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Main Article

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Necrotising otitis externa: a serious condition becoming more frequently encountered

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Abstract

Background. Necrotising otitis externa is an aggressive infection of the external ear, which extends to the surrounding bone and soft tissue. In recent years, there has been an apparent increase in the number of patients admitted to our hospital with this condition.

Methods. A retrospective review was conducted of all patients admitted to our hospital with necrotising otitis externa between July 2012 and June 2020.

Results. Among 39 patients included, only 9 were diagnosed in the first four years, and 30 were diagnosed in the last four years. There were 27 males and 12 females, and the mean age was 78.7 years. There were six non-diabetic immunocompetent patients. Cranial nerve palsies developed in 50 per cent of the patients. Disease-related mortality was 7.7 per cent. A favourable outcome was recorded in 66.7 per cent of the patients.

Conclusion. Necrotising otitis externa is associated with high morbidity and mortality. The incidence of the disease is rising in our local geographical area.

Introduction

Necrotising otitis externa is an aggressive infection of the external ear soft tissue, which extends to the periosteum and bone of the skull base and the surrounding soft tissue.¹ The condition was first given the name of 'malignant otitis externa' in 1968 by Chandler, who described it as a particularly severe type of infection that tends to invade cartilage, bone, nerve and adjacent soft tissue.² The term 'necrotising otitis externa' was later used to avoid confusion with malignant neoplastic causes. Additionally, the term 'skull base osteomyelitis' was introduced to describe the pathological changes related to this condition,³ although these may also be seen in conditions other than necrotising otitis externa.⁴

Untreated necrotising otitis externa may be associated with up to 50 per cent mortality.⁵ Even with treatment using appropriate antibiotics, mortality figures as high as 15 per cent have been reported.⁴ The disease may also lead to prolonged and recurrent hospital admissions.

Necrotising otitis externa has been described primarily in elderly diabetic patients. However, there have been some reports describing the disease in non-diabetics.⁶⁻¹¹ Pseudomonas is the most common pathogen and has been reported by some to be responsible for over 90 per cent of cases, but other organisms, including fungi, have also been implicated.¹²

The infection extends outside the external auditory canal, through the fissures of Santorini, to involve the bone of the skull base. From here, it may spread to the foramina, leading to involvement of the cranial nerves, and to the venous sinuses, leading to thrombophlebitis. The infection may also extend intracranially and/or extracranially.¹³

There is no precise data about the global incidence of necrotising otitis externa, but it is generally considered to be a relatively uncommon condition.¹ In recent years, we have observed an increase in the number of patients diagnosed with this condition and admitted to our hospital, particularly among non-diabetics. The current case series aimed to examine our institutional experience of patients admitted to our hospital with a diagnosis of necrotising otitis externa in the past eight years, focusing particularly on the observed changes in the incidence of this condition.

Materials and methods

A retrospective review of all patients diagnosed with necrotising otitis externa and admitted to Barking, Havering and Redbridge University Hospitals NHS Trust between 1 July 2012 and 30 June 2020 was performed. A search of medical records containing the hospital diagnostic codes for the terms 'malignant otitis externa' and 'necrotising otitis externa' was conducted. This was followed by a review of the identified patients' electronic and paper medical records, to ascertain eligibility and collect relevant data.

Patients were included in the study if they fulfilled both the clinical and radiological criteria for the diagnosis of necrotising otitis externa. The clinical diagnosis was based on the symptoms and signs of external auditory canal inflammation that had not

© The Author(s), 2021. Published by Cambridge University Press on behalf of J.L.O. (1984) LIMITED responded to standard treatment for otitis externa after a minimum of two weeks. In addition, the presence of at least one of the following radiological criteria was mandatory for inclusion in the study: computed tomography (CT) evidence of bone erosion involving the external auditory canal and/or adjacent bone of the skull base; magnetic resonance imaging (MRI) evidence of skull base osteomyelitis; radionucleotide evidence of skull base osteomyelitis; and CT or MRI evidence of extension of the inflammatory process to the soft tissue adjacent to the skull base.

Data analysis was performed using Microsoft^M Excel spreadsheet software, and statistical analysis involved the student's *t*-test, chi-square test and Fisher's exact test.

The study was registered with our hospital trust's audit department. The retrospective collection and analysis of anonymous patient data were conducted as part of a service evaluation and did not require approval by a research ethics committee.

