



Original Article

# Management of Necrotizing Otitis Externa: Our Experience with Forty-Three Patients

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**OBJECTIVE:** To assess the impact of the introduction of a dedicated management protocol of necrotizing otitis externa patients with joint care between otorhinolaryngology and infectious diseases.

**MATERIALS and METHODS:** Retrospective review of case notes and the otorhinolaryngology department database of all adults admitted with necrotizing otitis externa at our teaching hospital over a 5-year period. The patients were split into two groups (first group of 10 patients prior to the introduction of the dedicated management protocol, and a second group of 33 patients managed after the introduction of this protocol).

**RESULTS:** Of the 43 patients included in the study, diabetes mellitus was present in 83.7%. *Pseudomonas aeruginosa* was grown in 67.4% of patients. All 43 patients underwent computed tomography and magnetic resonance imaging (with contrast) scans. Surgical intervention was undertaken in 25.6% of patients. Mean follow-up was 10 months (SD,  $\pm 7$  months). Of the 43 patients, 79.1% made a full recovery and were discharged. Relapse occurred in 9.3% of patients. One patient died because of a myocardial infarction 4 months after treatment. The mean length of stay was significantly lower after the protocol was introduced ( $25.6 \pm 5.3$  vs.  $14.2 \pm 3.8$  days,  $p=0.001$ ), and the duration of treatment was also significantly lower after the protocol ( $21.2 \pm 6.8$  vs.  $14.3 \pm 4.3$  weeks,  $p=0.01$ ).

**CONCLUSION:** The introduction of a dedicated management protocol and joint care with otorhinolaryngology and infectious diseases resulted in improved care and decreased length of stay in patients. Early diagnosis and involvement with the relevant teams as well as prompt intervention are the key factors that reduce morbidity and mortality.

**KEYWORDS:** Necrotising otitis externa, malignant otitis externa, pseudomonas aeruginosa, osteomyelitis, otitis externa

## INTRODUCTION

Necrotizing otitis externa, also known as malignant otitis externa, is an aggressive and progressive infection of the external auditory canal and skull base. The first reported case was in 1959 that described in a case report as a fatal temporal bone osteomyelitis originating from otitis externa<sup>[1]</sup>. In 1968, Chandler created the term "malignant otitis externa" to describe this aggressive infection caused by *Pseudomonas aeruginosa*<sup>[2]</sup>. However, other organisms such as *Staphylococcus aureus* have been implicated in necrotizing otitis externa<sup>[3]</sup>.

Recent analysis of National Hospital Episode Statistics data shows a six-fold increase in the number of cases of necrotizing otitis externa in the UK from 1999 ( $n=67$ ) to 2013 ( $n=421$ )<sup>[4]</sup>. It is most common in elderly diabetic patients and the immunocompromised, although it can also occur in non-diabetics, young diabetics, patients on cytotoxic drugs, and infants<sup>[5]</sup>.

Previous literature has looked at case series of patients with necrotizing otitis externa and suggested management protocols, but these have been with relatively small numbers and have not looked at the impact of a dedicated management protocol with joint care between infectious diseases and otorhinolaryngology<sup>[6]</sup>.

The aim of this study was to assess the impact on the patient care pathway by the introduction of a dedicated management protocol for necrotizing otitis externa patients with joint care between otorhinolaryngology and infectious diseases.

## MATERIALS and METHODS

This study was approved by the local Trust Audit and Clinical Governance department and conducted in accordance with the Helsinki Declaration. Informed consent was obtained where appropriate.

This study was presented at the 21<sup>st</sup> International Federation of Otorhinolaryngological Societies World Congress, 24 June 2017, Paris, France.

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A retrospective review of case notes and the otolaryngology department database was performed on all adults admitted with necrotizing otitis externa at our teaching hospital over a 5-year period between July 2011 and October 2016. Diagnosis of necrotizing otitis externa was based on characteristic computed tomography (CT) findings of a skull base osteomyelitis originating from an ear canal infectious process. Patient demographics, co-morbidities, signs and symptoms, length of stay, microbiology, imaging (CT and magnetic resonance imaging (MRI)), inflammatory markers, treatment, surgical intervention, and follow-up were all recorded and analyzed. Patients in whom there was insufficient data recorded were excluded.

