otoscopic findings, radiographic & biochemical tests, previous treatment records, microbiology & antibiotic sensitivity, length of hospital stay. All relevant data were retrieved from the hospital notes or patients own discharge records. This was a retrospective non-interventional observational review of medical records and the priority was to focus on methods of diagnosis, and the detailed therapies given to these patients.

Inclusion Criteria was all patients admitted to both centres either to inpatient ward or ICU during one year period and were diagnosed as malignant otititis externa by their attending physicians.

Exclusion criteria – patients with skull base osteomyelitis only without any ear symptoms or findings. In these cases, the attending physicians may not have confirmed a diagnosis of malignant otitis externa, however it could have been in their list of differentials.

Study period was from December 2017 to August 2019. All patients with MOE admitted to either hospital during one year duration of December 2017 to November 2018 were included. The data of these patients was collected and analysed from January 2019 to August 2019.

RESULTS

49 patients were identified across both centres, but complete relevant data was available for only 43 out of which - 19 were at centre one and 24 at centre two

All patients included in the study presented with either severe deep seated otalgia or otorrhea, which had not responded to topical treatment of presumed simple otitis externa. As per physicians' notes, this formed part of their clinical criteria for diagnosing the cases as MOE. All patients had microbiological samples taken in the hospital by the attending ENT specialist (external auditory canal swab performed during otoscopy) after discontinuation of any topical and systemic antibiotic therapy prescribed in the outpatient setting. Susceptibility testing was performed on all bacterial strains. Computed tomography (CT) scanning demonstrating signs of MOE (thickening and enhancing soft tissue and sometimes cortical bone erosion in the region of the external auditory canal) as well as C-reactive protein levels were done across both centres. In addition, pre-treatment gallium scans were done at centre one to note active hot spots indicating bone destruction, following which post treatment gallium scans were used to assess effect of antibiotic therapy. No other clinical signs or laboratory or microbiology results were included in the diagnostic criteria at centre two.

General Patients' characteristics

Patients with age between 35 and 78yrs were identified, no pediatric cases were reported, with male to female ratio as 3.8 to 1. All the patients were found diabetic and the mean duration of diabetes was 11 years. All patients were treated at other hospitals prior to the presentation. Average hospital stay after presentation was 8-10 days at Centre one and 23-26 days at Centre two.

Deep seated otalgia was the most common symptom affecting all 43 patients typically worsening at night. Second commonest symptom reported in 38 patients was purulent otorrhoea. Hearing loss was reported in 39 cases with 32 patients showing a mixed hearing loss and remaining 7 patients with conductive loss alone. The hallmark examination findings was granulation present especially at the external auditory canal seen in 38 patients, while the remaining 5 patients shows canal oedema.

Pseudomonas was isolated from cultures of 38 patients out of which 3 patients showed additional candida albicans in culture; 1 patient showed Staphylococcus haemolyticus; 1 acinetobacter baumanni and 3 patients with Klebsiella. (Table 1)

Table 1: Organism isolated from ear swab cultures

Organism	Frequency
Pseudomonas aeruginosa	35
Pseudomonas + Candida albicans	3
Staphylococcus haemolyticus	1
Acinetobacter baumanni	1
Klebsiella	3

Management at Centre one : All 19 patients admitted to hospital in the ICU for initiation of treatment, later shifted to inpatient care once the diabetes status corrected and renal & other co-morbidities managed. Computed tomography (CT) and C-reactive protein (CRP) levels, ESR and other relevant lab tests done. Also, patients with suspected skull base involvement

and 1 patient with osteomyelitis and abscess formation underwent an MRI scan. In addition, **Gallium 37 citrate scans were done pre** (Image 1) **and post treatment** to note reduction in tracer uptake for monitoring disease progression. The treatment protocols were set according to recommendation of ICU intensivists and infection specialists. 13 pateints received injectable Meropenem 4 g/day in continuous IV infusion and injectable Amikacin 1.5gm once a day on alternate days. 1 patient received injectable Ceftriaxone 4g/ day in addition to be above, whereas 5 patients received injectable Ceftazidime 6g/day in addition to meropenem and amikacin. Reduction of hot spots on gallium scans after 4 weeks of intravenous antibiotic therapy was taken as the indicator to shift to oral antibiotic therapy. 1 patient showing signs of skull base osteomyelitis and abscess formation underwent endoscopic assisted surgical drainage of abscess via nasopharyngeal approach. All 19 patients with initial elevated C-reactive protein (CRP≥10 mg/L) had normal CRP levels after 4 weeks of intravenous antibiotic therapy. All 19 patients continued to receive oral treatment with Levofloxacin 750mg daily for an additional period of 3 weeks.

