

# Optimised diagnosis and treatment of necrotizing external otitis is warranted

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## ABSTRACT

**INTRODUCTION:** Necrotizing external otitis (NEO) is a devastating and life-threatening infection in the external auditory canal and the temporal bone. The aim of this paper is to evaluate the diagnostics and treatment of NEO and to recommend new guidelines.

**MATERIAL AND METHODS:** Eleven patients were retrospectively enrolled under the code DH609 otitis externa without specification from 1 January 2000 to 31 December 2009. Records were reviewed to register: age, symptoms, clinical findings, co-morbidity, imaging, microbiology and treatment.

**RESULTS:** The median age was 75 years and the median time of therapy at the hospital was 6.3 months. All patients belonged to a risk group. A diagnostic delay was found resulting in further progression of the disease. In contrast to current international recommendations, the treatment consisted mostly of local antibiotics in combination with surgery. All patients survived, but most patients were left with hearing loss and psychiatric problems.

**CONCLUSION:** A greater awareness of diagnostic criteria and a shift from local antibiotics to prolonged systemic monotherapy with ciprofloxacin in accordance with international concepts is recommended. Surgery should be left for extensive and refractory cases only. A list of diagnostic criteria and treatment guidelines is presented.

**FUNDING:** not relevant

**TRIAL REGISTRATION:** not relevant

Necrotizing external otitis (NEO), previously referred to as malignant external otitis, is a rare, devastating and potentially life-threatening disease of the external auditory canal (EAC) and the temporal bone [1]. NEO appears initially as a simple external otitis, but demonstrates irresponsiveness to topical treatment within one to two weeks.

The disease is typically localized to the bony-cartilaginous junction in the EAC with granulations and necrosis in the adjacent tissue. It successively causes mastoiditis, chondritis and osteomyelitis and eventually intracranial involvement including cranial nerve paralysis. Its pathophysiology is not completely understood, but NEO often affects immune-compromised persons, especially diabetics [2-5]. In the majority of cases, the

causative aetiological organism is *Pseudomonas aeruginosa* [6-10].

Due to the rarity of the disease, evidence-based criteria with regard to diagnostic procedures and treatment schedules are unavailable. According to international literature, no single criterion defines NEO and the diagnosis is based on clinical presentation, laboratory data and microbiology and imaging [1-13].

Necrotizing external otitis is associated with a relatively high risk of treatment failure and mortality rates reaching 50% have been reported. After the introduction of the quinolones, mortality has dropped to approximately 10%. However, co-morbidity may have influenced this outcome [14].

At present, there seems to be consensus on monotherapy with ciprofloxacin for a minimum of 6-8 weeks and surgery is reserved for local debridement and exclusion of malignancy [13-16]. A long follow-up period of several months with repeated imaging and erythrocyte sedimentation rates is also recommended.

Thus, the aim of the present study is to evaluate the management of NEO in a Danish ear-nose-and-throat department and to suggest revisions of existing guidelines.

## MATERIAL AND METHODS

The Patient Administration System (Det Grønne System) was searched for the International Classification of Diseases (ICD)-10 code DH609 "otitis externa without specification" from January 2001 to December 2009 at the Ear-Nose-and-Throat Department, Aarhus University Hospital, Denmark. Cases exclusively treated as out-clinic patients and responding to topic therapy in less than two weeks and patients with incorrect diagnostic codes were excluded. The remaining 11 patients had month-long courses with a minimum of one week of hospitalization and NEO was suspected in all cases. Their medical records were reviewed and the following data registered: age, symptoms, clinical findings, co-morbidity, image studies, microbiology and treatment.

According to the departmental guidelines, a computed tomography (CT) of the temporal bone is carried out on suspicion of NEO and in case of bone destruction, the patient is hospitalized for intravenous treatment

## ORIGINAL ARTICLE

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Dan Med Bul 2011;58(7):A4292

with amoxicillin and gentamicin and a ciprofloxacin gauche in the ear canal. Surgical debridement and mastoidectomy are also recommended.

The database pubmed.gov was searched for previous studies using medical subject headings (MeSH) combining the following terms: necrotizing external otitis, malignant external otitis, skull base osteomyelitis, gallium 67 ( $^{67}\text{Ga}$ ), technetium 99 ( $^{99}\text{Tc}$ ), erythrocyte sedimentation rate, computer tomography, MRI, ciprofloxacin and *P. aeruginosa*.

