Otolaryngology online journal

ISSN: 2250-0359 **Case Report** Volume 9 Issue 1: 183 2019

The Role of Hyperbaric Oxygen Therapy in Necrotizing Otitis Externa: 8 Case Reports Review

Borges-Costa Joana[1*], Abreu Pereira Diogo[1], Duarte Delfim[1], Viana Miguel[1], Fernandes Tiago[2]

[1]Department of Otorhinolaryngology, Pedro Hispano Hospital, Portugal
[2]Department of Hyperbaric Medicine, Pedro Hispano Hospital, Portugal

[*]**Corresponding author:** Borges-Costa Joana, Department of Otorhinolaryngology, Pedro Hispano Hospital, Portugal, Tel: +351913582058; E-mail: costa.jrb@gmail.com

Received date: December 21, 2018; **Accepted date:** January 11, 2019; **Published date:** January 18, 2019

Abstract

Introduction: Malignant or necrotizing otitis externa (NOE) is an invasive infection of the external ear canal that primarily affects elderly diabetic or immunocompromised patients. The role of hyperbaric oxygen therapy (HBO) in NOE management is not well established but some authors believe that HBO is a valuable and beneficial treatment method and recommend its use in NOE for refractory skull base osteomyelitis and intracranial involvement. This study's aim was to present our NOE's management experience, describing 8 case reports and correlating the clinical outcomes with HBO treatment.

Methods: This observational study is about NOE's patients treated with HBO in Pedro Hispano Hospital during the last 10 years (2007-2016). All patients' records were reviewed.

Results: During the studied period, 8 patients with NOE diagnosis were admitted to our hospital for investigation and HBO-treatment. Local and systemic antibiotic treatment and HBO treatment was proposed for all patients and, although only 5 patients have completed the HBO-40 sessions, we were able to control the disease in most of them.

Conclusion: There is an apparent beneficial effect of HBO on complicated and refractory NOE cases. It's gradually gaining acceptance as a useful adjunctive therapy and, considering NOE as a potentially fatal disease, the current recommendations state that HBO should be used whenever a therapeutic pressure chamber is available.

Keywords:

Malignant; Therapy; Otitis; Diabetic patients

Introduction

Necrotizing or malignant otitis externa (NOE) is a rare and invasive osteomyelitis that originates in the external acoustic canal (EAC) and can extend to the surrounding tissues through the fissures of Santorini and the bony-cartilaginous junction, involving the temporal bone, skull base and cranial nerves. This is an aggressive and life-threatening infection that usually affects immunocompromised individuals. Any immunosuppression condition may predispose a patient to NOE but diabetes mellitus (DM) remains the most important associated condition, with a 90%-100% prevalence in NOE patients. Diabetic patients are particularly vulnerable to NOE because the microangiopathy caused by DM coupled with the bacteria's capacity of invade blood vessels leads to multiple vasculitis phenomena, thrombosis and tissue necrosis;7 diabetic patients usually have depressed immunity and the higher pH of diabetic patients' cerumen may be a contributing factor [1-10].

Although the most frequent causative agent of NOE is Pseudomonas aeruginosa other bacteria have also been reported in NOE, as *Staphylococcus*

aureus or *Proteus mirabilis*. NOE can also be a fungal infection, particularly in non-diabetic immunocompromised patients and the most common fungal organism is *Aspergillus fumigatus*. The possibility of a fungal NOE must be considered if a patient with classic signs and symptoms of NOE is unresponsive to appropriate antimicrobial therapy and cultures have been negative.6 Fungal infection usually originates in patients with chronic otitis media history and most of these patients develop facial nerve palsy during the course disease [3,6,11-16]

Patients with NOE may complain of progressive nocturnal pain refractory to analgesics, aural fullness and hearing loss, fever and purulent otorrhea in more than a half of the cases. Headache, temporomandibular joint pain and trismus may also be present. The examination can reveal periauricular skin tenderness, purulent otorrhea and granulation tissue at the EAC, cranial nerve involvement, vertigo or meningeal signs [1,3,6,15].

Progression of the disease may lead to skull base osteomyelitis and cranial nerve palsies. The facial nerve is the most commonly affected cranial nerve in NOE, but cranial nerves IX, X, XI and XII can be affected if the disease progresses along the skull base. Cranial nerves V and VI can be affected if the disease extends to the petrous apex [1,3].

The diagnosis of NOE relies on specific elements of the history, physical examination and laboratory and imaging studies [6].

Computerized tomography (CT) is normally the first imaging test used to evaluate the extension and severity of the disease. However, more than 30% of affected bone needs to be demineralized to appear altered on CT, so it's not very useful to diagnose NOE in an early stage. Magnetic resonance imaging (MRI) is better than CT at identifying soft tissue changes and is recommended when central skull base invasion is seen on CT scan. Because bone remineralization may never occur and MRI changes may never disappear despite resolution of infection, neither CT nor MRI are appropriate examinations to evaluate response to treatment [3,16,17].

Although nuclear imaging scans show poor anatomic resolution, they have been the basilar stone in the diagnosis and follow-up of NOE patients. Technetium-99 scintigraphy localizes areas of increased osteoblastic activity with an almost 100% sensibility and doesn't depend on bone demineralization to be positive, allowing the early diagnosis of osteomyelitis. However, it can remain positive indefinitely and therefore isn't a useful marker of therapy response or disease resolution [6,15,18].

