ORIGINAL ARTICLE

Initial management of necrotizing external otitis: Errors to avoid

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Summary
Objectives: Diagnostic and therapeutic practice guidelines have been established for classical forms of benign otitis externa. However, these guidelines do not include unusual forms of the disease, especially “invasive” otitis externa. No consensual diagnostic flow diagram has been published in the literature, which frequently results in delayed diagnosis and inappropriate primary care management. The objective of this study was to analyse the primary care management practices of malignant otitis externa (MOE).

Material and methods: Retrospective study of 22 cases of MOE managed in our tertiary care centre over a 6-year period (2004–2010).

Results: All but one of the patients presented a systemic or local predisposing factor. The mean interval between onset of the first symptoms and referral to our tertiary care centre was 13 weeks (range: 1 to 12 months); 77% of patients were referred by a private ENT specialist, 14% were referred by an emergency department and 9% were referred by a hospital department. Seventeen patients (81%) had received one or more courses of inappropriate systemic antibiotics during this interval (oral in 15 cases, parenteral in two cases, multiple treatments in 13 cases). The mean duration of each course of antibiotics was 12 days (range: 7 to 21 days). All patients also received local antibiotic ear drops (aminoglycosides or fluoroquinolones).

Conclusions: The practice audit constantly revealed delayed management of MOE, often resulting in inappropriate antibiotic prescriptions. Publication of practice guidelines for primary and secondary care practitioners therefore appears to be essential.

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Introduction

Malignant otitis externa (MOE), also called necrotizing otitis externa, corresponds to osteomyelitis of the skull base, typically due to Pseudomonas aeruginosa, initially arising in
the external auditory canal (EAC). Extension to the deep soft tissues of the face and to the central nervous system determines the severity of this infection. The first cases described by Chandler in 1968 [1] classically concerned elderly diabetic men with extremely painful otitis externa associated with facial palsy.

Although this clinical presentation is well known and generally leads to rapid, appropriate management, diagnostic difficulties may be encountered, especially at the early stages, resulting in inappropriate primary care management that delays and complicates subsequent management [2], as, early in the course of this necrotic infection, the clinical features are identical to those of classical otitis externa. The presence of systemic predisposing factors, otoscopic signs and especially resistance to topical treatment should raise the suspicion of MOE, even in younger, non-diabetic subjects. An early clinical diagnosis confirmed by imaging and microbiology allows initiation of appropriate antibiotic therapy that very probably limits the extent of necrosis and the development of central nervous system complications [3].

We conducted a retrospective study of cases admitted to our tertiary care centre with particular attention to the primary care management of these cases. The objective of this study was therefore to define the traps and errors associated with the diagnosis and primary care management of MOE in order to propose improvement of clinical practice.

Material and methods

All consecutive patients managed in the Department of Otorhinolaryngology and Head and Neck Surgery of Nice University Hospital with a diagnosis of MOE between 1st July 2004 and 31 August 2010 were included in this study.

In our unit, the diagnosis of MOE was defined by the presence of clinical signs of inflammation of the EAC confirmed by radiological signs of bone involvement (computed tomography and/or magnetic resonance imaging [MRI] and/or scintigraphy).

Carcinomas of the EAC were excluded from this study.

The following data were retrospectively collected from the medical files of the ENT and infectious diseases departments for each patient included:

- epidemiological data;
- analysis of the clinical setting and systemic predisposing factors;
- initial clinical data:
  - clinical presentation (at the time of admission);
  - previous management;
  - laboratory, microbiological and histopathological analysis (at the time of admission).

Data were entered into spreadsheet software (Microsoft Office Excel® 2008 — Microsoft Corporation© — Redmond, USA).

Results

Twenty-two cases (21 patients) satisfying the inclusion criteria were included in this retrospective study.

Clinical setting and systemic predisposing factors

The epidemiological characteristics of these 22 cases are summarized in Fig. 1. One patient was managed twice: for a lesion on the right side in 2004 (case 1, Fig. 1) and then for a lesion of the left side in 2010 (case 19, Fig. 1). The mean age of the patients of this series was 73 ± 11 years and 77% of them were males (sex-ratio of 3.4/1).

Twelve patients (55%) were diabetic, and eight of them were considered to be poorly controlled (HbA1c > 8%). MOE was the presenting sign of diabetes in one case (case 21, Fig. 1). Serum protein electrophoresis was performed in 14 patients, revealing hypogammaglobulinaemia in four cases (29%), including one patient who was also diabetic. HIV serology was determined in 10 cases and was negative in all cases. Overall, at least one systemic predisposing factor was identified in 15 out of 22 cases (68%).

Climate and local predisposing factors

Onset of symptoms was situated between April and September in every case. Twenty patients (95% of cases) attended our outpatients department between May and December.