*Trial registration:* not relevant.

## RESULTS


The characteristics of the 11 patients are listed in **Table 1**. Their median age was 75 years, 64% were men and all patients belonged to a risk group previously identified in the literature. Nine (82%) of the patients were admitted after having been treated for several weeks by a practising ear-nose-throat (ENT) specialist. Pre-hospital treatment included a variety of systemic as well as topic antibiotics and aural toilet, but all had proven inefficient.

On admission the patients were in pain, had puru-

lent discharge and swelling, redness and granulation tissue in the ear canal (**Figure 1**). In one case, the patient was initially hospitalized with meningitis due to *Pseudomonas*. C-reactive protein (CRP) and white blood cell counts were usually normal. Characteristically, the pathology was located to the bony-cartilaginous junction in the bottom of the ear canal. Granulation tissue was the only single factor found in all cases. *P. aeruginosa* was the most commonly isolated pathogen and was found in the diabetic patients. All had a CT which demonstrated destruction of bone and/or cartilage in nine patients.

No systematic procedures and follow-up regimens were executed with regard to collection of specimen for microbiology, biopsy and choice of imaging modality. Accordingly, no systematic treatment strategy was followed. However, debridement of the external ear canal including a biopsy was performed in all cases. More extensive surgical procedures with mastoidectomy were carried out in nine patients. *Pseudomonas*-positive infections were treated with various intervention combinations: topically (gauge or ear drops) with ciprofloxacin with or without steroids; dexamethasone-framycetin-gramicidin; hydrocortisone-terramycin-polymyxin B; and rinsing with acetic acid. Orally, ciprofloxacin was used and intravenously either ciprofloxacin (between 400 mg  $\times$  2 and 750 mg  $\times$  2), tazocin (between 2 g  $\times$  2 and 4 g  $\times$  2), gentamicin (240 mg), nebcina (120 mg  $\times$  2) or imacillin (4 g  $\times$  4) were used. Gentamicin was withdrawn early in the process in several cases due to adverse effects such as increasing serum creatinine concentrations.

The individual patients had largely the same treatment regimen during the first three weeks. Thereafter, management became quite inconsistent and unsystematic with frequent changes of antibiotics. The median duration of the course was six months (1-15 months) (Table 1). Patients having a protracted course of more than one year generally received more divergent and inconsistent treatment than patients with shorter courses. The patients were re-hospitalized several times, but were promptly discharged upon relief – usually after a couple of days and in more cases without antibiotics. One patient was treated for 12 months with several acute admissions, numerous outpatient controls and divergent antibiotic treatments. The patient was cured and treatment completed only after seven weeks of treatment with ciprofloxacin 750 mg  $\times$  2 daily. At that time the patient had undergone surgery several times and had acquired a hearing loss. Another patient with NEO and meningitis relapsed with meningitis after finishing only two weeks on antibiotics. All the patients survived. Seven patients developed permanent sensorineural hearing loss during the course and one became deaf on the affected ear. Unfortunately, audi-

 **TABLE 1**

The demographic and clinical characteristics of the 11 patients with necrotizing external otitis at the Aarhus University Hospital.

	Patients, n (%) (N = 11)	Median (range)
Age, years	–	75 (30-88)
Men	7 (64)	
Women	4 (36)	
Side	5 sin, 3 dxt, 3 bilateral	
Diabetes mellitus	6 (55)	
Other co-morbidity	9 (82)	
<i>Clinical findings</i>		
Exudation from the ear	9 (82)	
Facial paralysis	5 (46)	
Bone/cartilage sequestrum	2 (18)	
Granulation tissue	11 (100)	
<i>Microbiology</i>		
<i>Pseudomonas aeruginosa</i>	7 (64)	
<i>Streptococcus faecalis</i>	1 (9)	
<i>Staphylococcus aureus</i>	2 (18)	
Fungus	2 (18)	
Enterobacteria	1 (9)	
Unknown	1 (9)	
<i>Computed tomography findings</i>		
Bone/cartilage destruction	9 (82)	
<i>Surgical treatment</i>		
Mastoidectomy	7 (64)	
Exploration of the middle ear	2 (18)	
Duration until cure, months	–	6.3 (1 -15)

Dxt = dexter; Sin = sinister.


