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MAIN ARTICLE

Necrotising otitis externa: clinical profile and management protocol

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Abstract

Background: Necrotising otitis externa, which is typically seen in elderly diabetics, is a severe infective disorder caused by *Pseudomonas aeruginosa*. There is lack of standard management policy for necrotising otitis externa, hence this study attempted to frame a protocol for management based on clinical parameters.

Method: A retrospective study of 27 patients with necrotising otitis externa was conducted over 6 years in a tertiary care hospital. Data were analysed with regards to demographic characteristics, clinical features, investigations, staging and treatment modalities.

Results: Out of 27 patients, 26 were diabetics. The commonest organism isolated was *P aeruginosa*, which was sensitive to third generation cephalosporins and fluoroquinolones. Nine patients had cranial nerve involvement. Twelve of 15 patients treated with medical therapy recovered, as did 11 of 12 patients that underwent surgery.

Conclusion: A high index of suspicion, early diagnosis and prompt intervention are key factors to decrease morbidity and mortality. Fluoroquinolones, third generation cephalosporins and surgical debridement are the mainstay of treatment.

Key words: Otitis Externa; Fluoroquinolones; Osteomyelitis; Temporal Bone; Pseudomonas; Ceftazidime

Introduction

Necrotising otitis externa or skull base osteomyelitis is an aggressive and potentially fatal infection of the external auditory canal and skull base. It is typically seen in elderly diabetic or immunocompromised individuals. Progressive osteomyelitis of the temporal bone was first reported by Toulmouche in 1838.[1] In 1959, Meltzer and Kelemen described a case of progressive pseudomonal osteomyelitis of the temporal bone.[2] In 1968, Chandler used the term 'malignant external otitis' to describe 13 cases of pseudomonal external otitis which began in the external auditory canal and mainly affected elderly diabetics.[3] The infection may spread to soft tissues of the skull base and progress to facial nerve palsy, mastoiditis, multiple cranial nerve palsies and death. The mortality rate of necrotising otitis externa has been reported to be 23 per cent in cases where no deep structures were involved, 67 per cent if the facial nerve was involved and 80 per cent if deeper cranial nerves and the jugular vein were involved.[4]

The diagnostic criteria for necrotising otitis externa are divided into obligatory (major) and occasional (minor) criteria.[5] Patients usually present with extreme otalgia and otorrhoea. The pain is classically worse at night. The infection penetrates through the osteocartilaginous junction in the floor of the external auditory canal and invades the connective tissues, cartilage, bone, nerves and blood vessels in the temporal bone and its surroundings (base of skull, masseter and pterygoid fossa).[6] The diagnosis requires a high index of suspicion in those not responding to conventional treatment. Immunocompromised patients are at high risk of developing necrotising otitis externa. However, it can also affect non-diabetics,[7–9] young diabetics,[10] patients on cytotoxic drugs[11] and infants.[12]

Most cases of necrotising otitis externa occur in elderly diabetics due to macroangiopathy (atherosclerosis) and microangiopathy, which result in poor local blood supply, compromising systemic antibiotic uptake. The diabetic immune response is compromised by poor migration, reduced chemotaxis and defective phagocytosis of polymorphonuclear leucocytes; this decreases the host response to pseudomonas.[13–15] In addition, the cerumen of diabetic patients has a higher pH, which makes for a hospitable environment for bacterial growth.[16]

Pseudomonas aeruginosa is the most common pathogen in skull base osteomyelitis.[17–19] Aspergillus has also been implicated in necrotising otitis externa;

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this infection typically begins in the middle ear or mastoid as opposed to the external auditory canal.[20–23] *Staphylococcus aureus*, *Staphylococcus epidermidis*, proteus and salmonella have all been reported as aetiologic agents.