Marked exposure to water (spa therapy in five cases, swimming or diving in three cases) was also formally identified in eight cases (38%) (Fig. 1). In two of these eight cases (corresponding to the same patient), the patient performed traumatic manoeuvres himself (cleaning of EAC with a knife!).

Two other patients also underwent potentially traumatic manoeuvres (extraction of a cerumen plug) during the days preceding onset of the infection.

MOE was the first sign of Wegener’s granulomatosis involving the EAC and parotid gland in one case. Finally, one patient had received external beam radiotherapy and chemotherapy 25 years previously for cervical lymphoma (precise irradiation fields not specified).

Overall, a potential local predisposing factor was therefore identified in 12 cases (55%). Only one of the 22 patients of this series did not present either a systemic or a local predisposing factor (case 13, Fig. 1).

Previous management

The mean interval between onset of the first symptoms and referral to our centre was 13.4 ± 6 weeks, i.e. about 3 months with a range of 1 month to 12 months and a median of 10 weeks.

Seventy-seven percent of cases were referred by a private ENT specialist, 14% were admitted via an emergency department and 9% were referred by a hospital department.

In 17 cases (81%), one or several courses of systemic antibiotics had been prescribed during this period (oral in 15 cases, parenteral in two cases, multiple treatments in 13 cases). The various types of antibiotics prescribed are indicated in Fig. 2. A fluoroquinolone was prescribed in nine out of 17 cases, including ciprofloxacin active against P. aeruginosa in eight cases, always as monotherapy and at the standard dosage.
The mean duration of each course of antibiotics was $11.6 \pm 3$ days (range: 7 to 21 days). These patients always received concomitant topical treatment with antibiotic eardrops (aminoglycosides or fluoroquinolones).

**Clinical presentation**

**Fig. 3** summarizes the clinical presentation of these 22 patients. Symptoms were unilateral in every case. Earache was the symptom most frequently reported and was
present in 100% of cases. All patients were taking or had been taking level 1 or 2 analgesics at the time of diagnosis. Otorrhoea was present in 16 cases (73%).

Otoscopic examination showed lesions of the EAC in every case, with a polyp or granuloma in 77% of cases, fluctuating abscess of the floor of the EAC in two cases, and global inflammatory stenosis of the EAC in the remaining two cases.

A cranial nerve lesion was observed at the time of the first visit in seven patients (32%): seven cases presented facial palsy, associated with ipsilateral vagus nerve palsy in one case (demonstrated by dysphonia). The median time to management of these patients was identical to that of patients without cranial nerve lesions.

Parotid swelling was present in two cases (cases 11 and 16, Fig. 3). Signs of temporomandibular joint dysfunction were present in three cases. Only four patients were febrile (18%).

### Imaging

The initial diagnostic work-up comprised computed tomography (CT) in 22 cases (100%), magnetic resonance imaging (MRI) in 13 cases (59%) and Technetium-99 (99mTc) scintigraphy in two cases. CT showed no signs of bone lysis in 23% of cases (five out of 22). The diagnosis was established by 99mTc scintigraphy in two cases (intense bone uptake) and MRI in three cases (infiltration of retrocondylar fat).

### Laboratory parameters and microbiology

Bacteriology specimens were obtained in every case. The pathogen was demonstrated in 20 cases (95%): in our unit in 15 cases, and before referral to our centre in five cases (Fig. 4).

Cultures were positive for *P. aeruginosa* in 17 cases (77%). *P. aeruginosa* was associated with another micro-organism in three out of 17 cases, considered to be a contaminant in two cases (enterobacteria and coagulase-negative Staphylococcus in one case, *Candida parapsilosis* in one case), and a potential pathogen in 1 case (*Candida albicans*).

The other bacteria isolated were:

- *Achromobacter xylosoxydans* in one case;
- *Actinomyces meyeri*, associated with an animal strain of *Corynebacterium* in one case;
- *Escherichia coli* in one case;
- A combination of bacteria of the gastrointestinal flora: *E. coli*, *E. faecalis*, *K. oxytoca*.

Antibiotic susceptibility testing was performed in every case. *P. aeruginosa* was sensitive to ciprofloxacin and ceftazidime in 100% of cases. Minimum inhibitory concentrations (MIC) for ciprofloxacin and ceftazidime were determined in each case. One *P. aeruginosa* strain had a high MIC (0.64 mg/L).

Laboratory signs of inflammation were investigated in 21 cases and were present in 15 cases (71%): elevation of C-Reactive Protein (CRP) greater than 10 mg/L in 13 cases (range: 16 to 101, mean: 51). Erythrocyte sedimentation rate was determined in 1 case and was elevated (81 mm at the first hour).