The patients were split into two groups: a group of 10 patients prior to the introduction of the dedicated management protocol in 2013, with joint infectious diseases and otorhinolaryngology care for these patients (Figure 1), and a second group of 33 patients managed after the introduction of this protocol.

Statistical analysis and comparisons were carried out using the Fisher's exact test and a paired Student's *t* test, and significance was set at  $p < 0.05$  (GraphPad Software, USA) [7].

**RESULTS**

Of the 43 patients included in the study, 28 were male and 15 were female. The median age of patients was 78 y (range, 23-100 y). Diabetes mellitus was present in 36 of 43 patients (83.7%), and 3 of 43 patients (7.0%) were on immunosuppressant treatment. No history of diabetes or immunosuppressant treatment was present in 4 of 43 patients (9.3%), and all of these patients were diagnosed with necrotizing otitis externa on CT due to prolonged symptoms despite adequate medical treatment.

The patients were split into Group 1 (10 patients prior to the introduction of the protocol) and Group 2 (33 patients after the introduction of the protocol), and both groups were compared.

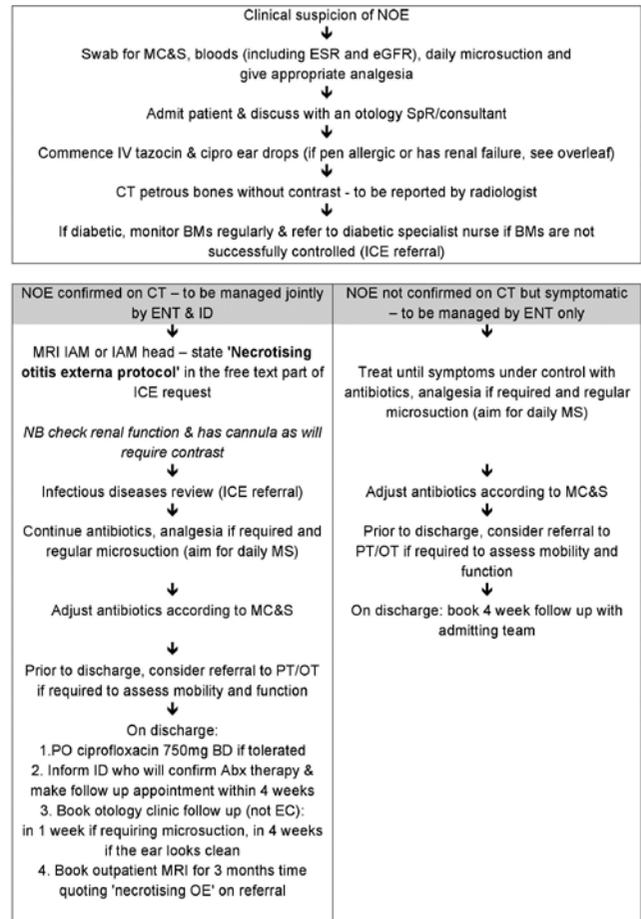
Otalgia was the most common symptom at presentation in both Group 1 and Group 2 (10/10 vs. 33/33 patients,  $p=1.00$ ). Facial nerve paralysis was more common in Group 1 than in Group 2, but with no statistically significant difference (3/10 patients in Group 1 vs. 5/33 patients in Group 2,  $p=0.36$ ).

In terms of microbiology, *Pseudomonas aeruginosa* was the most common microorganism grown in both groups (5/10 patients in Group 1 vs 17/33 patients in Group 2,  $p=1.00$ ).

In terms of imaging, all 43 patients underwent CT (10/10 patients in Group 1 vs. 33/33 patients in Group 2,  $p=1.00$ ), but there was a statistically significantly higher number of patients in Group 2 who had MRI (with contrast) scans than in Group 1 (6/10 patients in Group 1 vs. 33/33 patients in Group 2,  $p=0.002$ ).

Initial treatment with intravenous piperacillin/tazobactam (Tazocin®) was significantly more common in Group 2 than in Group 1 (3/10 patients in Group 1 vs. 24/33 patients in Group 2,  $p=0.02$ ). Surgical intervention (including examination under anesthesia and polypectomy and debridement) was similar in both groups (3/10 patients in Group 1 vs. 8/33 patients in Group 2,  $p=0.70$ ).