**FIGURE 1**

Necrotizing external otitis. Notice the typical granulation tissue in the floor of the ear canal.



ometries before NEO were not available. Two patients without prior psychiatric problems developed serious depressive symptoms demanding anti-depressive medication.

## DISCUSSION

The present study has indicated several problems with the management of NEO both according to the local guidelines and in comparison with the current international recommendations. These problems meant that diagnosis was delayed and disease courses protracted and characterized by involvement of several doctors, unsystematic use of diagnostic procedures and inconsequent treatment and follow-up regimens.

As in all other centres, NEO is a rare disease, but early suspicion and subsequent referral is of utmost importance for its course and prognosis.

In order to further explain the outcome and to adjust the guidelines, it seems relevant to focus on three main issues: the definition of NEO, diagnosis and treatment strategy.

A review of the literature reveals some obligatory and supplementary criteria for the definition of the disease (**Table 2**). Suspicion should be raised if a patient who is initially diagnosed as a case of simple external otitis does not respond to relevant therapy within two to three weeks (aural toilet, topic ear drops in accordance with the microbiological results). The mere finding of granulation tissue/abscesses at the bony-cartilaginous junction in the ear canal strongly indicates the diag-

nosis in those conditions where malignancy has been excluded by biopsy. Furthermore, external otitis in patients fulfilling one or more of the supplementary criteria is an early red flag.

Thus, NEO is mainly a clinical diagnosis [14, 16-18]. Additional diagnostic tools have been introduced with the purpose of evaluating the extension of the disease and to follow the effects of its treatment. As far as imaging modalities are concerned, abnormal CT scans demonstrating bone destruction should only be regarded as a supplementary diagnostic tool. On the other hand, MRI, bone scans and gallium scans would be useful in the diagnostic evaluation and monitoring of the disease and treatment response [7, 8, 11-12, 17-18]. Magnetic resonance imaging is superior to CT with respect to demonstrating involvement of soft tissue such as intracranial structures and bone marrow [18]. Bone scan using  $^{99m}\text{Tc}$  methylene diphosphonate is extremely sensitive as it is capable of detecting a 10% increment of the osteoclast activity and it is thus instrumental in early diagnosis of NEO [7].  $^{67}\text{Ga}$  scintigraphy detects dividing cells such as activated granulocytes and osteoclasts [8]. It is used for early diagnosis as well as for treatment monitoring. However, both the bone scans and the  $^{67}\text{Ga}$  scintigraphy are impeded by a relatively poor resolution and need to be combined with CT or MRI.

From a serological point of view, CRP plays a minor role in relation to NEO. As in the present study, the reported CRP values are often within the normal range. Despite the fact that most patients suffering from NEO have elevated erythrocyte sedimentation rates (ESR) due to their co-morbidity, fluctuations in the ESR values are considered useful in monitoring the treatment response [7, 14, 15, 17].

Treatment of the patients in the present study was characterised by a preference for topical rather


**TABLE 2**

Diagnostic criteria for necrotizing external otitis.