### Histopathology

Histological examination excluded a malignant tumour in the 13 cases with a doubtful diagnosis.
Discussion

This study revealed a clear-cut conclusion concerning the primary care management of MOE: severely delayed diagnosis, consequently associated with multiple inappropriate treatments. Evidence-based guidelines are available for classical forms of benign otitis externa [4], but these guidelines exclude particular forms of the disease, especially invasive forms: in some cases, this benign disease can evolve towards a necrotizing process arising in the bone of the EAC, and then spreading to cause osteomyelitis of the skull base, and involvement of the deep soft tissues of the face, or even the central nervous system, causing cranial nerve lesions and life-threatening implications.

Although various authors have proposed diagnostic criteria [3,5–20] (Fig. 5), no consensual diagnostic flow diagram has been published in the literature. This is particularly important, as early diagnosis, allowing rapid management, could be a major prognostic factor [3]. The most characteristic feature of MOE, rather than the classical clinical signs (granulation tissue of the EAC in a context of symptoms of otitis externa in an immunodepressed setting) is that it is refractory to conventional treatments. In the present series, seven out of 22 patients did not present any systemic predisposing factors, but all patients presented signs of otitis externa for more than 4 weeks. All patients had received several topical treatments, associated in every case with one or more courses of systemic antibiotics therapy, often prescribed by several practitioners. According to 70.6% of authors [3,5–20] (Fig. 5), the poor response to conventional treatment (not including systemic antibiotics) constitutes a mandatory diagnostic criterion.

Current guidelines for benign otitis externa support this dogma: according to the Good Clinical Practice guide of the Cochrane Database [4], benign otitis externa should respond to well conducted topical treatment within 48 or 72 hours after aspiration of the EAC and the diagnosis should be reviewed after 2 weeks.

However, practice audits constantly show delayed management, and often inappropriate initial management. Delayed management for up to more than 3 months after onset of the symptoms has also been reported in the literature [2]. In the present study, the mean time to diagnosis was 13 weeks.

As a result of this uncertain diagnosis, many empirical antibiotics with a spectrum that does not correspond to the bacterial epidemiology of MOE are prescribed (for example amoxicillin-clavulanic acid and pristinamycin, to which P. aeruginosa is naturally resistant). Moreover, antibiotics are generally useless in the case of benign otitis externa, and inappropriate and prescribed for an insufficient duration in the case of MOE, which requires prolonged antibiotic therapy in order to treat osteomyelitis. Multiple courses of local antibiotics are also used concomitantly, which can predispose to the development of resistant strains (especially to ciprofloxacin [14,21], but also and more recently to ceftazidime [22]) and the risk of negative cultures [23]. However, microbiological documentation is required to correctly adapt the antibiotic therapy of MOE. Due to the low frequency of ear swabs performed in the primary care setting (only 5/22 patients in this series), identification of the pathogen was usually performed in our unit, and cultures were repeated 48 hours after stopping all topical and/or systemic local antibiotics, if necessary. No resistant strains of P. aeruginosa were detected in the present series. However, one strain of P. aeruginosa with a high MIC was isolated from one patient who received ciprofloxacin, requiring 6 weeks of two-agent antibiotic therapy.

In a study conducted in Athens, Eleftheriadou et al. [24] concluded that patients referred by rural centres situated away from the capital had a poorer prognosis than patients managed immediately in Athens, although the difference was not statistically significant. They emphasized the role of primary care physicians in referral of high-risk patients to specialized centres to ensure more rapid management.

Rubin Grandis et al. [25] described an archetypal example of delayed diagnosis: a patient received 12 courses of antibiotics, often based on effective molecules, and always for periods of less than two weeks. The patient was referred to a reference centre only after 18 months without improvement.

According to Johnson and Ramphal [9], the growing diffusion of information to physicians is largely responsible for improvement of the prognosis of this disease over recent years.
Conclusion

This study illustrates the diagnostic difficulties encountered in the primary care management of patients with MOE, especially at the early stages of the disease, which delayed initiation of appropriate treatment. Publication of practice guidelines appears to be necessary in view of the diagnostic delay ranging from 4 weeks to 1 year and the inappropriate antibiotic prescriptions:

- first of all, the physician must consider the possibility of this diagnosis. Any case of otitis externa refractory to well conducted topical treatment must raise the suspicion of MOE, even in non-diabetic, non-immunodepressed and female subjects;
- the diagnosis must then be confirmed by cultures (after stopping antibiotic eardrops for 48 hours, and obviously after stopping any systemic antibiotics) and appropriate imaging (computed tomography of the petrous temporal bone completed, when negative, by 99mTc bone scan or magnetic resonance imaging). Depending on the clinical presentation, various differential diagnoses, especially malignant diseases of the EAC, must be excluded;
- finally, culture-directed antibiotic therapy, at maximum dosage with good bone diffusion, initially as dual-agent therapy to decrease the risks of failure and resistance, must be conducted in collaboration with an infectious diseases physician.

In this way, the time to initiation of appropriate antibiotic therapy could be reduced to 2 weeks, which could possibly decrease the risk of cranial nerve lesions.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


