ORIGINAL ARTICLE

Malignant Otitis Externa: A persistent challenge

Otite Externe Maligne: Le défi persiste

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Abstract

Introduction: Although rare, Malignant otitis externa is responsible for a high morbidity and could sometimes be fatal. The management of this condition is still challenging.
Aim: To analyse the clinical, microbiological and radiological profile of malignant otitis externa, and the management of this condition.
Methods: A descriptive, cross-sectional study was conducted at ENT Department of Kairouan's hospital including 38 patients hospitalised and treated for malignant otitis externa from January 2013 to August 2021.
Results: The mean age of patients was 67.7 ± 12.9 years (35-98). All patients presented with continuous otalgia that resists to usual analgesics. Otorrhea was noticed in 76.3% of cases, facial palsy in 2 cases (5.3%) and dysphonia in one case (2.6%). Pseudomonas Aeruginosa was the main responsible pathogen (42%). Concomitant bacterial and fungal infection was noticed in 6.4% of the cases. First-line intravenous antibiotherapy used was mainly based on an association of Cephalosporins and Fluoroquinolones. Complete remission was noticed in 30 patients (79%). However, 8 cases of recurrences (21%) and 2 cases of deaths (5.2%) were noticed in our series. The mean follow-up was 4.6±6.3 (1-26 months).
Conclusions: Pseudomonas Aeruginosa remains the main responsible pathogen for malignant otitis externa. Nevertheless, fungal infections are rising because of the overuse of antibiotics. Antibiotherapy should be adapted to culture results and resistance profile of pathogens in hospital. Practionners should be aware of the possibility of concomitant fungal infection, especially in the case of unfavorable evolution.

Key words: otitis, externa, microbiology, diagnosis, management.

Résumé

Introduction: Bien que rare, l'otite externe maligne est responsable d'une morbidité élevée parfois mortelle. La prise en charge de cette pathologie demeure un défi.
Objectif: Analyser le profil clinique, microbiologique et radiologique de l'otite externe maligne ainsi que sa prise en charge thérapeutique.
Méthodes: Une étude descriptive et transversale a été menée au sein du service d'ORL du CHU de Kairouan incluant 38 patients hospitalisés et traités pour otite externe maligne entre Janvier 2013 et Août 2021.
Résultats: L'âge moyen des patients était de 67.7 ± 12.9 ans (35-98). Tous les patients présentaient une otalgie continue résistante aux analgésiques habituels. Une otorrhée a été notée dans 76.3 % des cas, une paralysie faciale dans 2 cas (5.3%) et une dysphonie dans un cas (2,6 %). Le Pseudomonas Aeruginosa était le principal pathogène (42%). Une infection bactérienne et fongique concomitante a été objectivée dans 6.4 % des cas. L'antibiothérapie intraveineuse était basée principalement sur l'association de Céphalosporine et de Fluoroquinolone. Une rémission complète a été notée chez 30 patients (79%) avec 8 cas de récidives (21%) et 2 cas de décès (5.2%). Le suivi moyen était de 4.6 ± 6.3 mois (1-26).
Conclusions: Le Pseudomonas Aeruginosa reste le principal agent pathogène responsable de l'otite externe maligne. Néanmoins, les infections fongiques sont en croissance en raison de l'utilisation excessive des antibiotiques. Les praticiens doivent être conscients de la possibilité d'une infection fongique concomitante, notamment en cas d'évolution défavorable.

Mots clés: otite externe, microbiologie, diagnostic, traitement.

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LA TUNISIE MEDICALE-2024; Vol 102 (08): 478-482 DOI: 10.62438/tunismed.v102i8.4867

Introduction

Malignant Otitis Externa (MOE) is an aggressive infection of the external auditory canal (EAC) which can involve cranial nerves and cause osteomyelitis of the skull base. Although rare, it is responsible for a high morbidity and could sometimes be fatal. Only 10 cases per million per year were reported in the general population in United Kingdom (1). This entity is classically seen in the elderly population and immunosuppression conditions, particularly diabetes mellitus, but also chemotherapy, HIV/AIDS, or malnutrition. Mortality reached 50% of the cases and it is reduced to 10 to 20% thanks to early diagnosis and advanced therapeutic modalities (2). In Tunisia, the incidence of MOE has increased over the last recent years. Nonetheless, few reports were published. The incidence is estimated to be 10 new cases every year with the emergence of severe fungal forms (3).

The aim of this study is to analyse the clinical, microbiological and radiological status of MOE and the management of this condition.

Methods

A descriptive, cross-sectional study was conducted at ENT department of Kairouan from January 2013 to August 2021, including 38 patients hospitalised and treated for MOE.

