Acta Otorrinolaringol Esp. 2010;**61(6):**437–440

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

ORIGINAL ARTICLE

Malignant otitis externa. Our experience

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Received December 17, 2009; accepted February 17, 2010

KEYWORDS
Malignant otitis externa;
Necrotizing otitis externa

PALABRAS CLAVE
Otitis externa maligna;
Otitis externa necrotizante

Abstract
Malignant otitis externa is a devastating disease that poses a diagnostic and therapeutic challenge. The objective of our study was to demonstrate the importance of detailed clinical analysis and to provide an update on the current diagnostic and therapeutic tools available.

Otitis externa maligna. Nuestra experiencia

Resumen
La otitis externa maligna es una infección severa cuyo diagnóstico y tratamiento continúan suponiendo un reto para el clínico. El objeto de este estudio es demostrar la importancia de un análisis clínico detallado y aportar una puesta al día de las herramientas diagnósticas y terapéuticas actualmente disponibles.

Introduction

Malignant external otitis (MEO) is a severe disease whose diagnosis and treatment is a challenge for any specialist. The first description was carried out in 1959 by Meltzer and Kelemen,[1] but it was in 1963 and 1968 with the work of Chandler[2] that it was defined with the term MEO.

MEO occurs in patients with decreased immune systems mostly elderly diabetics (90%), generally insulin-dependant and poorly controlled. There are also forms of MEO in youths and children. The main differential diagnosis is with malignant tumours of the external ear canal (EAC).[3]

Although mortality was high for the past few years, at present the prognosis has improved due to good response to prolonged treatment with fluoroquinolones. The purpose of this study is to demonstrate the importance of detailed clinical analysis and to provide an update of currently available diagnostic and therapeutic tools.

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0001-6519/$ - see front matter

Material and method

We conducted a prospective study of 8 patients treated at our hospital with a diagnosis of MEO between the years 2005-2009 (Table). As for the diagnostic protocol, we performed a CT scan and a combination of Tc-99m and Ga-67, the latter essential for monitoring. In cases of neurological complications, MRI was requested. An EAC biopsy and bacterial culture were carried out in all cases.

All patients were admitted for treatment. This consisted primarily in local cure and topical administration of ciprofloxacin 2 times a day, as well as intravenous antibiotics. We proceeded to control glycaemia and began treatment with oral antidiabetic agents or insulin.

Our discharge criteria were: normal otoscopy, C-reactive protein values and erythrocyte sedimentation rate within normal limits and negative Ga-67 scintigraphy. After discharge, all patients continued treatment with oral ciprofloxacin for 6 weeks, at a dose of 500 mg/12 h.

Results

The bacteriological study isolated *Pseudomonas aeruginosa* in 3 cases, *Aspergillus flavus* in 1 case, *Candida albicans* in 2 cases and the cultures were negative in 2 patients.

Bone erosion and occupation of the external ear canal and middle ear were observed on the CT scan (Figure 1). The Ga-67 scintigraphy showed an increase of osteogenic response in the petrosal (Figure 2).

Laboratory tests showed elevated C reactive protein and erythrocyte sedimentation rates in all cases.

The average duration of intravenous therapy was 6 weeks (range 3-12). Patients were treated with 3rd generation cephalosporin and a fluoroquinolone or a broad-spectrum antibiotic from *Pseudomonas* (piperacillin-tazobactam, imipenem). Amphotericin B was also administered in cases where *Aspergillus flavus* or *Candida albicans* were detected as pathogens, except in one case with liver cirrhosis where imidazole was administered and another case in which no germ was isolated that responded satisfactorily.

A total of 4 patients suffered facial paralysis, one of them from the time of diagnosis. Of these 4 patients, 1 also presented involvement of other cranial nerves. Two patients recovered facial function during treatment.

One patient suffered a cerebrovascular pontine stroke during treatment.

We performed a mastoidectomy on 1 patient, due to the absence of improvement with medical treatment and to the persistence of granulation tissue and facial involvement.

The control of otalgia was very difficult in 3 patients despite treatment with morphine. They received hyperbaric oxygen therapy after discharge with satisfactory results.

Two patients suffered relapses at 3 and 12 weeks, respectively. One of them evolved favourably after treatment and the other, in whom a number of factors coincided (age, poorly controlled diabetes, involvement of cranial nerves and cerebrovascular pontine stroke), died. The rest are currently free of disease.

Table

Patient	Age	Gender	ID	Affected ear	Affected cranial nerves	Polyps and granulation	Germ	Elevated ESR and CRP	Treatment	Evolution
1	83	M	DM	LE	VII, IX	No	Aspergillus	Yes	Amphotericin B+piperacillin+ fluoroquinolone	Relapse at 3 weeks and death
2	77	M	DM	LE	VII	Yes	Candida	Yes	Amphotericin B+3rd-generation cephalosporin+fluoroquinolone	Cure
3	73	M	DM	Bilateral	VII	Yes	No germ isolated	Yes	Amphotericin B+tazobactam+ fluoroquinolone	Relapse at 12 weeks and cure
4	70	F	DM	RE	No	Yes	Pseudomona	Yes	Imipenem+fluoroquinolone	Cure
5	76	F	DM	RE	VII	Yes	Pseudomona	Yes	Tazobactam+fluoroquinolone	Cure
6	80	M	DM	RE	No	Yes	Pseudomona	Yes	Piperacillin+fluoroquinolone	Cure
7	70	M	DM	RE	No	Yes	No germ isolated	Yes	3rd-generation cephalosporin+ fluoroquinolone	Cure
8	57	M	DM	LE	No	Yes	Candida	Yes	Imipenem+imidazole+ fluoroquinolone	Cure

CRP indicates C reactive protein; F, female; ID, immunosuppression; M, male.

