ORIGINAL RESEARCH

Principles in Malignant Otitis Externa

Sergul Ulus[1], Eyup Baz[2], Bulent Evren Erkul[3], Ibrahim Engin Cekin[4]

Abstract

Objective: Malignant otitis externa (MOE) is a serious and recalcitrant disease with its morbidity and mortality. This infection and inflammation can spread easily and attack cranial nerves (CNs) and the skull base, even though it starts with simple otitis externa.

Methods: This retrospective observational study agglomerates 10 MOE cases, including their diagnosis, follow-up, and treatment.

Results: Otalgia that especially increases at night was the most common symptom. Diabetes was present in all patients. Seven cases had associated facial palsy. Half of the patients underwent mastoidectomy. Six patients were cured of MOE.

Conclusion: Management of diabetes is the first step of the treatment. In our study, we could not demonstrate the contribution of mastoidectomy to the outcome. Resolution of cranial neuropathy is associated with good prognostic signs.

Keywords: Malignant otitis externa, Mastoidectomy, Necrotizing otitis externa.

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Introduction

Malignant otitis externa (MOE), also known as necrotizing otitis externa, is a serious and recalcitrant disease with its morbidity and mortality. Meltzer first reported MOE in 1959. He described this disease as lateral temporal bone osteomyelitis of the external auditory canal owing to *Pseudomonas aeruginosa* (*P. aeruginosa*) in a patient with uncontrolled diabetes.[1] Clinicians must be aware of this disease, even in nondiabetic and immunocompetent patients.[2] Sex predilection is more toward males and the elderly age-group above 60 years of age.[3] The symptoms of otitis externa, like ear pain and fullness, are also common in MOE, which can make diagnosis difficult, so this situation may lead to a delay in treatment.

This infection and inflammation can spread easily and attack cranial nerves (CNs) and the skull base, even though it starts with simple otitis externa. Infection from the external ear canal spreads to the skull base through the fissures of Santorini. These are small perforations in the cartilaginous portion of the external auditory canal situated along the floor of the canal.[4] Computed tomography (CT) reveals details on bone destruction, the anatomic site of infection, abscess formation, reduction in skull base density, involvement of bone and soft tissue, detection of infection resolution, and recurrence.[5] *P. aeruginosa* had been known to be the most frequently isolated causative organism; however, with the increase in medical care and antibiotic usage, clinical presentation of pathogens changed.[6] The most effective treatment is to control diabetes and to use the proper antibiotic and debridement necrotic tissue; sometimes, aggressive surgical management is also done.[7] Controversies still exist in the medical and surgical indications and outcomes of mastoidectomy. The purpose of this study was to share our experience with MOE from diagnosis to treatment and identify the role of surgery in this disease.

Methods

This retrospective observational study was conducted in our hospital and agglomerates MOE cases, including their diagnosis, follow-up, and treatment. Ethical clearance was obtained. We gathered data of 10 MOE patients from October 2016 to August 2020. Diagnoses were based on anamnesis, physical examination, CT/MRI, and culture.

[1–4]Department of Otorhinolaryngology, Sultan 2. Abdulhamid Khan Training and Research Hospital, Istanbul, Turkey

Corresponding Author: Sergul Ulus, Department of Otorhinolaryngology, Sultan 2. Abdulhamid Khan Training and Research Hospital, Istanbul, Turkey, e-mail: sergululus@hotmail.com

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Results

During the study period, 10 (eight males and two females) MOE patients were identified. On the first examination, purulent otorrhea and ear canal edema were observed in all patients. Two of them were obstructed by granulation tissue or polyp (cases 3 and 6). Perforation was observed in one tympanic membrane. Three patients had contralateral involvement (cases 1, 7, and 9). A total of 13 sides of ten patients were added to the study. The average age was 72 ± 10.6 years at the time of diagnosis (median: 75.5, min: 50, max: 85 years) (Table 1). Prolonged otalgia and ear discharge were the common symptoms at presentation. It was remarkable that otalgia was severe and often seen at night. Otoscopic examination revealed edema and hyperemia in the external ear canal in all patients. All of them had a preexisting indication of diabetes mellitus. Hemoglobin A1c levels were recorded in 6 of the 10 diabetic patients (Table 1). All the patients underwent high-resolution computed tomography (HRCT) of the temporal bone on admission. If someone's prognostic factors deteriorated during hospitalization, magnetic resonance imaging (MRI) was performed (Table 1). The criteria were: no improvement in the otoscopic examination, pain increase, increase in the erythrocyte sedimentation rate (ESR), prolonged length of stay, and deterioration in general condition. MRI helped us to show extralateral temporal bone involvement. We performed a