Clinical data were retrieved from medical and surgical records with respect to anonymity after the approval of the Ethical Committee of the hospital. They included: age, gender, comorbidities, clinical presentation and findings, biological results (Erythrocyte sedimentation rate: ESR and C-reactive protein: CRP), microbiological culture results, imaging results, histological findings, management modalities (antimicrobial treatment, with any subsequent changes; treatment duration; other treatments or surgical procedures) and outcome (complications, recurrences and death). Patients with incomplete records were excluded from the study.

Results

A total of 38 patients were diagnosed with MOE within 7 years with a mean age of 67.7 ± 12.9 years (35-98). We noticed that 73.6% of the patients were over 60 with a female predominance (sex ratio: 1.2). All patients were diabetic and 60.5% of them had arterial hypertension. Chronic renal failure was noticed in 3 cases and one patient was previously treated with chemotherapy for breast cancer (Table 1). All patients presented with continuous otalgia that resists to usual analgesics. Otorrhea was noticed in 76.3% of cases, facial palsy in 2 cases (5.3%) and dysphonia in one case (2.6%) (table 1).

Physical examination revealed EAC stenosis in all cases. Otorrhea was noticed in 92% of the cases. Granulation tissue and EAC polyp were objectified in 21 and 28.9% of cases, respectively. Facial palsy was noticed in 2 cases (5.3%).

Table 1. Demographic and clinical characteristics of the series.

Characteristics	Number	Percentage
Comorbidities		
Diabetes mellitus	38	100
Arterial hypertension	23	60.5
Dyslipidemia	12	31.6
Hypothyroidism	2	5.3
Chronic renal deficiency	3	7.8
Cardiovascular disease	11	29
Chemotherapy	1	2.6
Clinical presentation		
Otalgia	38	100
Otorrhea	29	76.3
Headache	2	5.3
Facial palsy	2	5.3
Dysphonia	1	2.6
Consciousness disorder	1	2.6
Physical examination findings		
Stenosis of the EAC	38	100
Purulent Otorrhea	35	92
Congestive painful pinna	3	7.8
Granulation tissue	8	21
EAC Polyp	11	28.9
Facial palsy	2	2.6

EAC: External Auditory Canal.

Biological investigations revealed high level ESR, CRP and leukocyte counts in 60.5%, 21% and 7.8% of cases, respectively. Microbiological investigation was positive in 81.7% of the cases with a predominance of Pseudomonas Aeruginosa (42%), Staphylococcus Aureus (29%) and Candida Albicans (16%) (table 2). The infection was mainly bacterial; however, concomitant bacterial and fungal infection was noticed in 6.4% of the cases. Concerning fungal infection, Candida Albicans was the main fungal agent (50%) followed by Candida Glabrata (25%) and Aspergillus Flavus (25%).

Table 2. Microbiological results in our series

Organisms isolated from discharge in MOE	Number (percentage)
Pseudomonas Aeruginosa	13 (34.2)
Staphylococcus Aureus	9 (23.6)
Candida Albicans	4 (10.5)
Candida Glabrata	2 (5.2)
Aspergillus	2 (5.2)
Pseudomonas Aeruginosa + Candida Albicans	1 (2.6)
Staphylococcus Aureus + Candida Albicans	1 (2.6)
Other pathogens	4 (10.5)

Computed tomography (CT) scan was performed in 27 cases (71%). For the other cases, CT scan was not available, and the diagnosis was based on clinical, biological and microbiological findings. All patients demonstrated abnormalities of the EAC such as involvement and thickening of EAC and mastoid air cells. Erosion and/or lysis of tympanic part of the temporal bone were noticed in 15 cases (55.5%), ossicular chain lysis in 37% of cases, parapharyngeal extension in 29.6% of cases and temporo-mandibular joint involvement in 22% of cases (table 3).

Complications related to MOE were objectified in 7 cases (18.4%). Three of them were suspected clinically: 2 patients presented facial nerve palsy and one patient had dysphonia (X nerve palsy). On CT scan, retropharyngeal abscess was noticed in 3 cases (responsible pathogen was

Candida Albicans in one case). Sigmoid sinus thrombosis was noticed in one case (the responsible pathogen was Pseudomonas Aeruginosa) and facial nerve denudation in 2 cases (the responsible pathogen was Pseudomonas Aeruginosa in one case).