Results

Thirty-nine patients fulfilled the diagnostic criteria of necrotising otitis externa and were included in the study. There were 27 males and 12 females (male-to-female ratio of 2.25:1). The patients' age ranged from 55 to 94 years, with a mean age of 78.7 years. Necrotising otitis externa affected the right ear in 15 patients and the left ear in 21 patients, whereas 3 patients (7.7 per cent) had bilateral disease.

Between July 2012 and June 2016 (i.e. in the first half of the study period), nine patients fulfilling the clinical and radiological criteria for the diagnosis of necrotising otitis externa were admitted to our hospital. In comparison, between July 2016 and June 2020 (i.e. in the latter half of our study period), 30 patients were admitted using the same criteria. The number of admissions in the second half of the study therefore increased more than three-fold in comparison with the first half of the study (Table 1).

From July 2016 onwards, we have observed a steady increase in the number of patients admitted to our hospital with necrotising otitis externa year on year. The only exception to this was the first six months of 2020, when the number of admissions suddenly dropped. This time period coincided with the onset of the current coronavirus disease 2019 (Covid-19) pandemic, when a significant reduction in all non-Covid-19 related admissions was noted in our hospital, as in most other UK hospitals.

The length of hospital admission per patient, including re-admissions where applicable, ranged from 8 to 130 days, with a mean admission period of 36.5 days.

Cranial nerve palsies and other complications were studied in 38 patients in this cohort, as the clinical data were missing for 1 patient. Cranial nerve palsies were seen in 19 patients (50 per cent). The facial nerve was involved in 17 patients (45 per cent). One or more of the lower four cranial nerves were involved in four patients (10.5 per cent). Of these, swallowing function was impaired in three patients secondary to the cranial nerve palsies, requiring the fashioning of gastrostomies for long-term feeding. One patient in this cohort developed abducens nerve palsy.

Vascular complications were identified in 13 per cent of patients in this cohort. Four patients (10.5 per cent) developed internal jugular vein thrombosis, with a fifth patient developing lateral sinus thrombosis not extending to the internal jugular vein.

Soft tissue abscesses secondary to the spread of the inflammatory process were seen in three patients (8 per cent). Nasopharyngeal prevertebral abscesses were diagnosed in two patients, whereas one patient had an abscess of the zygomatic arch and the masseter muscle.

It was not possible to ascertain the diabetic status of one patient in our study group because of missing clinical data. Out of the remaining 38 patients, 30 were diabetic (79 per cent) and 8 were non-diabetic (21 per cent). Of the nondiabetics, two patients were on long-term corticosteroid treatment for rheumatoid arthritis, with a resultant impact on immune function. There remained six patients in this cohort (16 per cent) who were non-diabetic and did not have any history of any diseases or medications that might have affected their immune status.

When comparing the non-diabetics with the diabetics, there was no significant difference in the age of patients between the groups. Regarding gender, when all eight nondiabetic patients were considered, there were five females and three males; and when only the six immunocompetent non-diabetics were considered, there was an equal distribution of three males and three females. This was in contrast to the diabetic patients, for whom there was a clear male predilection (male-to-female ratio of 3.4:1 for diabetics and 2.25:1 for the whole cohort combined).

There was no significant difference regarding the length of hospital admission when the 8 non-diabetic patients were compared with the 30 diabetics. However, when the six non-diabetic immunocompetent patients were compared with the diabetics, the immunocompetent group was found to have a significantly shorter duration of hospital admission (p < 0.05).

Only two non-diabetic patients (25 per cent) developed cranial nerve palsies. Excluding the two patients who were receiving steroids, only one of the six immunocompetent non-diabetic patients (17 per cent) developed cranial nerve palsies. In comparison, 50 per cent of the whole cohort and 57 per cent of the diabetics developed cranial nerve palsies. The difference, however, between diabetics and non-diabetics (both including and excluding the two patients on steroids) was not statistically significant regarding cranial nerve palsies. Similarly, no significant difference was found between diabetics and non-diabetics regarding the incidence of other complications like venous thrombosis and abscess formations.

Out of the eight non-diabetic patients in this cohort, seven patients, including five of the six immunocompetent patients, were diagnosed within the last four years of the study period, and only one patient was diagnosed in the first four years. These figures highlight the increase in the number of hospital admissions for non-diabetic immunocompetent patients diagnosed with necrotising otitis externa in recent years.