A technetium-99m bone scan is a valuable test in diagnosis as the results are positive in early cases of temporal bone osteomyelitis. Gallium-67 citrate serial scans are useful in evaluating the effectiveness of treatment as the uptake of gallium decreases with control of the infection.[24] Computed tomography (CT) defines the location and extent of the disease process at initial evaluation. Early in the course of the disease, soft tissue changes and bony erosion may be noted in the external auditory canal. More advanced cases manifest active bone destruction in the skull base, temporomandibular joint and mastoid that sometimes extends into the petrous apex, jugular foramen and carotid canal. Bony sequestration and abscess formation, as well as soft tissue oedema in the parapharyngeal space and nasopharynx, may also be seen in advanced cases.[25]

The treatment of necrotising otitis externa involves different parenteral antipseudomonal antibiotics (quinolones), local debridement of ear canal granulations, wide surgical excision and hyperbaric oxygen as an adjuvant therapy for refractory cases.[26–28]

The rise in prevalence of diabetes and human immunodeficiency virus (HIV) has led to a corresponding increase in the incidence of necrotising otitis externa. This paper presents the clinical profile and management policy followed for 27 cases diagnosed with necrotising otitis externa at our institution from 2006 to 2012. The main goal of this study was to develop a protocol based on clinical parameters for the diagnosis and treatment of necrotising otitis externa in otolaryngological practice.

Materials and methods

We conducted a retrospective study of 27 patients diagnosed with necrotising otitis externa in the Department of Otorhinolaryngology & Head and Neck Surgery, Goa Medical College & Hospital, India. The study spanned a period of six years, from May 2006 to May 2012. The data were obtained from the medical records department of the institution. All patients included in the study were in-patients except one who was treated on an out-patient basis.

A diagnosis of necrotising otitis externa was established according to the following criteria: (1) persistent otalgia and otorrhoea for more than 10 days despite receiving routine otitis externa treatment; (2) the presence of external auditory canal granulations or oedema; (3) concurrent diabetes or an immunocompromised state; (4) the isolation of causative organisms of necrotising otitis externa such as *P aeruginosa* or *S aureus* from external auditory canal exudates; and (5) a high resolution CT scan showing soft tissue changes and bone erosions in the external auditory canal, with extension along the skull base and adjacent structures.

A review of the literature revealed several staging systems based on clinical, radiological and combined clinico-radiological findings. We used a staging system based on clinical and high resolution CT scan findings, and categorised our patients into four stages as follows. Stage I: clinical evidence of soft tissue infection of the external auditory canal and beyond, without bone erosion on high resolution CT of the temporal bone. Stage II: the above features with bone erosion. Stage III: the above features with cranial nerve involvement. Stage IIIa is associated with facial (VIIth cranial) nerve involvement and stage IIIb with multiple cranial nerve involvement. Stage IV: the above (stages I, II and III) features with the presence of complications, including meningitis, empyema, sigmoid sinus thrombosis and brain abscess.

This staging system is a modification of the clinicopathological classification described in the textbook *Scott-Brown's Otorhinolaryngology, Head and Neck Surgery*.[29] We could not implement the same staging system due to the unavailability of a bone scan facility at our institution.

All patients were treated with 3–4 weeks of parenteral antibiotics (depending on the antibiotic sensitivity report) and the daily insertion of medicated (polymyxin B and neomycin sulphates ointment) wicks. Patients were monitored using a visual analogue scale (VAS) for otalgia. Surgical intervention was considered necessary in those patients who suffered persistent otalgia for more than 10 days (VAS score of more than 50 per cent), and those with persistent granulations with or without facial nerve palsy. Diabetes was treated with rapid- and intermediate-acting insulin, and glycosylated haemoglobin (HbA_{1C}) levels were monitored during follow-up visits.

Hospital discharge criteria were: resolution of otalgia and granulations, normal otoscopy, and controlled diabetes status. All patients were prescribed oral ciprofloxacin (0.5–1 gram twice daily) for 8–10 weeks and followed up periodically for 4–6 months.

The study was approved by the Institutional Ethics Committee of Goa Medical College and Hospital, Goa.