Table 3. Imaging findings in our series

Imaging feature	Number (percentage)
Ossicular chain lysis	10 (37)
Temporo-mandibular joint involvement	6 (22)
Parapharyngeal extension	8 (29.6)
Retropharyngeal abscess	3 (11)
Sigmoid sinus thrombosis	1 (3.7)
Masticator space extension	2 (7.4)
Middle skull base involvement	2 (7.4)
Nasopharyngeal extension	2 (7.4)
Carotid space extension	2 (7.4)
Second portion facial nerve denudation	2 (7.4)

All patients presented with uncontrolled diabetes. First-line intravenous (IV) antibiotherapy used was mainly based on an association of Cephalosporin (Ceftazidime: Fortum®) and Fluoroquinolone (Ciprofloxacin®) (89.4%). Combined Cephalosporin (Cefotaxim®) and Fosfomycin were used in 2 patients (5.2%). Two patients received Imipenem (Tienam®) associated with Aminoglycoside (Gentamycin®). The mean intravenous treatment duration was 21.8 ± 8.5 days (10-50). The main oral antibiotic was Ciprofloxacin® in 32 cases (84.2%). The most used antifungal therapy was Fluconazole (Flukas®) (5 cases) followed by Itraconazole (Sporanox®) (3 cases). The total treatment duration (IV + oral) was 37.4 ± 23.6 days (21-120).

Factors that led to treatment discontinuation were the isolation of a different pathogen and the side effects related to treatment. The disease cured based on clinical (otalgia and otorrhea disappearance) and biological (decrease of ESR) evolution.

Surgical treatment based on local debridement was performed in 8 cases (21%). Complete remission was noticed in 30 patients (79%). However, 8 cases of recurrences (21%) were noticed in our series. They were related to short treatment duration, the presence of an aggressive pathogen, particularly, fungal infection and the presence of complications on initial CT scan. Two cases of deaths (5.2%) related to consciousness disorder due to intracranial complications were noticed in our series. The mean follow-up was 4.6±6.3 (1-26 months).

Discussion

The incidence of MOE in the world is unclear but is still infrequent. Up today, there are only series of less than 80 cases. In Tunisia, the incidence is estimated to be 10 new cases every year (3).

MOE affects patients over 65 years old with a male predominance (2,3). In our series, 73.6% of patients were over 60 years old with a female predominance. The most predisposing factor is diabetes mellitus (90-100%) mainly through microangiopathy, suppressed immune system and hypoperfusion (4). Other immunosuppression situations were noticed, such as HIV, transplant patients, advanced cancer, chemotherapy, etc. In our series, all patients were diabetic. One patient was under chemotherapy. Previous radiotherapy in the head and neck was also mentioned as a predisposing factor. In their study, Bechraoui et al. (3) noticed arterial hypertension associated with diabetes mellitus in 47% of cases. In our series, hypertension was noticed in 60.5% of diabetic patients. Chronic renal deficiency has been reported in 30% of cases by Kumar et al. (5). In our series, 7.8% of our patients presented with chronic renal deficiency.

The most common symptom of MOE is otalgia (100%) which is resistant to usual therapy for more than one month, followed by otorrhea in 60 to 100% of cases. Other clinical presentations include headache, dysphonia and facial palsy related to cranial nerve involvement found in up to 20% of cases, hearing loss and temporo-mandibular joint pain (2). In our series, otalgia was found in 100% and otorrhea in 76%. Facial nerve palsy and dysphonia were noticed in 5.3% and 2.6%, respectively. Otoscopy findings may show stenosis of the EAC, otorrhea, granulation tissue or polyp in the EAC. Clinical presentation may reveal a congestive/painful pinna or facial nerve palsy (2). In our series, there was stenosis of EAC in 100% of cases, granulation tissue and polyp of EAC in 21 and 28.9% of cases, respectively.

Pseudomonas Aeruginosa is the commonest micro-organism isolated (50-90%) followed mainly by fungii (6-8). In other studies, Staphylococcus Aureus occupied second place which goes in line with our study (9). Aspergillus is the main fungal agent reported in the literature (10); however, Candida Albicans was the main fungal pathogen in our series. Nonetheless, diagnosis could be delayed and isolating the responsible organism could sometimes be impossible. Thus, most authors recommend performing biopsies on granulation tissue and bone sequester (11). Besides, Aspergillus serology can be contributive (12).

Predictive factors of delayed diagnosis are prior quinolone antibiotic and the use of quinolone ear drops (3, 13). The invasive behavior of fungal infection has been demonstrated with more facial nerve palsy: 75% with Aspergillus vs 24% with Pseudomonas and more intra-cranial complications (14, 15). Surgical debridement was more required in the fungal infection than the non-fungal one. The hyperbaric treatment was more indicated in fungal infection (14).