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Table 1: Patient demographics, hemoglobin A1c levels, application of MRI, and scintigraphy (F, female; M, male)

Case number	*Age*	*Gender*	*HgbA1c level*	*MRI*	*Tc99m*
1	75	M		+	+
2	76	F		–	–
3	67	M		+	–
4	83	M		–	–
5	61	M	6.9	–	–
6	85	M	8.7	+	+
7	68	F	11.6	+	–
8	76	M	7.8	+	–
9	79	M	6.2	+	–
10	50	M	7.1	–	–

technetium-99m bone scan in just two patients (cases 1 and 6). We did not make use of scintigraphy as a diagnostic criterion.

Before topical or systemic antibiotic therapy was started, ear secretions were cultured. We sampled swabs from the external ear canal, and some of the samples were taken as a tissue culture intraoperatively. Some swabs were obtained multiple times. Culture and resistance results were noted (Table 2). One patient did not have an external auditory canal culture (case 8). One patient did not have a contralateral external auditory canal culture (case 1). Therefore, 11 sides of nine patients had external auditory canal culture and five of them were culture negative. Two of six culture-positive sides were positive for *P. aeruginosa* (cases 3 and 6). Three of them were positive for fungal microorganisms (cases 1, 3, and 7). Culture samples were taken from four of five patients intraoperatively. Only one of these patients had a positive microbiologic sample (case 7).

Topical ear treatment with ciprofloxacin was applied to all regularly. All of them were referred to an endocrinologist to have their diabetes medication and insulin therapy reassessed. Four of the cured patients (cases 2, 5, 8, and 10), including one with facial palsy (case 2), just received intravenous (IV) ciprofloxacin. Cases 2 and 5 received IV ciprofloxacin 200 mg twice a day and cases 8 and 10 received IV ciprofloxacin 400 mg twice a day. Treatment lasted between 1 and 3 weeks. Case 8 had no culture, and the other cultures were negative. Case 4 was treated with oral ciprofloxacin 500 mg and piperacillin/tazobactam 4/5 g for 4 weeks. His culture was also negative. They were all discharged with the medication of oral ciprofloxacin. Weekly follow-up was planned with examination and ESR. According to the result of culture, the treatment was reorganized. Voriconazole was preferred as an antifungal by the infectious disease specialist if needed. Cases 1, 3, 6, 7, and 9 were treated with broad-spectrum antibiotics, including antifungal drugs. The preferred antifungal was voriconazole except in case 9. Case 9 was treated with fluconazole. Cases 6 and 9 received antifungal therapy despite being culture negative for fungal microorganisms. Their treatment lasted at least 6 weeks. Only case 7 recovered.

We noted their ESR frequently. During the follow-up, we measured minimum ESR as 5 mm/hour and maximum as 127 mm/hour. Details of results are shown in Table 3. Except for patients with a rapid response to treatment, the patients received hyperbaric oxygen therapy (HBOT), if there was no contraindication. HBOT was administered for nine sides of six patients. Three patients with contralateral involvement received HBOT for both sides. Treatments were administered daily for a 20-day period. In case the length of stay was prolonged, another 20-day treatment was given.

The House–Brackmann facial nerve grading system was used to describe the degree of facial paralysis. Seven patients developed facial nerve palsy, and one of them was together with contralateral abducens nerve palsy (case 1). One patient presented with 7th, 10th, and 12th cranial nerve palsy (case 3). Five patients demonstrated extralateral temporal bone involvement (Table 3). This description includes nasopharynx, parapharyngeal area, parotid space, and petrous apex. Six sides of five patients underwent surgery. Five sides of four patients underwent canal wall down (CWD) mastoidectomy and one patient underwent canal wall up (CWU) mastoidectomy (case 4). One patient underwent CWD mastoidectomy bilaterally (case 9) (Table 3). Three operated patients died (cases 1, 3, and 9), and two patients cured (cases 4 and 7).