Results

Of the 27 patients included in the study, 22 were male (a male to female ratio of 4.4 to 1). Patients were aged between 50 and 80 years; there were no paediatric cases of necrotising otitis externa. All patients were diabetic with the exception of one patient. The mean duration of diabetes was 12.37 years, ranging from 1 to 40 years. Amongst the diabetics, one patient was immunocompromised (HIV with hepatitis B), while three patients had end stage renal disease. The average hospital stay of patients was 23.2 days. All patients were treated at other hospitals for otitis externa prior to their consultation at our institution. Patients' demographic

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TABLE I
CLINICAL PROFILE

Age (y)	
– Range	50–80
– Mean	63.59
Gender (*n* (%))	
– Male	22 (81.5)
– Female	5 (18.5)
Diabetic pt status (*n* (% of DB pts))	
– Uncontrolled	22 (84.6)
– Controlled	4 (15.4)
Non-diabetic pts (*n*)	1
Symptoms & signs (*n* (%))	
Otalgia	27 (100)
Otorrhoea	22 (81.5)
Hearing loss (*n* (% of HL pts))	21 (77.8)
– CHL	8 (38.1)
– SNHL	7 (33.3)
– Mixed	6 (28.6)
EAC granulations	25 (92.6)
Cranial nerve palsy	9 (33.3)
– Single (VII)	7 (25.9)
– Multiple (VII, IX, X, XI)	2 (7.4)

Y = years; pt = patient; DB = diabetic; HL = hearing loss; CHL = conductive hearing loss; SNHL = sensorineural hearing loss; EAC = external auditory canal

characteristics, and clinical symptoms and signs are summarised in Table I.

Otalgia was the most prominent symptom at presentation; this affected all 27 patients (100 per cent), typically worsening at night. Purulent otorrhoea, which was reported in 22 patients (81.5 per cent), was the second most common symptom. Of the 27 patients, 9 (33.3 per cent) had cranial nerve palsy, 7 (25.9 per cent) had infranuclear facial palsy, and 2 others (7.4 per cent) had multiple cranial nerve involvement (implicating the VIIth, IXth, Xth and XIth cranial nerves). Although hearing loss was not a frequent complaint, specific enquiry revealed that 21 of the patients (77.8 per cent) had decreased hearing. The hallmark sign of granulations in the external auditory canal situated at the osteocartilaginous junction, in the floor as well as the anterior and posterior walls, was observed in 25 patients (92.6 per cent), while 2 others (7.4 per cent) had oedematous canal skin. This clinical picture was accompanied with tinnitus, headache, and nausea and vomiting in different intensities. Three patients had preauricular swelling due to infiltration of the temporomandibular joint by rapidly spreading inflammatory process.

Bacteriology

Aural swab culture and antibiotic sensitivity testing was performed in all patients; however, the data for three patients could not be traced. The commonest organism isolated was *P aeruginosa* in 10 of 24 patients (41.7 per cent), followed by *S aureus* in 3 of 24 patients (12.5 per cent). Of the 24 patients, 2 showed a combined growth of *P aeruginosa* with *S aureus* (8 per cent), 1 had *P aeruginosa* with klebsiella (4 per cent), 1 had *P aeruginosa* with *Candida albicans* (4 per cent) and 1 had *S aureus* with enterococcus (4 per cent). One patient showed growth of *non-albicans Candida*, the significance was doubtful. The cultures of five patients were sterile.

All pseudomonas organisms isolated were sensitive to third generation cephalosporins (ceftazidime, cefoperazone with sulbactam, and ceftriaxone) as well as ciprofloxacin.

Staging

Nine patients were categorised as having stage I disease (33.3 per cent), eight were stage II (29.6 per cent), six were stage IIIa (22.2 per cent), one was stage IIIb (3.7 per cent) and three were stage IV (11.1 per cent).

Radiology

High resolution CT scans were obtained for all 27 patients. These scans aided in the diagnosis of bone erosion of the skull base. They also helped in assessing the spread of infection medially into the middle ear, mastoid and petrous apex; and anteriorly into the temporomandibular joint and infratemporal fossa. Most of our patients showed erosion of the bony external auditory canal.

Treatment

All patients were initially treated with parenteral antibiotics and the mechanical debridement of granulations in the external ear, followed by medicated wick insertion. Exclusive medical therapy was received by 15 patients (9 with stage I disease, 3 at stage IIIa and 3 at stage IV). Twelve of these patients showed clinical improvement (i.e. resolution of otalgia and granulations) within a period of 10–14 days. The three patients with stage IV disease continued to suffer from otalgia; one of these patients died on the fourth day of admission. We were unable to intervene surgically in these three patients due to systemic complications (including sepsis, meningitis and status epilepticus).

