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Lessons learnt from the diagnosis and antimicrobial management of necrotising (malignant) otitis externa: our experience in a tertiary referral centre

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Abstract. *Lessons learnt from the diagnosis and antimicrobial management of necrotising (malignant) otitis externa: our experience in a tertiary referral centre*. Necrotising otitis externa is an uncommon and aggressive infection of the external auditory canal with a tendency to present in the elderly and immunocompromised patient. We report a series of twenty-five patients admitted to our institution over a four-year period with this diagnosis. We review the diagnosis and antimicrobial management of these cases, and propose a treatment algorithm based on our experience.

Introduction

Necrotising otitis externa (nOE) is an uncommon and aggressive infection of the external auditory canal, often progressing to involve adjacent structures, notably the skull base. It was first formally described in 1968 by Chandler as 'malignant' otitis externa, due to its aggressive nature and poor response to available treatment.[1]

Necrotising otitis externa has a tendency to present in the elderly immunocompromised patient, especially those with co-existing diabetes mellitus. Syringing of the external auditory canal, as a treatment for impacted cerumen, has been linked to the development of nOE.[2]

Psuedomonas aeruginosa has been well established as the most commonly isolated causative organism but there are numerous reports of other causative pathogens, including fungal organisms seen most notably in individuals with human immunodeficiency virus (HIV).[3]

Historically, the management of nOE frequently required extensive surgical intervention. Whilst the development and availability of antibiotics has largely superseded the need for such surgery (now largely confined to local debridement and, most commonly, biopsy) a definitive therapeutic strategy to combat nOE has yet to be established.

In this report we present and discuss the clinical features, investigation and management of a series of cases of nOE to our department.

Materials and methods

A retrospective review of admissions to an otolaryngology tertiary referral centre with a diagnosis of nOE over a four year period (2007-2011) was carried out. Diagnosis was made, in each case, on clinical grounds (Table 1). Criteria included a consistent history: that of severe otalgia out of proportion to examination findings, symptoms of at least 7 days duration, and symptoms refractory to empirical topical medication and examination findings: notably those of granulation tissue on the floor of the external auditory canal, with or without associated cranial nerve palsy. Radiological findings were also frequently employed to confirm diagnosis.

Analysis of patient records focussed on epidemiological data, pre-admission clinical features, radiological and microbiological investigation and treatment strategy.

Results

Twenty-seven patients were admitted to our centre with a diagnosis of nOE, as per our study criteria, over the four-year sample period. Two sets of notes were unavailable leaving a total of 25 patients, 9 of which had had multiple admissions during this period.

Demographics

The mean age was 73.5 years (range 37-94; SD 18.7 years). Of the 25 individuals, 16 were male and 9 female (p=0.12 two-tailed binomial test).

Table 1

Diagnostic criteria

Diagnostic criteria
Consistent history:
• severe otalgia out of proportion to examination findings
• symptoms of at least 7 days duration
• symptoms refractory to empirical topical medication
Examination findings:
• notably those of granulation tissue on the floor of the external auditory canal
• +- associated cranial nerve palsy
Radiological findings:
• frequently employed to confirm diagnosis

Immunosuppression

Fifteen patients had co-morbidities which could be considered to place them in an immunosuppressed state. Ten of the patients had diabetes mellitus. Other co-morbidities were chronic renal insufficiency (2 cases), a diagnosis of cancer (1 case), polymyalgia rheumatica (1 case) and the use of immunosuppressive medication (1 case). Of those considered not immunosuppressed (10 cases), 7 patients were aged over 80 years.

Clinical findings

Ninety-six percent of patients (n=24) in the study sample described otalgia on the affected side. Other common symptoms were otorrhoea (68% of patients, n=17) and hearing deficit (40% patients, n=10). Facial palsy was noted in 3 cases (12%) and there was one case with associated glossopharyngeal palsy. Sanguinous discharge from the ear canal was reported by 1 patient.

The most common examination findings were granulations (52%, n=13), the presence of mucopus (48%, n=12), swelling of the external auditory canal (40%, n=10) and the presence of a polyp (36%, n=19). A defect in the canal was observed in 12% (n=3), 1 patient had an identifiable cyst and 1 patient was noted to have a furuncle.