It has been demonstrated that CT scan is the most available and effective technique to diagnose MOE (7, 16, 17). It usually shows bone erosion, central nervous system extension, and soft tissue involvement in the parapharyngeal spaces. Therefore, it is the first test to perform when the diagnosis is suspected (7). Magnetic resonance imaging is useful for soft tissue involvement, but less adequate for bone involvement. The role of Tc99m and Galium-67 scan is still debating and may be useful in follow-up and deciding the end point of antibiotic therapy for MOE (18, 19). In our series, CT scan was performed in 27 cases (71%).

MOE can extend to the skull base if diagnosed late and may cause complications. The main common one is

facial nerve involvement noticed in almost 20% of cases. Other intracranial nerve involvement can occur, such as the glossopharyngeal nerve (IX), the vagus nerve (X), the accessory nerve (XI) and rarely the hypoglossal (XII) one. In our series, there were 2 cases (7.4%) of facial palsy and one case of dysphonia (20). MOE may be responsible for osteomyelitis of the skull base, meningitis, venous thrombosis or cerebral abscess (21). In our series, there was one case of internal jugular vein thrombosis and 3 cases of nasopharyngeal abscess confirmed on CT scan.

Regarding the management of MOE, most literature consists of small case series or case reports. When Pseudomonas aeruginosa is suspected to be the responsible agent, a combination of cephalosporins and ciprofloxacin followed by ciprofloxacin monotherapy for 6 weeks: 3 weeks of initial combination therapy (ceftazidime® + ciprofloxacin®, high doses) followed by 3 weeks single therapy with ciprofloxacin, is the first line recommended management. A monotherapy of ciprofloxacin® should be avoided since it may lead to a resistance up to 50% (22). The recommended duration is still unclear. However, the advocated duration for osteomyelitis recovery is estimated from 6 to 8 weeks (23).

The most common fungal organism causing MOE is Aspergillus Fumigatus and Voriconazole is the first treatment option for Aspergillus infections. Amphotericin B and/ or Itraconazole therapies are the other treatment options for fungal MOE (24).

Anti-fungal therapy is associated with antibiotherapy in case of prior prescription of fluoroquinolones (which is a predictive factor of fungal infection) or in case of previous fungal MOE. Anti-fungal therapy is secondly added to antibiotherapy in case of unfavorable evolution under antibiotherapy even if bacterial positive culture has been documented and, in this case, repeated tissue cultures (from granulation) are highly recommended.

Hyperbaric oxygen therapy (HBOT) should be used only as an adjunct to antimicrobial therapy. It may be helpful for patients with complications, experiencing a poor response to therapy, or with recurrent cases (25). HBOT is beneficial; however, efficacy remains unproven and further research is required (26).

Surgical therapy in MOE includes local debridement, removal of bony sequestrum or abscess drainage. There is no indication of facial nerve decompression in patients with facial nerve involvement. Altogether, surgery did not show any prognostic benefits (27).

The poorer prognosis was seen in patients who experienced facial nerve involvement, additional cranial nerve involvement, extensive granulations (or edema) in the EAC, Aspergillus species as the causative organism (28). The recurrence rate of MOE is high and estimated from 15 to 20% (29). In our series, the recurrence rate was 21%. MOE can recur up to one year after treatment. The patient should be followed up regularly for one year before being considered cured. MOE remains a lethal infection. In the last few years, mortality has dropped from a high of 50% in the past to 10% to 20% thanks to early diagnosis stages (30).

Conclusion

MOE is still challenging because of its high morbidity. Pseudomonas Aeruginosa remains the commonest responsible pathogen, nevertheless, fungal infections are rising because of the overuse of antibiotics, particularly, systemic, oral and topical fluoroquinolones. Resistance of Pseudomonas to fluoroquinolones reaches 50%. Sensitivity to cephalosporins seems to be preserved. Combined systemic antibiotherapy including 3rd generation cephalosporins and fluoroquinolones followed by oral fluoroquinolones for 6 to 8 weeks is, up to now, the best way to increase complete remission. Antibiotherapy should be adapted to culture results and resistance profile of pathogens in hospital. Practionners should be aware of the possibility of concomitant fungal infection, especially in the case of unfavorable evolution. Prolonged antibiotherapy can lead to emergent fungal infection. Repeated culture from tissue is highly recommended in case of unfavorable evolution of the disease. A large multicenter study is necessary to establish the microbiological profile of this condition.

List of abbreviations

MOE : Malignant Otitis Externa
ESR : Erythrocyte sedimentation rate
CRP : C-reactive protein
EAC : External auditory canal
IV : Intravenous
HBOT : Hyperbaric oxygen therapy

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