**Necrotising Otitis Externa Guidelines**



**Figure 1.** Management algorithm for suspected necrotizing otitis externa

The mean length of stay in hospital was significantly lower after the protocol was introduced (25.6 ±5.3 days in Group 1 vs. 14.2±3.8 days in Group 2,  $p=0.001$ ). The duration of treatment was also significantly lower after the protocol was introduced (21.2±6.8 weeks in Group 1 vs. 14.3±4.3 weeks in Group 2,  $p=0.01$ ). While there was a trend for C-reactive Protein (CRP) to gradually decrease over time with treatment, there was no significant difference between the two groups in terms of the length of time to normalization of CRP.

There was no significant difference between the two groups in terms of those patients who made a full recovery and were discharged from follow-up (7/10 patients in Group 1 vs. 27/33 patients in Group 2,  $p=0.67$ ). There was no significant difference in the relapse rates between the two groups (2/10 patients in Group 1 vs. 2/33 patients in Group 2,  $p=0.23$ ). One patient in Group 2 died because of a myocardial infarction 4 months after initiating treatment.

Further results are summarized in Table 1.

**DISCUSSION**

Necrotizing otitis externa is a potentially life-threatening disease and needs early aggressive treatment to prevent long-term morbidity. Any diabetic or immunocompromised patient with persistent otal-

**Table 1.** Comparison of variables between Group 1 (pre-intervention) and Group 2 (post-intervention)

Variable	Group 1	Group 2	p
Otalgia	10/10	33/33	1.00
Otorrhoea	8/10	28/33	0.66
Hearing loss	5/10	18/33	1.00
Facial swelling	2/10	5/33	0.66
Facial nerve palsy	3/10	5/33	0.36
Multiple cranial nerve palsies	1/10	1/33	0.42
<i>Pseudomonas</i>	5/10	17/33	1.00
<i>Staphylococcus Aureus</i>	1/10	3/33	1.00
<i>Aspergillus flavum</i>	1/10	2/33	0.56
No growth	4/10	12/33	1.00
CT	10/10	33/33	1.00
<b>MRI</b>	<b>6/10</b>	<b>33/33</b>	<b>0.002</b>
<b>Tazocin</b>	<b>3/10</b>	<b>24/33</b>	<b>0.02</b>
Ceftazidime	2/10	5/33	0.66
Ciprofloxacin (intravenous)	1/10	4/33	1.00
Ceftriaxone	1/10	1/33	0.42
Colistin	1/10	1/33	0.42
Ciprofoxacin (oral)	9/10	32/33	0.34
Cefuroxime (oral)	1/10	1/33	0.42
Surgery	3/10	8/33	0.70
<b>Length of stay</b>	<b>25.6±5.3 days</b>	<b>14.2±3.8 days</b>	<b>0.001</b>
<b>Treatment length</b>	<b>21.2±6.8 weeks</b>	<b>14.3±4.3 weeks</b>	<b>0.01</b>
Length of follow up	10.4±2.2 months	10.6±2.5 months	1.00
CRP at 4 months post treatment	4.6±1.9	5.1±2.2	0.80
Resolution and discharged	7/10	27/33	0.67
Relapse	2/10	2/33	0.23

CT: computed tomography; MRI: magnetic resonance imaging; CRP: C-reactive protein

gia and otorrhea should be considered high risk for necrotizing otitis externa and should have a CT scan to aid diagnosis. Given that 4 of 43 patients (9.3%) were not diabetic or immunocompromised but developed necrotizing otitis externa, we would also suggest that non-diabetic patients with otitis externa who fail to improve despite adequate medical treatment should be investigated further for possible necrotizing otitis externa.

Improved imaging technology means that MRI can be used to assess for disease resolution, and recent literature has highlighted the benefits of diffusion-weighted MRI in assessing for disease resolution when compared to standard MRI sequences<sup>[8]</sup>. Indeed all of our necrotizing otitis externa patients post-protocol now receive an MRI with contrast as well as diffusion weighted imaging, and this is demonstrated by our data which show that prior to the protocol this was not always the case.