Microbiology

Considering all microbiology samples cultured for all patients during all admissions, canal swabs were analysed for 19 individuals (76%) and their results are shown in Table 2. Culture isolated *Pseudomonas aeruginosa* in 11 individuals (57.9% of cases with microbiology). 3 patients were found to have *Staphylococcus aureus*, 2 patients *Aspergillus flavus*, and 2 patients grew Coagulase-negative staphylococcal species. In addition, *Candida albacans*, *Enterococcus*, *Proteus mirabilis*, *Staphylococcus epidermis*, diphtheroid bacteria and anaerobic species were individually isolated in single cases.

Biopsy

Thirteen biopsies were performed (52%), considering all patients during all admissions. Biopsies underwent both microbiological and histopathological examination. Seven biopsy specimens were noted to culture pathogen species in cases previously devoid of positive microbiological findings. There were no signs of malignancy in any of the specimens.

Imaging

Ninety-two percent of patients (n=23) underwent cross sectional computer tomography (CT) imaging during their assessment and the most prominent radiological feature was noted. Prominent findings included mastoid opacification (43.5%), bony erosion (39.1%) and soft tissue thickening (17.4%).

Antibiotics

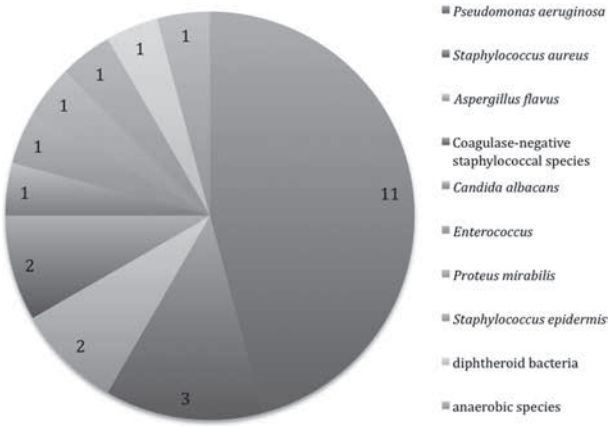
All antibiotic prescriptions were made following discussion with our institution's microbiology department. Recommended antibiotic regimens varied considerably and involved both single and combination therapy. Classes of antibiotics used included quinolones (ciprofloxacin), beta-lactam penicillins (amoxicillin and clavulanic acid [co-amoxiclav]; piperacillin/tazobactam), carbapenems (meropenem), glycopeptides (vancomycin), lincosamides (clindamycin), cepahlosporins (ceftriaxone; ceftazidime) and nitroimidazoles (metronidazole). Antibiotic regimens (depicted in Table 3) were considered in three phases: (i) those prescribed empirically on admission, (ii) those prescribed for an initial primary extended course (commonly based on microbiology profile), (iii) those prescribed for any secondary extended course (based on both microbiology profile and response to earlier antibiotics).

On admission, antibiotics were prescribed empirically in 88% of cases (n=22). Seven patients were placed on co-amoxiclav (31.8% of prescriptions), 3 on ciprofloxacin, 3 on meropenem and 3 on piperacillin/tazobactam (13.6% each).

Table 2

Microbiology

Culture of canal swabs



Combination therapy was prescribed for 2 patients with co-amoxiclav and metronidazole, 1 patient with vancomycin and piperacillin/tazobactam, 1 patient with vancomycin and meropenem and 1 patient with co-amoxiclav and ciprofloxacin. One patient was prescribed clindamycin alone.

All 25 patients in the series were subsequently prescribed an extended course of antibiotics for a median of 2 weeks (range 1-9 weeks). Antibiotic choice again varied: seven patients were placed on piperacillin/tazobactam (28%), 4 on ciprofloxacin, 4 on co-amoxiclav and 4 on meropenem (16% each). Combination therapy was prescribed for 1 patient with ciprofloxacin and clindamycin, 1 patient with ciprofloxacin and vancomycin and 1 patient with co-amoxiclav and metronidazole. In addition, 1 patient was prescribed ceftazidime, 1 patient ceftriaxone and 1 patient clindamycin.