The microbial pathogens involved in the necrotising otitis externa infections were identified from microbiological swabs and/or tissue cultures grown from ear or mastoid biopsies. The results were not available for two patients. Among the remaining 37 patients, pseudomonas was identified as a causative pathogen, either alone or in combination with other pathogens, in 27 patients (73 per cent), although in 3 of these patients the pseudomonas was found to be scanty or very scanty. The second commonest pathogen was candida, which was identified in four patients (11 per cent), but was found as a single pathogen in one patient only, where it was identified in scanty amounts. Other pathogens identified included *Staphylococcus aureus* (including methicillin-resistant *S aureus*), coliforms, enterococci, proteus, mixed

Table 1. Numbers of patient	s diagnosed with NOE admitted to	hospital within study period
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Parameter	July 2012–	July 2013–	July 2014–	July 2015–	July 2016–	July 2017–	July 2018–	July 2019–
	June 2013	June 2014	June 2015	June 2016	June 2017	June 2018	June 2019	June 2020
Patients (n)	2	3	2	2	6	8	11	5*

*Including four patients in 2019 and one patient in 2020. NOE = necrotising otitis externa

anaerobes, mixed faecal flora and *Aspergillus flavus*. In three patients (8 per cent), there was no microbial growth from the specimens obtained.

All patients in this cohort underwent radiological studies to confirm the diagnosis of necrotising otitis externa. A dual radiological modality of CT and MRI was the commonest radiological investigation conducted, and was utilised for 29 patients (74 per cent). A triple modality of CT, MRI and radionucleotide study was used for four patients (10 per cent). Magnetic resonance imaging and radionucleotide scans without CT were used for one patient. Another patient underwent MRI as a single radiological modality, and a further four patients (10 per cent) had CT scans as a single modality.

All patients received a minimum of six weeks of intravenous antibiotics based on culture and sensitivity and local microbiology antibiotic guidance, together with topical ciprofloxacin ear drops. When the culture results were not available in a timely manner, or if no growth was identified from the specimens, empirical treatment was started with intravenous piperacillin and tazobactam (Tazocin®) or oral ciprofloxacin in addition to the topical treatment, as per the guidelines for treating necrotising otitis externa in our trust. The single patient in whom A flavus was isolated was treated with intravenous voriconazole and then switched to oral treatment after clinical improvement. In general, the intravenous medications were administered in the hospital until the patients' symptoms and signs improved; once patients were fit enough to be discharged, the medications were continued outside the hospital via a peripherally inserted central catheter.

In addition to medical treatment, 12 patients (31.5 per cent) underwent aural polypectomy or polyp biopsy, 5 patients (13 per cent) had grommets inserted, 4 patients (10.5 per cent) had biopsies from the nasopharynx and 16 patients (42 per cent) underwent mastoid exploration surgery. Other surgical procedures included facial nerve decompression (n = 1), canaloplasty (n = 1) and biopsy of the zygomatic arch (n = 1).

The outcomes of the patients after treatment were also recorded. In terms of mortality, three patients (7.7 per cent of the whole cohort) died while being treated in hospital for their necrotising otitis externa. All three patients developed hospital-acquired pneumonia, which was the primary cause of death, while necrotising otitis externa was considered the secondary cause of death in each of them. The ages of these three patients were 82, 83 and 89 years, with a mean age of 84.7 years, which was found to be significantly higher than the mean age of the rest of the cohort (p < 0.05). However, the small sample size may affect the validity of this comparison. These three patients were all diabetic and all of them had facial nerve palsies.

Re-admission to hospital after discharge was needed in 10 patients (25.6 per cent of the whole cohort), either because of relapse of the disease or the failure of peripherally inserted central catheter lines, disallowing the continuation of treatment outside the hospital. Among these, six patients (15.4 per cent of the whole cohort) were re-admitted once, three

patients (7.7 per cent of the whole cohort) were re-admitted twice, and one patient (2.5 per cent of the whole cohort) was re-admitted four times.

The follow-up period after discharge from the latest hospital admission ranged from 0 to 44 months, with a mean follow up of nine months. The lack of follow-up data recorded for eight patients has impacted on this range. These included two patients who died within the first year after their discharge from hospital from unrelated causes, and a third patient who died a few years after discharge for unrelated reasons; unfortunately, no data pertaining to the follow up of necrotising otitis externa were found in their medical records. It was thus not possible to assess the outcomes of these eight patients.

Among those who had documented follow up, two patients (5.1 per cent of the whole cohort) continued to develop symptoms and signs of active necrotising otitis externa; one of these patients eventually died of unrelated causes, whereas the other was eventually referred to another centre. The remaining 26 patients (66.7 per cent of the whole cohort) showed improvement or complete remission of their symptoms and signs (except for the cranial nerve palsies). Among these 26 patients, 8 were followed up in the out-patient clinic and were later found to require no further ENT surveillance because of full recovery. Another five patients are currently still under regular follow up, but are no longer in need of systemic or topical antibiotics. A further nine patients have died during the follow-up period from unrelated causes, and four patients were lost to follow up but with the documentation from the last encounter with them showing disease improvement.