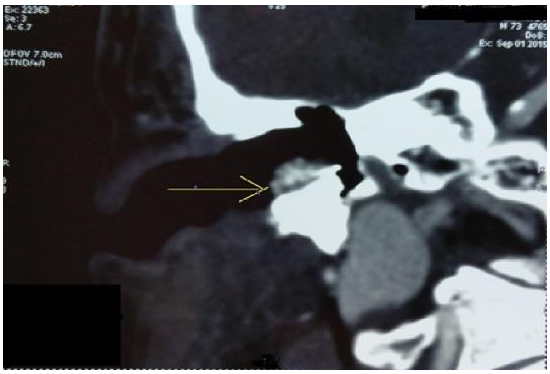

Image 1: CT scan showing granulations in EAC and bony sequestra.

Management at centre two

All 24 patients were admitted to the hospital in the inpatient wards. The diagnosis was confirmed on clinical, microscopy and CT temporal bone findings (Image 2). CRP levels were noted pre-treatment as prognostic indicator. Response to treatment was gauged by reduction of night time otalgia, change in physical findings (Image 3) and fall of CRP levels. No additional tests were done. Patients were started on intravenous Ciprofloxacin 750mg daily and Streptomycin 1.5gm alternate day dose. (Table 2 for details) Oral Ciprofloxacin 500mg/twice daily was started after completing 3 weeks of IV therapy and continued for additional 4 weeks. 5 patients with relapses after initial period of improvement received IV therapy for 6 weeks.

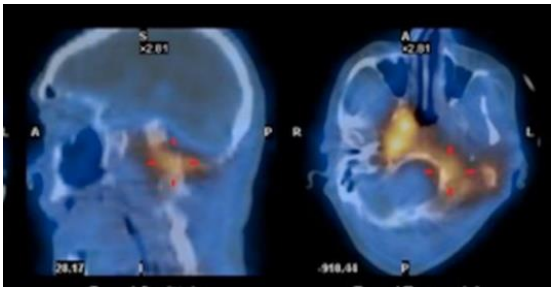

Image 2: Gallium scan showing radiotracer uptake in temporal bone.

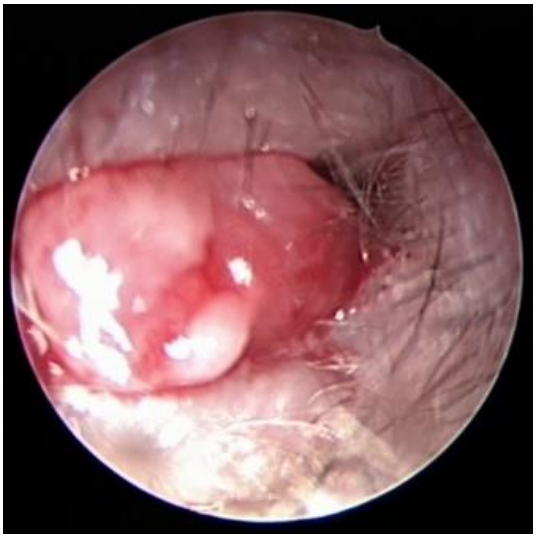

Image 3a: Endoscopy image showing granulation occluding external auditory canal at presentation at centre two.