The follow-up time of the patients ranged from 6 to 46 months (median: 15 months). Six patients were cured of MOE. Totally, four patients died because of direct and indirect results of the disease. One case diagnosed with lung cancer died of it (case 1). The patients' outcomes are summarized in Table 3.

Two cases are summarized to illustrate the efficiency of surgery.

Selected Case Presentations

Case 4

An 83-year-old man was referred to our clinic with left ear pain for 1 month. He was diabetic and had hypertension. Otoscopic examination revealed purulent discharge from the external auditory canal. Cultures were taken from the canal. HRCT was performed. On HRCT, there was fluid level in the middle ear and the mastoid air cells; these were reported as otomastoiditis. The ossicular chain was intact, and bony erosions were rare on the left side (Fig. 1).

The treatment started with oral ciprofloxacin. HBOT was started to be applied. One week later, ESR gradually increased, and grade II (according to the House–Brackmann grading system) facial palsy was observed. Therefore, mastoidectomy was planned. In the surgery, we observed that the tympanum and mastoid bone were normal but full of clear yellow non-purulent liquid. Cultures were taken from the cavity. CWU mastoidectomy was performed, and a grommet tube was inserted in the tympanic membrane to provide drainage. Culture results were reported as "no growth." Because of an increase in ESR and nocturnal ear pain, an infectious disease consultant recommended continuing antibiotic therapy with intravenous piperacillin–tazobactam and oral ciprofloxacin. Four weeks later, oral ciprofloxacin was prescribed at discharge. During the 6 months follow-up period, symptoms improved and facial palsy also completely recovered.

Case 7

A 68-year-old woman with poorly controlled diabetes mellitus, hyperlipidemia, chronic heart failure, and hypertension was referred to our clinic with right ear pain for 4 months and facial weakness for 3 weeks. Grade V facial palsy on the right side was observed. Otoscopic examination revealed diffuse edema and purulent discharge. The patient's diet and medications for diabetes were reassessed. Cultures were taken and HRCT was performed. Cultures from the right ear canal grew non-*albicans* yeast and *Staphylococcus epidermidis*. IV ceftazidime and oral levofloxacin treatment was initiated. On HRCT, there was soft tissue in the epitympanum, Prussak's space, and mastoid area (Fig. 2). HBOT was started. The patient underwent contrast-enhanced temporal MRI, which

Table 2: Culture and resistance results for MOE patients on admission

		External auditory canal				
Case		*1. Swab*	*2. Swab*	*3. Swab*	*4. Swab*	*Intraoperative*
1	Culture (right)	*Staphylococcus hominis*, *Candida parapsilosis*	*Staphylococcus aureus*	*Escherichia coli*		No sample
	Resistance		Penicillin G	Ciprofloxacin, levofloxacin piperacillin/tazobactam, piperacillin, trimethoprim/ sulfamethoxazole		
2	Culture	No growth				
3	Culture	*Staphylococcus haemolyticus*, *Candida albicans*	*Pseudomonas aeruginosa*	*Candida albicans*		No growth
	Resistance	Amphotericin B (for *Candida*)	Levofloxacin ciprofloxacin			
4		No growth	No growth			No growth
5		No growth				
6	Culture	*P. aeruginosa*	*P. aeruginosa*	*P. aeruginosa*	*P. aeruginosa*	
	Resistance	Gentamicin, ciprofloxacin	Gentamicin, piperacillin/ tazobactam vs ciprofloxacin	Gentamicin, piperacillin/ tazobactam, cefepime, ceftazidime vs ciprofloxacin	Gentamicin, ciprofloxacin	
7	Culture (right)	Non-*albicans* yeast	*Staphylococcus epidermis*			*Candida albicans*, *Escherichia coli*
	Resistance					Levofloxacin, netilmicin, piperacillin, cefepime, ceftazidime, ciprofloxacin tobramycin, trimethoprim/sulfamethoxazole, aztreonam (for *E. coli*)
	Culture (left)	No growth				
8	Culture	No sample				
9	Culture (left)	*Klebsiella pneumoniae*				No sample
	Resistance (left)	Amoxicillin clavulanic acid, ampicillin, nitrofurantoin, piperacillin/tazobactam, cefixime, ceftazidime, ceftriaxone, cefuroxime, cefuroxime axetil, ciprofloxacin, trimethoprim/ sulfamethoxazole				
	Culture (right)	*K. pneumoniae*	No growth	No growth		No growth
	Resistance (right)	Amoxicillin clavulanic acid, ampicillin, piperacillin/tazobactam, cefazolin, cefepime, ceftazidime, ceftriaxone, cefuroxime, cefuroxime axetil, ciprofloxacin, trimethoprim/ sulfamethoxazole, tigecycline				
10		No growth				