Following this initial extended course of intravenous therapy, 19 patients were prescribed a secondary course of antibiotics of varying duration (median 6 weeks, range 1-11 weeks). Thirteen patients (68.4% of all prescriptions) were prescribed a course of ciprofloxacin. Four patients (21.1%) were prescribed co-amoxiclav and combination therapy was given to 1 patient with clindamycin and ciprofloxacin and 1 patient with co-amoxiclav and metronidazole.

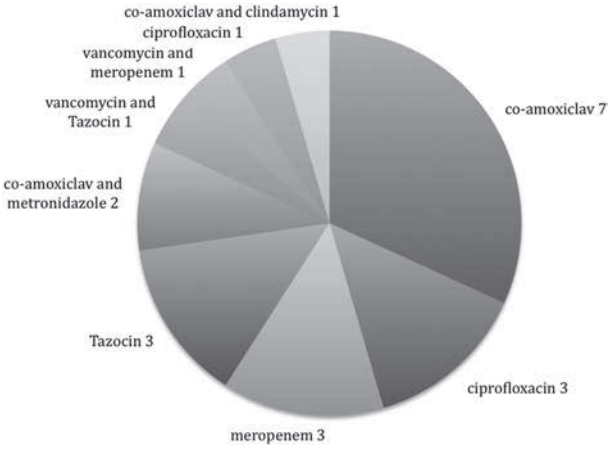
Management

Length of hospital stay varied between 1-45 days (median 15 days). The treatment of nOE frequently requires long courses of intravenous antibiotics. In

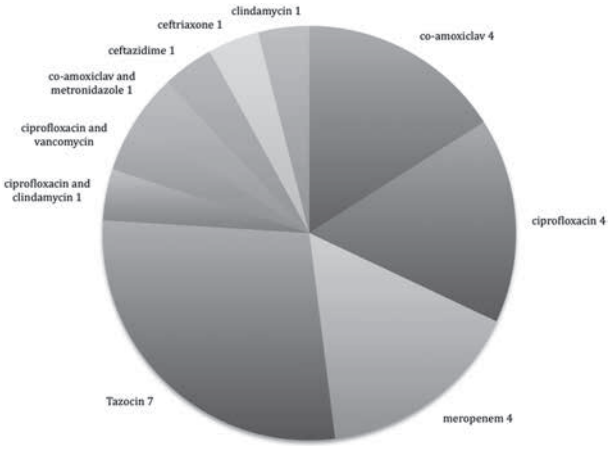
Table 3

Antibiotics

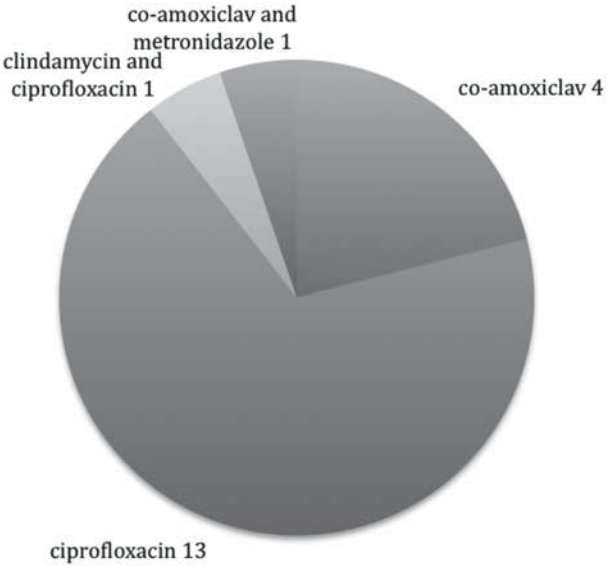
(i) empirical treatment (n=22)



(ii) primary extended course (n=25)



(iii) secondary extended course



our region, we try to achieve this outside the hospital setting. This requires the patient to have suitable intravenous access (such as a peripherally inserted central catheter, PICC line) and for adequate community-based staff to be available to administer medication. It has been our experience that, despite a patient being suitable for community level care, delays in PICC line placement and/or the co-ordination of district nursing teams to supervise intravenous administration can dramatically, and unnecessarily, increase length of inpatient stay.