There was no available documentation regarding the outcomes of the cranial nerve palsies in three patients. Of the remaining 16 patients who experienced cranial nerve palsies, 8 (50 per cent) had significant improvement or full recovery, and 7 (43.8 per cent) had persistent nerve palsies. A further patient who had both facial nerve and lower cranial nerve palsies recovered from the latter, but suffered from a persistent facial palsy. The facial nerve palsies resolved in 46.7 per cent of the cases, the lower cranial nerves recovered in 66.7 per cent of the cases, and the single case of abducens nerve palsy also recovered.

With regard to the outcomes of the six non-diabetic immunocompetent patients, all showed improvement or remission of the disease. Among these six patients, two are still under follow up, having so far completed 25 months and 44 months of follow up, respectively; two other patients were lost to follow up after three and four months of follow up, respectively, but with the documentation from their latest follow-up appointment showing disease improvement; and a further two patients died of unrelated causes at 13 months and 18 months from the date of hospital discharge, respectively, again with documentation of improvement available from their last follow-up appointment. The non-diabetic immunocompetent patients were more likely to experience improvement or recovery in comparison to the diabetic ones (100 per cent vs 60 per cent, respectively), although the difference did not reach statistical significance.

Discussion

Necrotising otitis externa is a serious disease with the potential for mortality. It is associated with significant patient morbidity, and can involve lengthy hospital stays with resultant burdens on the already stretched healthcare resources. In the current study, 7.7 per cent of the patients died of disease-related causes, and 25.6 per cent required hospital re-admission after discharge because of poorly controlled disease, with 10.2 per cent requiring multiple re-admissions. The mean hospital stay per patient was 36.5 days, indicating that most patients spent over a month in hospital for their treatment. Serious complications were common in the current study, with 50 per cent of the patients developing cranial nerve palsies and 13 per cent developing significant venous thrombosis.

In keeping with our data, Glikson et al.⁶ reported 8 per cent disease-related mortality for necrotising otitis externa, while another study reported a higher figure of 14 per cent.¹² Glikson et al.⁶ reported a mean hospital stay of 14.5 days, which is comparatively shorter than our finding. The patients in their series also experienced fewer cranial nerve complications compared with our cohort, with only 8 per cent of their patients developing this complication. Shavit et al.¹² reported that 17 per cent of their necrotising otitis externa patients suffered from facial nerve palsies, while Mani et al.¹⁴ observed a comparable result to our study, with 43.5 per cent of their necrotising otitis externa patients developing cranial nerve palsies. In all studies, similarly to ours, the facial nerve was the most commonly involved cranial nerve. Shavit et al.¹² also reported that diabetes, older age, facial palsy and positive CT findings were predictors for higher mortality. In accordance with these findings, all three patients who died of disease-related causes in our study were diabetic, aged over 80 years and suffered from facial palsy.

In the present study, 42 per cent of our patients required mastoid exploration. This rate is higher than the figures reported in the literature.^{6,12} However, 66.7 per cent of patients in the present study improved or recovered from necrotising otitis externa, which is a lower rate than that reported by others.^{5,6} This disparity potentially stems from a loss of patients to follow up: it is possible that the patients with no documented follow up who were thus excluded from outcome analysis had actually experienced improvement.

The present study has shown that the incidence of necrotising otitis externa in the local geographical area of our hospital is increasing. The number of patients admitted to our hospital with necrotising otitis externa in the last four years of the study period was more than triple the corresponding number in the earlier four years. There have been some previous reports from other areas in the UK showing similar findings. Bhasker et al.¹⁵ reported a significant increase in the number of admissions for necrotising otitis externa in York over an eight-year period between 2004 and 2012. However, their cohort consisted of only 11 patients. Chawdhary et al.¹⁶ diagnosed five cases of necrotising otitis externa in Slough in 2013, and noticed that this figure was double the number of patients diagnosed in the previous years in their area. Considering the significantly larger cohort in the present study in comparison with other UK-based necrotising otitis externa publications in the reported literature, we present, to the best of our knowledge, the most conclusive evidence so far of the increasing incidence of necrotising otitis externa within a local geographical area. This may reflect a national increase in the incidence of this disease, although further larger studies on a national level are required to investigate this.