Antimicrobial therapy was selected in order to cover Gram-negative organisms. Of the 27 patients, 13 (48.2 per cent) received ceftazidime, 6 (22.22 per cent) received ciprofloxacin, 5 (18.5 per cent) received ceftriaxone and 3 (11.1 per cent) received cefoperazone-sulbactam. The course of parenteral antibiotics lasted for a mean of 24 days (4–61 days; the patient who received 4 days of parenteral antibiotics had presented with stage IV disease and expired on the fourth day of admission). Oral ciprofloxacin was given to all patients for a mean duration of 8 weeks (3–38 weeks) following discharge from hospital.

Twelve out of 27 patients underwent surgical intervention. Canal wall down mastoidectomy was performed in all cases. In three of these cases, the facial nerve was decompressed from the first genu to the stylomastoid foramen, with mastoid tip amputation. One patient recovered from facial palsy, but there was no improvement in the remaining two patients. Skull base resection was not performed in our case series.

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TABLE II
TREATMENT PROTOCOL AND OUTCOME

Disease stage	Patients	Medical therapy*	Medical therapy + surgery†	Outcome	
				Recovered	Death
I	9	9	–	9	–
II	8	–	8	8	–
IIIa	6	3	3	6	–
IIIb	1	–	1	–	1
IV	3	3	–	–	3

Data represent numbers of patients. *Medical therapy includes local debridement, parenteral antimicrobials and diabetes control. †Surgery includes canal wall down mastoidectomy with or without facial nerve decompression.

One of the patients who underwent surgery died (this patient was categorised as having stage IIIb disease).

Outcome

The prognosis of necrotising otitis externa is good in the initial stages of the disorder. Twenty-three out of 27 patients recovered with our treatment protocol (Table II). Morbidity and mortality due to necrotising otitis externa have been major concerns for several decades. In our case series, the mortality rate was 14.8 per cent (4 out of 27 patients died), while the remaining patients improved. The terminal events in these patients were meningitis, septicaemia, status epilepticus and metabolic encephalopathy.

Discussion

Necrotising otitis externa is a potentially lethal disease, which demands aggressive medical treatment and occasionally surgical intervention. There are difficulties associated with correctly diagnosing necrotising otitis externa and thus a high index of suspicion is necessary. If diagnosed and treated early, morbidity and mortality can be significantly reduced. Any elderly diabetic that presents with otalgia and otorrhoea should be suspected to be suffering from necrotising otitis externa unless proven otherwise.

The mean age of patients in our study was 63.59 years, which is similar to that reported in previous studies.[3,6,30–32] Our study revealed a male preponderance comparable to previous studies,[31–34] the reasons for which are unknown.

The high incidence of necrotising otitis externa in diabetics has been well documented ever since James Chandler described his series of 13 patients. The majority of our patients had uncontrolled diabetes, as revealed by raised glycosylated haemoglobin levels (mean of 9.38 per cent). Glycosylated haemoglobin (HbA_{1c}) levels of 4–6 per cent were considered as non-diabetic and 6–8 per cent as controlled diabetes. The duration and severity of hyperglycaemia in diabetic patients contributes to microangiopathy, which causes ischaemic degeneration of the cartilage and dermis in the external auditory canal, and impairs healing capacity. We observed that the patients with good glycaemic control did not progress beyond stage II of the disorder, while those with poor glycaemic control were in disease stage II, III or IV. The endocrinology unit (diabetes control team) has a pivotal role to play in glycaemic control of such patients. Our diabetic treatment consisted of a strict diabetic diet, and rapid- and intermediate-acting insulin therapy, with everyday monitoring of sugar levels. One patient in our series was a non-diabetic; however, this patient was hypertensive. The exact cause of necrotising otitis externa in non-diabetics is unknown, but it could be associated with age-related small vessel disease and altered immune function.[7–9,30,35]