The number of days taken to co-ordinate PICC line placement varied from 1-8 days (n=13, median 4). The number of days taken to co-ordinate community level care varied significantly. Twelve individuals experienced delays: for the 8 patients for whom community level care was instituted successfully, median length of time to co-ordinate care was 7 days (range 4-18); for the 4 patients for whom community level care requested but not instituted, inpatient stay was delayed whilst intravenous therapy was completed (median 15.5 days, range 8-40 days).

Discussion

Chandler originally defined nOE, back in 1968,[1] in an immunosuppressed patient group and these findings ring true for our experience of the disease today. Ninety-two percent of the patients in our series either had co-morbidities which could be said to render them immunosuppressed or were aged over 80 years; 40% were diabetic. The microangiopathy observed in diabetics and the elderly is thought to be what predisposes such individuals to nOE, as the pathogen invades the local vasculature causing vasculitis and subsequent necrosis of surrounding tissue. Diabetics also demonstrate higher external auditory canal cerumen pH and this has been postulated to further increase the risk of nOE in this patient group.[4]

Patients with nOE typically present with severe otalgia, out of proportion to that seen in otitis externa, frequently associated with otorrhoea. There was only one individual in our series who did not present with severe otalgia (96% did) and 68% reported otorrhoea, reflecting the frequent nature of these symptoms in patients with nOE.

Spread of infection anteriorly, through the fissures of Santorini at the bone-cartilaginous junction of the external auditory canal, can lead to osteomyeltitis of the skull base and mastoid, often associated with cranial nerve involvement. The most frequently involved is the facial nerve, as it passes through the stylomastoid foramen, but the glossopharyngeal, vagus, accessory and hypoglossal nerves are also a risk in this region. Facial nerve palsy was a presenting feature in 12% of our patients. This is markedly lower than that reported in similar studies.[5,6]

Otoscopic examination findings in nOE can be similar to otitis externa but the presence of granulation tissue at the floor of the oseocartilagonous junction is considered to be a significantly more specific finding.[7] All patients in our series had findings on otoscopic consistent with nOE and, notably, 52% demonstrated regions of granulation tissue in the external auditory canal.

Radiologically, CT is considered the imaging modality of choice to demonstrate bony erosion and soft tissue thickening at presentation.[8] Indeed, in our practice 92% of the patients in our series underwent CT imaging to assess disease location and extent.

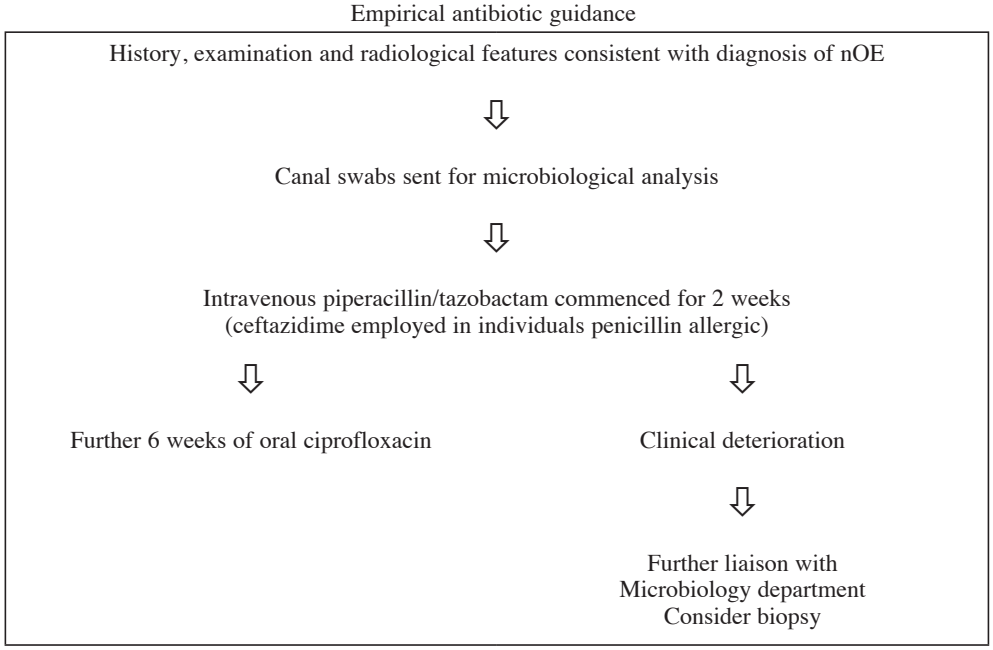
Whilst *pseudomonas aeruginosa* remains the most prevalent causative organism in nOE,[9] the increased use of quinolones in the management of otitis externa, particularly in the primary care setting, has led to the increasing finding of nOE caused by other bacterial strains.[10] This is reflected in our experience, as whilst the majority (57.9%) of positive cultures isolated *pseudomonas aeruginosa*, other bacterial species were also frequently found. The poly-microbial nature of nOE and, critically, the increasing isolation of bacterial strains resistant to quinolone antibiotic therapy, is a concerning entity.