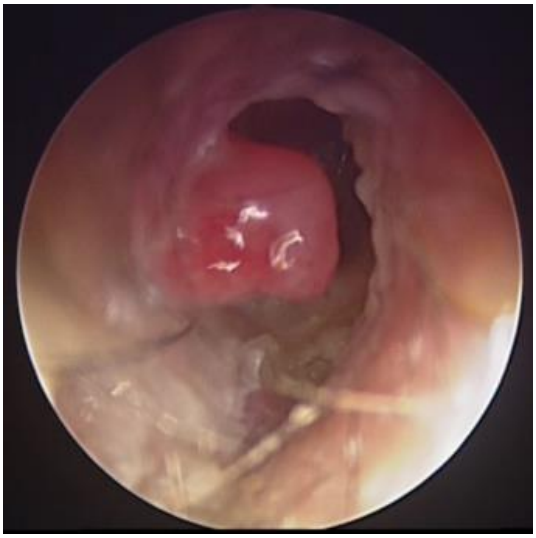

Image 3b: Image post 2 weeks of treatment at centre two- granulations reduced significantly

Table 2: Antibiotic therapy at private tertiary centre

No of patients	Duration	Antibiotics given	
9	3 weeks	Ciprofloxacin 750mg/day	Streptomycin 1.5g OD on alternate days
3 (With facial paresis)	4 weeks	Ciprofloxacin750mg/day + Cefpodoxime 4g/day	
12 (11 resistant to pseudomonas 1 with Klebsiella)	4 weeks	Cefpodoxime 4g/day	

DISCUSSION

Computed tomography, magnetic resonance imaging and isotope bone scanning have been used to assess progress of therapy in cases of malignant otitis externa [4]. Gallium-67 citrate serial scans are useful in evaluating the effectiveness of treatment as the uptake of gallium decreases with control of the infection and the scan rapidly turns negative which is essential to note response to therapy [5]. However, in our study, only patients at the tertiary care centre underwent serial imaging with computed tomography and gallium scan. At the primary centre, CT scans were done only for diagnosis, where the appearance of soft tissue swelling was noted in all 24 cases along with bone erosion in 11 cases. The progression of disease on CT scan alone was difficult but it provided useful information for confirmation of disease extent in the absence of isotope or bone scans.

Ciprofloxacin was introduced in the late 1980s. This oral treatment greatly reduced the need for surgical intervention and hospital admission and rapidly became the antibiotic of choice [1,6,7]. Unfortunately, ciprofloxacin resistant Pseudomonas aeruginosa is an emerging problem with several recent studies reporting ciprofloxacin resistant cultures [1,8-10].

In our study, chief organism isolated from ear swabs was pseudomonas – 86%, where ciprofloxacin resistant strains of Ps Aeruginosa were isolated from total 16 samples (38%) – **5** at centre tertiary centre and **11** at primary centre. This is consistent with other studies reporting resistance rates ranging from 3 – 50% [8]. This resistance is perhaps a consequence of previous fluoroquinolone topical and/or systemic treatment even for simple otitis externa.

At the tertiary care centre all the patients were treated with either Meropenem 4gm or Ceftazidime 6gm daily in combination with Amikacin 1.5gm alternate day regime.

At the primary care centre all patients showing ciprofloxacin sensitivity were started on Ciprofloxacin 1gm daily with amikacin 1.5 gm alternate day. Response to treatment was gauged by reduction of otalgia (especially night time otalgia). However, relapses were noted in 5 patients even when there was a good early response and intravenous treatment was continued for six to eight weeks. 2 patients did not respond to ciprofloxacin, and were later shifted to Steptomycin with Cefpodoxime 4gm. All had typical characteristics i.e elderly and suffering from type-2 diabetes (which was monitored and controlled).

Cranial nerve palsies arise from the progression of osteomyelitis in the petrous temporal bone leading to constriction at the stylomastoid foramen and the more distant jugular foramen. In keeping with this anatomy, facial nerve palsy is more frequent than glossopharyngeal, vagus, and accessory nerve palsies [2,11]. In our study, facial nerve palsy presented in 2 cases out of 19 at the primary centre and was treated with Ciprofloxacin 1gm per day, streptomycin 1.5gm alternate day and Cefpodoxime 4gm daily.

These cases illustrate the need to reconsider intravenous antibiotic therapy regimens, one which is readily available and affordable to the patients. The prolonged duration of treatment regimen (i.e minimum 6 weeks or more) often leads to non-compliance of patients and discontinuation of treatment. Thought needs to be given to the logistics of arranging intravenous therapy to primary care centres on an out-patient basis, to avoid the expense and demoralization of a long stay in hospital.