The increasing incidence of a disease with such high morbidity and mortality as necrotising otitis externa is potentially concerning. The reasons behind this increase need to be investigated. It is inaccurate to assume that an increase in the population alone can explain such an increase in the number of patients diagnosed with the disease. The last census in the UK took place in 2011 and estimated the UK population to be 63.2 million. The last population estimate was 66.8 million in mid-2019, showing the UK population to have increased by only 5.7 per cent in these eight years. When considering the population of the local geographical catchment area for our hospital, represented in the three London boroughs of Havering, Barking and Redbridge, the population increased within the same eight years from around 702 000 to around 778 000, an increase of 10.8 per cent. Such figures clearly cannot account for the three-fold increase in necrotising otitis externa cases.

It might be tempting to consider that population ageing is an important factor in the increased incidence of necrotising otitis externa, a disease known to be associated with old age. However, the figures again do not support this hypothesis. The proportion of the population aged 65 years and above represented 16 per cent of the UK population in 2011, and by 2019 had only increased to represent 18.5 per cent of the UK population. At a local level, the percentage of the population aged 65 years and above in the Barking, Havering and Redbridge areas has remained almost unchanged between 2011 and 2019. This suggests that an ageing population on its own cannot explain the observed rise in necrotising otitis externa cases.

One could postulate that increased awareness together with improved diagnosis of this condition has led to an increase in documented numbers of necrotising otitis externa cases. However, clinical diagnosis and management of otitis externa in our unit have not changed for a number of years, following agreed multidisciplinary microbiology and ENT departmental guidelines. The majority of patients are initially started on aural toilet and topical treatment with antibiotic and steroid ear drops, which are commenced empirically on the first visit and modified according to culture and sensitivity findings of the ear swab on the second visit. Patients who do not respond to this treatment (in whom necrotising otitis externa is then suspected based on clinical suspicion) are admitted to hospital for more aggressive management, usually involving systemic antibiotics and stronger pain control. If the disease still proves to be resistant to treatment, or if complications such as cranial nerve palsies are diagnosed, radiological investigations are performed to detect evidence of necrotising otitis externa. The fact that all patients in the present cohort had radiological investigations, and almost 90 per cent of the patients were assessed by at least two different radiological modalities, indicates that the practice for investigating patients with suspected necrotising otitis externa was highly consistent in our unit for a number of years. It is therefore unlikely that the increase in number of necrotising otitis externa cases can be solely attributed to increased awareness of, and hence investigations for, necrotising otitis externa.

It is the authors' opinion and practical observation that the increase in necrotising otitis externa incidence reflects a genuine rise in the number of overall cases which could be related to increased resistance of the microbial pathogens to treatments currently used for otitis externa, leading to progression of a higher proportion of these cases into the more aggressive condition of necrotising otitis externa than in previous years. Proving this theory, however, is outside the scope of the current study, and further higher-powered epidemiological studies are required to substantiate this link.

- Necrotising otitis externa is an aggressive external ear infection that extends to surrounding bone and soft tissue
- The disease is most common in elderly diabetic patients; pseudomonas is the commonest causative pathogen
- This study provides strong evidence that necrotising otitis externa incidence is increasing in a geographical locality and may reflect a national increase
- This is the first report showing rising necrotising otitis externa incidence
 among non-diabetic immunocompetent patients
- Disease-related mortality was 7.7 per cent, half of patients developed cranial nerve palsies and mean hospital stay was 36.5 days
- More than a quarter of patients needed hospital re-admission because of poorly controlled disease

This study has also shown an increase in the number of non-diabetic immunocompetent patients diagnosed with necrotising otitis externa. Only one such patient was admitted to our hospital between 2012 and 2016, in comparison to five patients between 2016 and 2020, representing a five-fold increase. This again corroborates an increase in the incidence of necrotising otitis externa in our local geographical area, even among groups of patients not traditionally known to suffer from this disease. Other studies have previously reported cases of necrotising otitis externa among non-diabetic immunocompetent patients,^{7–11} but following a search of the published scientific literature, and to the best of our knowledge, this is the first report to show that the incidence of necrotising otitis externa in this group of patients is rising.

Conclusion

Necrotising otitis externa is a serious condition with a high rate of morbidity and mortality. This study has shown that the incidence of this disease is increasing in the local geographical area of our hospital, with a particular increase seen for the first time among non-diabetic, immunocompetent patients. Our findings may reflect a national trend, but further studies are required to prove this and to investigate the causal factors.

Competing interests. None declared

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