Hospital Episode Statistics data have demonstrated that the incidence of necrotizing otitis externa is increasing<sup>[4]</sup>. We have also demonstrated that although *P. aeruginosa* remains the most common pathogen, others are contributory for the condition, and treatment should be tailored to the individual patient. This emphasizes the need for multidisciplinary advice from microbiology and infectious diseases. We have shown that early treatment results in lower morbidity, and indeed our mortality rates are lower than previously published data<sup>[5]</sup>. Our data also suggest that CRP can be used as a marker to demonstrate response to treatment, but this should be combined with clinical and radiological findings.

Crucially, our data have also shown that the introduction of a dedicated protocol for the management of this condition, along with joint infectious diseases and otorhinolaryngology care for these patients, results in decreased length of stay in hospital and decreased length of treatment. This is because the introduction of the protocol meant that patients with necrotizing otitis externa were managed by a multidisciplinary team, and therefore discharge planning and follow-up arrangements were more coordinated; for example, the availability of long-term peripheral lines for intravenous antibiotics in the community was available more rapidly following the introduction of the protocol.

The protocol was instituted in the first place, as it was recognized that patients with necrotizing otitis externa were being managed in heterogeneous ways, particularly with very limited input from the infectious diseases team. After the introduction of the protocol, each patient with necrotizing otitis externa was managed jointly by the otorhinolaryngology team and infectious diseases team, with appropriate imaging and treatment as per the protocol, tailored to the individual patient. It is possible that following the introduction of the protocol, as there was a greater awareness of necrotizing otitis externa, patients were identified at an earlier stage of their disease process, hence treatment was instigated earlier, resulting in a more rapid resolution of the condition, and decreased length of stay in hospital.

There were two cases of the total 43 patients who grew multi-drug-resistant *Pseudomonas* and required treatment with intravenous antibiotics for 12 weeks. This highlights the importance of the joint care with infectious diseases, as these patients required long-term close follow-up with monitoring of hepatic and renal function. Unfortunately, despite this, one of the cases went on to have a relapse and required readmission, likely due to the poor prognosis associated with multi-drug-resistant disease.

There were four cases where the patients had relapses (two during treatment and two after treatment) that required readmission to hospital. One of these cases was in a patient with multi-drug-resistant *P. aeruginosa*, and two of these cases were patients who did not attend follow-up appointments regularly.

There is no previous literature that looks at the synergistic beneficial effects of a dedicated management protocol utilizing multidisciplinary input. We have reported novel findings regarding the benefits of this approach. Our article also involved a larger number of patients than most of the case series published previously, and we compared patient groups pre-and post-introduction of a dedicated protocol, which has not been published previously<sup>[4-6, 9, 10]</sup>.

This study is limited in that we cannot be sure that the introduction of the management protocol and joint care is the only factor for a reduction in length of stay and length of treatment. It is possible that in this type of retrospective study other factors may have led to the improved results, such as sooner treatment with Tazocin®, more information on the course of the disease by the use of diffusion weighted MRI imaging, sooner discharge because of quicker application of long-term intravenous lines to allow home treatment, or other factors. There is potential for selection bias, as those patients who did not have adequate follow-up were excluded. Although, to our knowledge, this is the first and largest study to look at the effect of the introduction of a joint management pathway for patients with necrotizing otitis externa, the number of cases is relatively small due to the low incidence of this condition, which means it is difficult to make meaningful statistical conclusions. However, our results are similar to other studies from elsewhere in the world [4-6, 9, 10].

The most common presenting features found in our study of otalgia and otorrhea are in common with other larger case series and highlight the need for high clinical suspicion in immunocompromised or diabetic patients with these symptoms [9]. Facial nerve palsy was a less common presentation in the group post-intervention, although this was not statistically significant, and may have been due to the fact that post-intervention, there was greater awareness of necrotizing otitis externa, so these patients were managed earlier, before developing complications such as facial nerve palsy.