Table 3: Summary of outcomes and complications (INV, involvement; EX, exitus; CWD, canal wall down; CWU, canal wall up; HBOT, hyperbaric oxygen therapy treatment)

Case	*ESR range (max–min)*	*Cranial nerve (CN) inv. (nerve/grade)*	*Extralateral temporal bone inv.*	*Skull base inv.*	*Contralateral spread*	*HBOT*	*Operation (mastoidectomy)*	*Follow-up time (months)*	*Outcome*
1	81–5	7CN/Grade III		+	+	+	CWD		
Contralateral		6CN	+	–		+		24	Ex
2	67–31	7CN/Grade VI	–	–	–	–	–	46	Cured; palsy resolved
3	98–26	7CN/Grade IV —10CN—12CN	+	–	–	+	CWD	12	Ex
4	127–77	7CN/Grade II	–	–	–	+	CWU	8	Cured; palsy resolved
5	115–57	–	–	–	–	–	–	18	Cured
6	126–34	7CN/Grade IV	+	–	–	–	–	8	Ex
7	95–51	7CN/Grade V	–	–	+	+	CWD		
Contralateral	119–41	–	+	+		+	–	36	Cured; palsy resolved
8	74–24	–	–	–	–	+	–	42	Cured
9	119–40	7CN/Grade III	+	–	+	+	CWD		
Contralateral		–	–	–		+	CWD	6	Ex
10	83–33	–	–	–	–	–	–	6	Cured

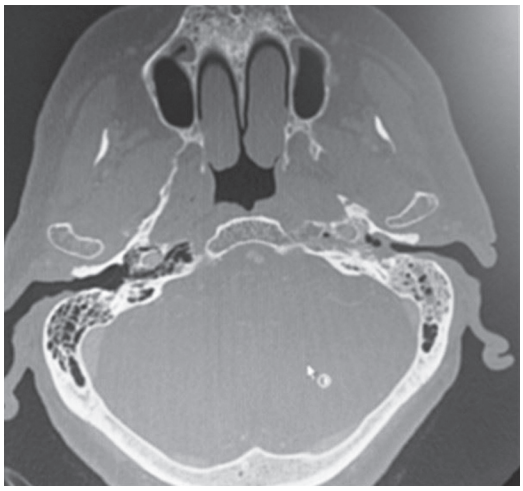

Fig. 1: HRCT axial image of the left temporal bone shows otomastoiditis findings

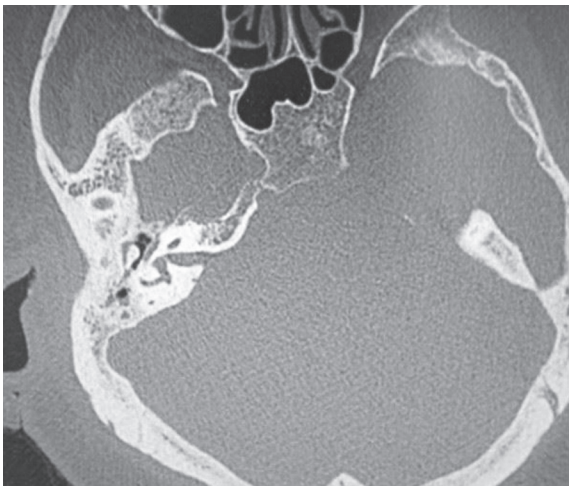

Fig. 2: Axial image of the temporal bone shows right soft tissue in epitympanum and mastoid cells