Figure 1 CT scan.

Figure 2 Ga-67 scintigraphy.

Discussion

A rare and serious infection of the EAC, MEO or progressive necrotizing external otitis can endanger the life of patients. The pathogenesis of the disease results from the conjunction of a predisposed area and EAC invasion by an opportunistic pathogen. The predisposed area in a diabetic patient is the diabetic microangiopathy responsible for tissue hypoperfusion,[4] present in all our patients. The opportunistic germ is *Pseudomonas*; its prevalence is higher in most of the literature than in our series, probably due to previous treatment with quinolones, which would explain the negativity of some of the cultures.

The infection spreads from the EAC causing extensive osteitis. Rubin[5] found a triggering factor in 60% of cases, mainly EAC trauma (removal of a wax plug, hearing aid) and also emphasised the importance of climate, as in banal external otitis.

An MEO process begins with a discrete otalgia, which would explain the late diagnosis. Facial paralysis, often complete, appears in 20%-30% of cases.[4,5] The involvement of other cranial nerves (IX, X, XI, XII) occurs in 15%-35% of cases,[2] indicating the spread of infection to the skull base. Of our patients, 4 presented facial palsy, 1 of them from the time of diagnosis. In 1 patient, the hypoglossal nerve was also affected. Traditionally, the involvement of cranial nerves has been considered as an indicator of a worse prognosis,[6] but recent studies found no differences in survival.[7,8]

While it is more common in elderly diabetics (90%), MEO also appears in other immunodeficiencies such as blood disorders, immunosuppressive treatments and AIDS. In the last of these, it affects younger patients with advanced disease, there is no granulation tissue, the predominant germ is *Aspergillus* and infection is more serious, with a mortality rate above 42%.[9]

Occurrence in children is rare and is associated with diabetes, anaemia and malnutrition, as well as with chemotherapy treatment.

Although *Pseudomona* is the most common germ, there have also been reports of cases of *Staphylococcus aureus* or *epidermidis* and *Proteus mirabilis*. Fungal infection (such as by *Aspergillus* and *Candida*) is more severe and mortality is higher (42%).[10] In our series, the patient with the worse outcome was the one in whom *Aspergillus* was isolated.

The analytical tests often show elevated inflammatory and infectious markers, which represent an interesting evolutionary parameter despite a lack of specificity.

The diagnosis and monitoring of MEO has improved considerably with the development of modern imaging techniques.[10] CT is useful in confirming the diagnosis.[11] In evolved forms, it makes it possible to assess the extent of the disease to the petrosal mass, subtemporal peritubal and parapharyngeal spaces and temporomandibular joints. However, it is not a specific test and is of little interest in monitoring. An MRI is useful in defining the involvement of soft tissues, especially the infratemporal, but is also of little value in monitoring.[11]

Scintigraphy plays an important role in diagnosis and monitoring. Bone scintigraphy with Tc-99m is regarded as the key test for an early diagnosis.[12,13] Technetium fixation is correlated with osteolytic activity, which explains its high sensitivity (100%), but its specificity is low.[14] It remains positive long after recovery and is therefore not applicable in monitoring.

Ga-67 scintigraphy is considered essential in evolution control and monitoring due to its high specificity. The standardisation of the test confirms the healing of the disease.[15,3]

Currently, the basis of treatment is antibiotic therapy, leaving surgical debridement and additional treatments such as hyperbaric oxygen therapy, for those cases with poor response and torpid evolution.[10]

In general, hospitalisation is recommended to perform a complete study and establish early treatment. Several guidelines have been proposed; most authors combine a 3rd-generation cephalosporin with a fluoroquinolone to avoid resistences.[13,16,17] Others use the association of semi-synthetic penicillin with an aminoglycoside, but its potential toxicity recommends its use only in cases of multidrug resistance in the antibiogram. Some authors advocate a monotherapy (3rd-generation cephalosporin or fluoroquinolones) with excellent results in the limited MEO form. Control of diabetes is very important. The duration of intravenous therapy ranges from 4-6 weeks. In our experience, extending oral antibiotic treatment (fluoroquinolone) for an average of 6 weeks is very important. The suspension of treatment requires regular monitoring until there is complete clinical recovery and normalisation of the Ga-67 scintigraphy.

Mortality has currently decreased from 30%-40% to 20%.[13,10] Recurrences may occur up to 1 year after the end of the treatment; consequently, it is considered necessary to maintain regular, prolonged patient monitoring.

Conclusions

Malignant external otitis is a rare but severe illness that can occur as a complication of external otitis in diabetic and immunocompromised patients. It can be fatal if not properly treated.

Early diagnosis and treatment of temporal osteomyelitis is essential for the prognosis of the disease.

Treatment, if the culture is positive, must be established on the basis of the antibiogram, given the emergence of resistances to ciprofloxacin.

Conflict of interest

The authors declare no conflict of interest.

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