In common with other studies, the most common causative organism was *P. aeruginosa*, but other organisms, such as *S. aureus*, are increasingly prevalent in these patients [5, 10]. A French study of 32 cases of necrotizing otitis externa found that mean length of stay (18.2±8.7 vs. 11.6±6.9 days,  $p=0.03$ ) and duration of antibiotic therapy (9.4±3.2 vs. 5.8±0.7 weeks,  $p<0.001$ ) were significantly lower after 2009 when a management protocol for necrotizing otitis externa was introduced. This supports our data and our conclusions [9]. Our mortality rate is significantly lower (2.4%) than that of other studies (14.8%), possibly due to the fact that these patients are managed jointly with infectious diseases [5].

As the osteomyelitis progresses to the foramina of the skull base, the most common cranial nerve involved is the facial nerve, which is what was noted in our study. Involvement of those cranial nerves in the jugular foramen is less common, and this is also noted in the literature [5]. In terms of imaging, there is some literature to suggest that CT scans can only detect disease when at least 30%-50% of bone erosion has already occurred [5]. However, our use of both CT and MRI allows imaging to be more sensitive, and the use of diffusion-weighted MRI aids to assess disease progression [8]. MRI is useful at the initial presentation to give a baseline level of inflammation, which can then be compared with subsequent scans to demonstrate progression of the disease. Radionuclide scans, such as technetium-99 m methylene diphosphonate or gallium-67 citrate, are sensitive in detecting disease activity but lack specificity. These imaging techniques were not available at our institution [6].

Our rate of surgical intervention (tympanomastoid surgery) is lower than other centers, but this may be due to better directed medical therapy in our patients due to the joint involvement of the infec-

tious diseases team, as surgical intervention is generally reserved for those patients who did not improve with medical treatment [10]. There is literature to suggest that hyperbaric oxygen has a role in normalizing oxygen tension in the inflamed tissues (necessary for bacterial destruction caused by polymorphonuclear leucocytes) [6]. However, we do not have hyperbaric oxygen facilities available at our institution.

This study showed that the introduction of a dedicated management protocol and joint care with otorhinolaryngology and infectious diseases resulted in improved care and decreased length of stay in 43 patients. Imaging should include both high-resolution CT temporal bones as well as MRI with contrast. Management of these patients includes broad-spectrum intravenous antibiotics and topical therapy tailored to the individual patient in conjunction with infectious diseases doctors, and then long-term oral antipseudomonal antibiotics upon discharge with close follow-up by both otorhinolaryngology and infectious diseases teams. Early diagnosis and involvement with the relevant teams as well as prompt intervention are the key factors that reduce morbidity and mortality in these patients.

## CONCLUSION

Necrotizing otitis externa is typically caused by *P. aeruginosa* and commonly affects diabetics and immunocompromised individuals. Our imaging protocol recommends both a high-resolution CT temporal bones to define bony erosion and serial MRI with contrast to monitor treatment response. Management of these patients includes broad-spectrum intravenous antibiotics and topical therapy tailored to the individual patient and then long-term oral antipseudomonal antibiotics upon discharge with close follow-up. Early diagnosis and involvement with the relevant teams as well as prompt intervention are the key factors that reduce morbidity and mortality in these patients. Future research should look at the influence of the protocol on larger numbers of patients and, perhaps, the influence of other treatment modalities such as hyperbaric oxygen. Crucially, our data have also shown that the introduction of a dedicated protocol for the management of this condition, along with joint infectious diseases and otorhinolaryngology care for these patients, results in decreased length of stay in hospital and decreased length of treatment.

**Ethics Committee Approval:** Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

**Informed Consent:** Informed consent is not necessary due to the retrospective nature of this study.

**Peer-review:** Externally peer-reviewed.

**Author contributions:** Concept - S.D., T.C., A.S.; Design - S.D., T.C., A.S.; Supervision - S.D., T.C., A.S.; Resource - S.D., T.C., A.S.; Materials - S.D., T.C., A.S.; Data Collection and/or Processing - S.D., T.C., A.S.; Analysis and/or Interpretation - S.D., T.C., A.S.; Literature Search - S.D., T.C., A.S.; Writing - S.D., T.C., A.S.; Critical Reviews - S.D., T.C., A.S.

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**Conflict of Interest:** No conflict of interest was declared by the authors.

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