demonstrated abnormal infiltration of the lateral temporal region. Canal wall down mastoidectomy was performed. As the tomography report mentioned, epitympanum and mastoid cells were partially filled with soft tissue. Tissue culture was taken from the mastoid cells and grew levofloxacin, netilmicin, piperacillin, cefepime, ceftazidime, ciprofloxacin, tobramycin, trimethoprim/sulfamethoxazole, aztreonam-resistant *Escherichia coli*, and *Candida albicans*. The patient was discharged with a prescription of voriconazole and amoxicillin–clavulanate. During the follow-up period, the maximum and minimum ESR results were noted as 95–51 mm/hour. The patent's facial palsy resolved in 6 months.

About 1 year later, the patient was admitted to our clinic with left ear pain and discharged after 1 month. Facial palsy was not observed on both sides. High-resolution computed tomography and MRI were performed. Magnetic resonance imaging demonstrated extensive involvement, including prevertebral and parapharyngeal muscles, posterior side of the left mandibular corpus, and skull base. Culture from the left ear canal was reported as "no growth." Oral voriconazole, IV ciprofloxacin, and IV ceftazidime treatment initiated together with HBOT. During this length of stay period, the maximum and minimum ESR results were 119–41 mm/hour. The patient recovered without surgery, and after the recovery, no recurrence was reported during the 18 months of follow-up period.

Discussion

Malignant otitis externa is a potentially lethal infection of the lateral temporal bone. As in our study, the most common symptom of MOE is earache, and ear discharge follows it.[8]

Many people have trouble controlling their diabetes. Gaining control of diabetes should be considered the first line of treatment.[7] Driss et al. suggested the patients not to leave the hospital without control of his/her diabetes if possible.[9]

High-resolution computed tomography is the initial imaging of choice because it is more accurate in pointing out bony involvement. Also, it is economical. Magnetic resonance imaging is effective in identifying soft tissue involvement and delineating the intracranial extension. The technetium-99m MDP radiotracer concentrates in areas with osteoblastic activity, as found in infection, trauma, and neoplasm. Gallium Ga (Ga 67) citrate concentrates in regions of active inflammation due to attaching to lactoferrin, which is present in large amounts in leukocytes, and through binding to transferrin and bacteria directly.[10] Scintigraphy with technetium-99m bone scanning and gallium (Ga 67) scanning are used to emphasize an infection focus and determine the presence of osteomyelitis.[5] Osteomyelitis of the temporal bone is not always related to MOE.[2] In our study, we did not use scintigraphy if we did not need to confirm the diagnosis. In one of our patients not included in the study who was subsequently diagnosed with keratosis obturans, bone involvement was detected in technetium-99m scintigraphy. Karaman et al. in their study requested scintigraphy (technetium 99 and gallium 67) in patients with facial nerve palsy.[7] Soheilipour et al. diagnosed MOE patients without gallium and technetium scintigraphy because they did not have devices in their area.[5] Computed tomography is a fast and economical tool for confirming the diagnosis of MOE but has limited value in predicting outcomes.[11] Both gallium and technetium-99m MDP scans show poor anatomic resolution but are complementary in the diagnosis of MOE.[4]

As we mentioned in the presentation of case 4, temporal bone HRCT revealed fluid in the tympanic and mastoid space. The bony structures of the mastoid air cells and the ossicular chain were intact. This made us think that this is the early stage of this disease. Some of the patients' HRCT reports demonstrated soft tissue lesions filling mastoid air cells and sometimes with bony destruction. This image seemed like an advanced stage of the disease compared to case 4. When the collection is in fluid form, ventilation tube insertion can be considered to provide drainage and apply topical treatment. In the study of Kaya et al., the Shepard ventilation tube was used in four patients.[12]

Standard medical treatment was started with ciprofloxacin as a monotherapy. In case of poor response, broad-spectrum antibiotics, including piperacillin, imipenem, ceftazidime, and gentamicin, were added. The use of antibiotics was recommended according to the microbiological culture if any. If the first result of cultures is negative, repeat cultures are necessary, but withholding therapy until cultures are positive is not recommended.[4] Drugs other than ciprofloxacin were used in case of suboptimal clinical response and different culture results.[13] While we were preferring antibiotics, we considered patients' liver and renal pathologies. Voriconazole is an excellent alternative modality treatment in patients with MOE.[14]

According to our experience, an increase in bacterial resistance leads to poor treatment outcomes, and culture-negative results lead to better treatment outcomes.