Necrotising otitis externa classically presents as otalgia, otorrhoea and granulation in the external auditory canal. The otalgia is described as a deep, boring, nocturnal, usually lancinating and throbbing pain, which is resistant to analgesics.[36] The pain may radiate to the preauricular and temporoparietal regions. A review of the literature showed otalgia to be the most common presenting symptom, with an incidence rate of 75–100 per cent.[5,32,36,37] In accordance with previous studies, the results of our case series revealed that 100 per cent of patients suffered otalgia, and otorrhoea was the second most common symptom observed.[5,32,36,37]

The most common clinical sign observed was the presence of granulation tissue in the external auditory canal, located at the osteocartilaginous junction, and at the anterior and posterior walls, which is similar to the findings of previous studies.[3,6,32,35,38] The granulation tissue and oedema can lead to narrowing of the external auditory canal lumen;[37–39] however, the tympanic membrane is usually normal when visualised. These granulations should be subjected to histopathological studies in order to rule out malignancy, and other differential diagnoses such as histiocytosis and tuberculosis.

Hearing loss was observed in the majority of the cases; conductive hearing loss can be due to external auditory canal obstruction by granulation or oedema, while sensorineural hearing loss can be due to ageing or diabetes mellitus.

As the osteomyelitic process progresses to the foramina of the skull base, multiple cranial nerves become involved, the most common of these being

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the facial nerve.[6,32,37] Similarly, in our study, facial nerve involvement was the most common of all cranial nerve palsies. Involvement of the jugular foramen, which results in IXth, Xth and XIth cranial nerve damage, is less frequent,[6,37,40] as was observed in our study. Cranial nerve involvement is not diagnostic of necrotising otitis externa and the outcome is independent of it.[32,41–43]

Pseudomonas aeruginosa was the most common organism cultured in our study. It is a Gram-negative, obligate aerobe that opportunistically affects patients with a defective immune system. Pseudomonas has the capacity for selective vasculitis. It may invade the arterial, capillary or venous wall, and cause focal coagulation necrosis of the surrounding tissues. The pathogenic action is due to the production of endotoxins, exotoxins and various enzymes such as haemolysins, lecithinases, lipases, esterases and numerous proteases. The virulent strain produces a mucoid layer which protects against phagocytosis and antibiotic action. O'Sullivan *et al.* described some strains of pseudomonas which produce neurotoxins that are likely to play a role in the development of cranial neuropathy.[44]

The second most common organism isolated in our study was *S aureus*, which is similar to previous findings.[34,41,42] In contrast to those studies that reported growth of *Aspergillus fumigatus*, our study failed to find any fungal growth.[34]

With regards to the antibiotic sensitivity pattern, all pseudomonas organisms isolated in our study were sensitive to ciprofloxacin (fluoroquinolones), as well as third generation cephalosporins such as ceftazidime, ceftriaxone and cefoperazone, which is in contrast to reports of emerging resistance to fluoroquinolones.[45] The majority of the other organisms isolated, including *S aureus*, klebsiella species and enterococci, were also sensitive to these antibiotics.

Numerous imaging modalities have been used to assess patients with necrotising otitis externa. High resolution CT is the preferred modality for defining the anatomical extension of the osteomyelitic process. The value of CT scans is limited due to the inability of this technique to detect bone erosions in the early stages of disease. Computed tomography scans can only detect the disease when at least 30–50 per cent of bone erosion has already occurred.[46] Magnetic resonance imaging is sufficiently sensitive to evaluate intracranial extension of the disease. Radionuclide scanning techniques, such as those using technetium-99m methylene diphosphonate or gallium-67 citrate, are useful in detecting the lesions of early disease. The radionuclide accumulates at the site of osteoblastic activity, and the bone scan can detect a minimum of 10 per cent osteogenic activity. There was no radionuclide imaging facility available at our institution; hence, our imaging was limited to CT scans only.

Although necrotising otitis externa has been reported on for nearly six decades, there is still no universally accepted staging system. Several systems have been suggested based on clinical,[37] radiological[47] and clinico-radiological[39] findings. Our staging system is essentially dependent on clinical parameters (which are easy to assess) and CT scan findings (a technique which is widely available), making it clinician friendly and easy to implement in practice.