Study Limitations: Our study lacked a predetermined frame for clinical assessment and documentation, which is a limitation with most retrospective studies. In addition to this, multiple confounding factors and as well as variables in the study made it impossible to produce a sound statistical analysis and comparison between patient groups.

CONCLUSION

No standardised protocols were identified at the primary care centre for treatment of malignant otitis externa. Also, a longer hospital stay with its associated problems were a concerning factor for treatment at the primary care centre. There was limited or no role of surgical management in the treatment of malignant otitis externa in both the centres in our study. Lastly, our study reported a significant presence of Pseudomonas strains resistant to ciprofloxacin, similar to other studies.

Future Considerations : There is an urgent need to reconsider intravenous antibiotic therapy regimens, ones which are readily available as well as affordable to the patients. Prolonged duration of treatment and/or financial constraints often lead to non-compliance of patients and discontinuation of treatment. We must advocate more practical and widely applicable guidelines to diagnose and further follow disease progression. In additions, we must arrange for logistics to provide intravenous therapy at primary care centres on an outpatient basis, to avoid the expense and demoralisation associated with a long hospital stay. Finally, it is imperative that we explore effectiveness of Streptomycin or similar affordable drugs, especially for wider distribution in developing countries, as they are more cost effective for long term regimens and seem to be equally effective.

COMPETING INTERESTS

The authors declare no competing interests with this study.

REFERENCES

[1] Grandis JR, Branstetter IV BF, Yu VL. The changing face of malignant (necrotising) external otitis: Clinical, radiological, and anatomic correlations. Lancet Infect Dis. 2004 Jan;4(1):34–9. DOI: 10.1016/s1473-3099(03)00858-2

[2] Chandler JR. Malignant external otitis. Laryngoscope. 1968 Aug;78(8):1257–94. DOI: 10.1288/00005537-196808000-00002

[3] Carfrae MJ, Kesser BW. Malignant otitis externa. Otolaryngol Clin North Am. 2008 Jun;41(3):537–49, viii–ix. DOI: 10.1016/j.otc.2008.01.004

[4] Al-Noury K, Lotfy A. Computed tomography and magnetic resonance imaging findings before and after treatment of patients with malignant external otitis. Eur Arch Oto-Rhino-Laryngology. 2011 Dec 15;268(12):1727–34. DOI: 10.1007/s00405-011-1552-8

[5] Okpala NCE, Siraj QH, Nilssen E, Pringle M. Radiological and radionuclide investigation of malignant otitis externa. J Laryngol Otol. 2005 Jan;119(1):71–5. DOI: 10.1258/0022215053222978

[6] Hickey SA, Ford GR, O'Connor AF, Eykyn SJ, Sönksen PH. Treating malignant otitis with oral ciprofloxacin. BMJ. 1989 Aug;299(6698):550–1. DOI: 10.1136/bmj.299.6698.550

[7] Levenson MJ, Parisier SC, Dolitsky J, Bindra G. Ciprofloxacin: drug of choice in the treatment of malignant external otitis (MEO). Laryngoscope. 1991 Aug;101(8):821–4. DOI: 10.1288/00005537-199108000-00004

[8] Berenholz L, Katzenell U, Harell M. Evolving resistant pseudomonas to ciprofloxacin in malignant otitis externa. Laryngoscope. 2002 Sep;112(9):1619–22. DOI: 10.1097/00005537-200209000-00017

[9] Hsu DI, Okamoto MP, Murthy R, Wong-Beringer A. Fluoroquinolone-resistant Pseudomonas aeruginosa: risk factors for acquisition and impact on outcomes. J Antimicrob Chemother. 2005 Apr;55(4):535–41. DOI: 10.1093/jac/dki026

[10] Giamarellou H. Therapeutic guidelines for Pseudomonas aeruginosa infections. Int J Antimicrob Agents. 2000 Oct;16(2):103–6. DOI: 10.1016/s0924-8579(00)00212-0

[11] Lucente FE, Parisier SC. James R. Chandler: "Malignant external otitis." (Laryngoscope. 1968;78:1257-1294). Laryngoscope. 1996 Jul;106(7):805–7. DOI: 10.1097/00005537-199607000-00003