It is general consensus that, due to poor bone penetrance, an extended course of antimicrobial therapy is required for successful treatment of nOE. However, the specific agent, and indeed route of administration, varies between the recommendations of different groups: some suggest that an extended course of oral quinolone therapy (which can be administered in the outpatient setting) is sufficient for the management of all but the most recalcitrant cases of nOE,[3] whilst others find intravenous therapy, with a variety of different agents is almost invariably indicated.[10]

The patients in our study group frequently received a spectrum of antimicrobials with anti-pseudomonas efficacy, including penicillins, carbapenems, glycopeptides and cephalosporins,

Table 4

Empirical antibiotic guidance



often in combination with one another or with a quinolone. Our study has identified a lack of consistency with regard to the empirical prescription of antibiotics of patients admitted to our centre with nOE. Whilst, such initial treatment will vary, in accordance with a given individual's allergies, intolerances and, importantly, any previous courses of treatment, our department has subsequently drawn up empirical antibiotic guidelines and currently recommends a two-week course of piperacillin/tazobactam as first line therapy (or ceftazidime for those with penicillin allergy), followed by a six-week course of oral ciprofloxacin. This treatment algorithm was devised by our Microbiology department following the internal discussion of the cases reviewed here. Piperacillin/tazobatam is recommended as it combines potent anti-pseudomonal activity with broad spectrum action against Gram-postive and Gram-negative bacterial pathogens. Progression to oral quinolone therapy is based on both response to initial treatment and the sensitivity profile of any microbiology specimens cultured. Any deterioration in clinical condition will trigger deviation from this empirical guidance (see Table 4).

Antibiotics should ultimately be selected on the basis of microbiological cultures and response to previous antimicrobial therapy. We found that analysis of a biopsy sample from the canal could aid the isolation of the causative organism in cases where canal swabs were negative.

Gallium citrate radioisotope scans have been previously suggested as a possible method by which disease activity, and as such response to treatment, can be monitored but a number of studies have reported normal scans in the presence of ongoing disease.[11] If disease activity does not improve clinically, despite ongoing targeted anti-microbial therapy, we utilise repeat CT scanning looking again at levels of bony erosion and thickening of the surrounding soft tissues to assess disease activity and extent. The use of repeated CT imaging in this way has also been recommended by other groups.[2]

Extended courses of intravenous antibiotics can, in theory, be delivered effectively in the community but to be established promptly can often involve overcoming hurdles in coordinating multi-disciplinary input. The median time to successfully co-ordinate input was 11 days, however this does not include the 4 cases in which discharge to community-level care was delayed to the extent that their course of treatment was completed in hospital. The cost, to both the patient and hospital, of such an extended hospital stay is significant.

Conclusions

Necrotising otitis externa is an uncommon and aggressive infection of the external auditory canal with a tendency to present in the elderly and immunocompromised patient.

Patients typically present with severe otalgia, out of proportion to that seen in classic otitis externa, frequently associated with otorrhoea.

The widespread use of quinolones has led to the increasing finding of polymicrobial nOE, frequently involving bacterial strains other than *pseudomonas aeruginosa*.

It is our policy to initially empirically prescribe a two week course of piperacillin/tazobactam, followed by an extended six week course of ciprofloxacin, though antibiotic choice should ultimately be selected on the basis of microbiological culture.

Patients can often be managed in the community for the mainstay of their treatment but this is often fraught with logistic difficulties.

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