The treatment of necrotising otitis externa has always been controversial, and several modifications have been made to the therapeutic approach. Over several decades, it has been treated with prolonged courses of antipseudomonal antibiotics. Monotherapy has been successfully practised; however, the emerging resistance has demanded combination therapy.[45]

Third generation cephalosporins were introduced during the latter half of the 1980s. These were very effective against pseudomonas, and were used in the treatment of osteomyelitis caused by necrotising otitis externa. Ceftazidime in a dosage of 2 grams 8-hourly has been proven to be effective in controlling necrotising otitis externa when administered as a monotherapy[48,49] or in combination with ciprofloxacin. We recommend intravenously administered ceftazidime in a dosage of 1 gram 8-hourly for 4–6 weeks (similar to a previous study[34]), followed by maintenance therapy of an orally administered antipseudomonal antibiotic for 8–10 weeks.

The introduction of oral fluoroquinolones (ciprofloxacin), which are active agents against pseudomonas, has made new inroads in the treatment of necrotising otitis externa. When administered orally they achieve a high concentration in serum, urine and other tissues. Ciprofloxacin has been used as a primary parenteral therapy[50] as well as a domestic maintenance therapy[39] in the treatment of necrotising otitis externa. We recommend oral ciprofloxacin for maintenance therapy in a dose of 0.5–1.0 gram 12-hourly for 8–10 weeks, as supported by other studies.[37,39,51] In addition to systemic antibiotics, local therapy plays a significant role in the control of infection.[6] Local therapy may constitute the regular insertion of medicated wicks composed of neomycin and polymyxin B sulphates, bacitracin zinc, and hydrocortisone ointment.

It is widely accepted that the role of surgery in necrotising otitis externa is adjuvant or complementary. The goal of surgery is to achieve maximum possible debridement of granulations from the external auditory canal, middle ear and mastoid. Surgery is indicated if the patient is deteriorating clinically, in spite of medical therapy.[33] In our study, patients classified as having stage II or III disease underwent surgical intervention. This resulted in better control of the disease, the otalgia subsided and the granulations regressed. No recurrence was observed in those patients treated surgically. All of the stage IV patients had advanced osteomyelitis and uncontrolled diabetes, and could not therefore undergo surgery. On the basis of these

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findings, we conclude that most stage I patients respond well to medical therapy, whereas stage II and III patients are likely to require surgical intervention to improve their outcome.

Hyperbaric oxygen therapy has been shown to be effective in normalising oxygen tension in the inflamed tissues, which is necessary for bacterial destruction caused by polymorphonuclear leucocytes.[24] This therapy also stimulates vascular proliferation, and osteoblastic and osteoclastic activity, which facilitates faster wound healing.

- **Necrotising otitis externa is often caused by *Pseudomonas aeruginosa* and typically affects elderly diabetics**
- **No definitive management protocol has yet been described**
- **This study of 27 patients showed that otalgia, otorrhoea and external canal granulations are central to diagnosis**
- **Antipseudomonal antibiotics supplemented with surgical debridement are the mainstay of treatment**
- **A high index of suspicion, early diagnosis and prompt intervention are key factors for decreasing morbidity and mortality**

Sophisticated imaging modalities are not available at all levels of healthcare; hence, there is a need for a simple, clinically-oriented, diagnostic protocol. Our study can provide a framework towards an approach for managing necrotising otitis externa. The outcome of necrotising otitis externa has changed drastically since the introduction of antipseudomonas antimicrobials. The mortality rate has substantially decreased. In our series, the mortality rate was 14.8 per cent, which is much lower than that reported in earlier studies.[4]

Conclusion

In the current study, necrotising otitis externa predominantly affected elderly men with uncontrolled diabetes, and the most common organism isolated was *P aeruginosa*. Otalgia, otorrhoea and granulations are the most important clinical parameters for diagnosis and for monitoring treatment outcomes. As the disease progresses along the skull base, the cranial nerves become involved; however, this is not an indicator of poor prognosis (as was previously believed). Computed tomography scanning is helpful to assess the extent of the disease process, but it is not a replacement for scintigraphy studies. Third generation cephalosporins and fluoroquinolones are the mainstay of treatment, and this may be supplemented by surgical debridement in those with stage II and III disease. However, there is a need for a large-scale prospective study in order to standardise the management policy for patients with this disorder.

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