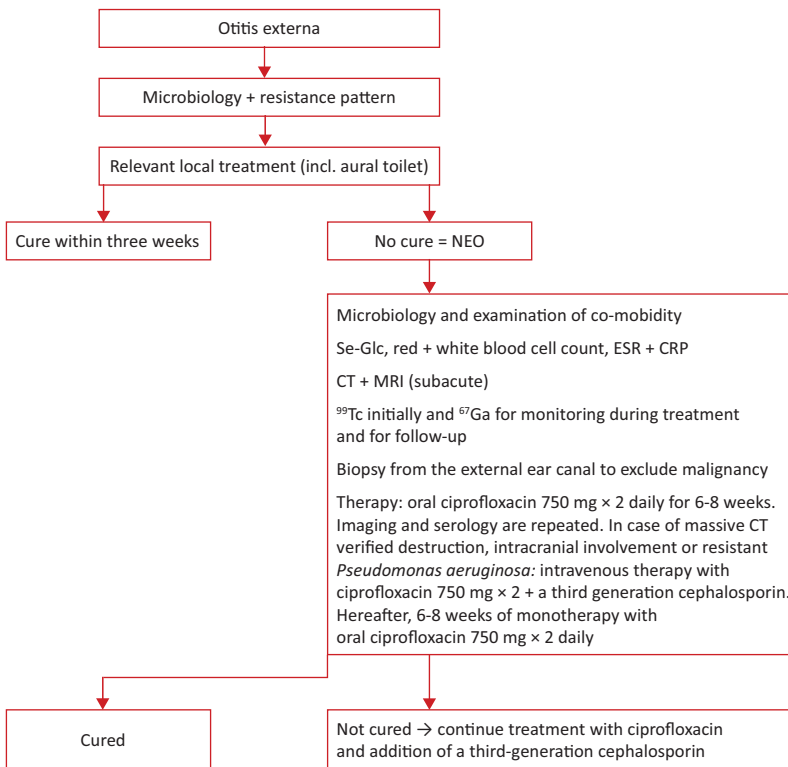
### Obligatory criteria

1. Signs of external otitis not responding to adequate treatment for 2-3 weeks
2. Granulation tissue eventually also micro abscesses localized to the bony-cartilaginous junction
3. Absence of carcinoma

### Supplementary criteria

1. Severe otalgia
2. *Pseudomonas aeruginosa*
3. Diabetes mellitus and other immunocompromising diseases
4. Age > 65 years
5. Abnormal computed tomography
6. Facial paralysis or another cranial nerve paralysis
7. Raised erythrocyte sedimentation rate

Guidelines for necrotizing external otitis depicted in accordance with international standards.



<sup>67</sup>Ga = gallium 67; <sup>99</sup>Tc = technetium 99; CRP = C-reactive protein; CT = computed tomography; ESR = erythrocyte sedimentation rate; MRI = magnetic resonance imaging; NEO = necrotizing external otitis; Se-Glc = serum glucosyl.

than systemic antibiotics, use of sub-therapeutic and short-term systemic treatment and a high frequency of surgery.

Previous studies on the treatment of NEO have mainly been retrospective and due to the rarity of the disease, rather few patients have been included [3-6, 9, 13]. Thus, depending on the size of the treatment centre's catchment area, the annual incidence in most centres is 1-3 patients, i.e. similar to our findings. Before the introduction of the quinolones, a combination of aminoglycosides and  $\beta$  lactam antibiotics was preferred [6, 7, 10, 16]. However, in contrast to the quinolones, these drugs are administered intravenously and associated with relatively many adverse effects [7, 9, 10, 16]. Furthermore, the quinolones provide high bioavailability in bone and cartilage [4, 13]. As a consequence, most authors advocate oral ciprofloxacin 750 mg twice daily as the drug of choice in patients with *P. aeruginosa*-positive cultures and in culture-negative cases [3, 4, 7, 9, 10, 13-16]. In general, long-term treatment (at least 6-8 weeks) is recommended due to the presence of osteomyelitis [3, 4, 7, 9, 13-16].

In complicated cases such as widespread disease (i.e. intracranial involvement and affection of cranial nerves), *P. aeruginosa* resistant to ciprofloxacin or refractory cases, a third generation of cephalosporin or an aminoglycoside in combination with ciprofloxacin is suggested [3, 4-6, 10]. Finally, treatment with antibiotics should be adjusted according to the isolated micro-organisms and consulting a microbiologist is recommended.

Local antibiotics play no role in the treatment of NEO internationally. Their use only causes problems in isolating the pathogenic micro-organisms by altering the microbiological flora [7, 10, 14, 17]. Furthermore, secondary fungal infection may emerge due to additional steroid in the chosen ear drops.

Another deviation from international practise observed in the Danish case material was the high frequency of surgical intervention. Surgery seems to play only a minor role internationally and should comprise diagnostic biopsy and removal of necrotic tissue in the external ear canal [3, 10, 15].

Guidelines in accordance with the issues discussed above are suggested in **Figure 2**.

In conclusion, the present review of 11 patients suffering from necrotizing external otitis (NEO) at the ENT department, Aarhus University Hospital, has demonstrated that the diagnosis was associated with an inexpedient delay, inappropriate use of diagnostic tools and inconsistent treatment. Based on international literature, up-dated diagnostic criteria and guidelines are presented to ensure the quality and effectiveness in the management of NEO.

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**ACCEPTED:** 15 April 2011

**CONFLICTS OF INTEREST:** none

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