Erythrocyte sedimentation rate is always elevated and considered as a nonspecific inflammatory marker for diagnosis and recovery of disease.[15] We realized that a high ESR does not mean poor prognostic factors. However, the increase and decrease in ESR are co-related with the severity of patients' symptoms and signs. This shows that ESR can be used in follow-up.

Previously, MOE patients underwent extensive surgery because it was believed that "an extensive surgery with removal of all infected tissues is necessary to cure".[16] Today, the role of surgery changed. In our study, we could not demonstrate the contribution of mastoidectomy to the outcome. Rhinosinusitis is one of the diseases that cause osteomyelitis. For instance, we see osteomyelitis on single photon emission computed tomography (SPECT) in the form of complicated acute rhinosinusitis and in the particular group of chronic rhinosinusitis,[17] and we use long-term antibiotics to eradicate the disease, not extensive resection of the sinus wall. In MOE patients, surgery currently plays a limited role only, restricted to cases that develop bony sequestra or abscesses.[18] Obtaining biopsy samples for histopathological examination and culturing, and drainage of abscesses are some indications for surgery.

Hatch et al. indicated in their study that mastoidectomy was the most commonly performed procedure in MOE.[19] According to this study, patients undergoing surgery had a significantly longer length of stay when compared to those that did not have surgery. But they could not demonstrate a significant difference in mortality. As in our study, the most likely explanation for the increased length of stay in this population is that patients requiring surgery may have more severe diseases requiring longer hospitalizations. Hatch et al. also reported that surgery in MOE may be considered to obtain adequate cultures. In our study, culture sampling was performed in four patients during surgery, and just one patient's culture obtained from the tympanic or mastoid cavity grew. In the study of Karaman et al.,[7] four patients presented with facial nerve palsy: two patients were grade II, and one each was grades IV and V according to the House–Brackmann facial grading system. After treatment with antibiotics, HBOT, and facial nerve decompression, the grade II cases showed good improvement, the grade IV case regressed until grade II, and the grade V case did not improve. However, in our study, no facial decompression was applied to any of the patients. Four of the seven MOE patients with facial paralysis died. Three of the patients were cured without decompression surgery. As a result, there is no indication for facial nerve decompression in patients with facial nerve involvement.

According to Amaro et al., HBOT was a candidate to be a helpful adjuvant treatment in MOE and should be considered for patients who are not benefitting from treatment and in severe cases.[20] Phillips et al. could not demonstrate any efficacy of HBOT.[21] Hyperbaric oxygen therapy was administered to nine sides of six refractory cases in our study. These numbers are insufficient to compare its efficacy.

According to Carlton et al., cranial neuropathies in MOE were a grave prognostic sign.[18] While Franco-Vidal et al.[22] were emphasizing that facial palsy points out to poor prognosis and needs for a longer course of treatment before recovery, Mani et al. indicated that cranial nerve palsy in itself is not a poor prognostic factor.[23] Our study demonstrated that resolution of the facial nerve palsy was associated with good prognostic signs.

In conclusion, MOE starts with simple external otitis; therefore, physicians must be aware of this possibility that early diagnosis and treatment lead to better results. Computed tomography and MRI scans have proven valuable in the diagnosis of MOE, and scintigraphy is complementary in the diagnosis. In MOE patients, surgery plays a limited role only.

Orcid

Sergul Ulus https://orcid.org/0000-0002-3232-8225
Eyup Baz https://orcid.org/0000-0002-4088-9735
Bulent Evren Erkul https://orcid.org/0000-0002-0360-1309
Ibrahim Engin Cekin https://orcid.org/0000-0002-9582-0743

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