Gallium-67 citrate accumulates in areas of active inflammation and its uptake returns to normal after the infection has resolved, that's why it's the best scan to monitor antibiotic response and to detect recurrence [15,19,20].

The historically high mortality rate from NOE has been decreased with the use of systemic antibiotics. Extension to skull base, cranial nerve involvement and intracranial extension are usually associated to poor prognosis. Long-term antibiotic therapy is the mainstay of NOE treatment and should be continued for at least 6 to 8 weeks 1 and monotherapy with ciprofloxacin has been proposed as the initial antibiotic regimen; 8 however, there are reports that describe a Pseudomonas' fluoroquinolones resistance rate of one third 1 so that third-generation cephalosporins with antipseudomonal activity provide an alternative to ciprofloxacin in the NOE treatment. Use of topical antibiotics in NOE is controversial because it may change bacterial flora, making culture more difficult and may be a potential source of antibiotic resistance without adding significant benefit [1,4,21,22].

The role of hyperbaric oxygen therapy (HBO) in managing NOE is not well established. However; it has been used with success in the treatment of osteomyelitis, particularly in refractory cases of skull base osteomyelitis and intracranial involvement. HBO increases the partial pressure of oxygen, which improves hypoxia, allows oxidative killing of bacteria and amplifies the oxygen diffusion gradient into avascular tissues; promotes fibroblastic division, collagen production, capillary angiogenesis and osteoblast activity, helping the soft-tissue and bone healing. Its use requires daily treatments lasting several hours for weeks; oxygen toxicity, barotrauma and other side effects can result [22,23].

Material and Methods

This is an observational, retrospective study that intends to evaluate the HBO effect in NOE treatment and prognosis.

All NOE cases treated by Hyperbaric Medicine Department of Hospital Pedro Hispano between January 2007 and December 2016 were identified based on Cohen and Friedman NOE diagnosis criteria. For each 8 cases that met those criteria, the respective clinical records were analyzed and several characteristics as gender, age, diabetes and other immunosuppression conditions, clinical presentation, microbiology results, computed tomography and magnetic resonance imaging, antibiotherapy regimen, surgery performed, complications, HBO cycles and outcome were reviewed. The patients' records and results were compared and described according to the principles expressed in the Declaration of Helsinki. Therapeutic success was defined as a significant improvement or complete resolution of complaints of otalgia and otorrhea, improvement of scintigraphy results and absence of recurrence during one-year-follow up in otolaryngology consultation [24].

A meta-analysis of NOE related articles was also performed, based on terms "malignant otitis externa", "necrotizing otitis externa", "skull base osteomyelitis" and "hyperbaric oxygen therapy".

Results

We identified 8 patients with a NOE diagnosis. There were 5 males (62.5%) and 3 females (37.5%), with a mean age of 76 ± 11 years (from 60 to 90 years). Type 2 diabetes mellitus was present in every patient and 5 of them (62.5%) were insulin-dependent, which assume that these patients had a long term and poor controlled diabetes (Table 1).

Table 1: The diagnostic criteria of malignant external otitis.

Major (obligatory) signs
1) pain
2) exudate
3) edema
4) granulations
5) microabscesses
6) positive technetium-99 (99tc) scan of
Failure of local treatment after more than 1 Week
Minor (occasional) signs
7) pseudomonas
8) positive radiograph
9) diabetes mellitus
10) cranial nerve involvement
11) debilitating conditions
12) old age
The diagnostic criteria of necrotizing otitis external (NOE) was divided into two categories: obligatory and occasional. All the obligatory criteria must be present to establish the diagnosis.

The most common inaugural symptom was purulent otorrhea (5 patients, 62.5%) and severe otalgia (5 patients, 62.5%), followed by headache (2 patients, 25%) and hearing loss (1 patient, 12.5%). Five patients (62,5%) were submitted to microbiologic cultures: 4 in 5 patients had a Pseudomonas aeruginosa identified and one of them had an *Aspergillus fumigatus* as the main offending organism.

Computed tomography, magnetic resonance and scintigraphy imaging were successively performed in every patient and for each one of them imaging

scans showed a CAE opacification, mastoid involvement and bone erosion. Three patients (37.5%) had an involvement and osteomyelitis of temporomandibular joint (TMJ) and 2 out of them respectively developed a TMJ septic arthritis and a mandibular osteonecrosis. Three cases of temporal and skull base osteomyelitis were also identified. Four cases (50%) of facial paralysis were recognized during the disease course, although one of them has appeared as a presenting symptom.

Long-term antibiotic therapy was completed in all patients: ciprofloxacin was the most frequently used antibiotic (6 patients, 75%); third generation cephalosporins was prescribed for 2 patients (25%). The patient with a fungal NOE caused by *Aspergillus fumigatus* was initially treated with ciprofloxacin and after fungal isolation in culture completed the treatment with itraconazole, with a satisfactory response.

Four out of 8 patients (50%) underwent surgery. Surgery was performed for local debridement and to collect biopsy specimen for histological confirmation of the disease.

Since January 2006, Pedro Hispano Hospital has had an available and full working hyperbaric chamber. Every NOE patient that is diagnosed in our hospital or in neighbour institutions are referred to HBO department and are proposed to HBO treatment, if patients accept and if there are no contraindications for the treatment. Therefore, the 8 patients identified was submitted to HBO, even though only 5 of them (62.5%) have completed the 40 sessions, which is the recommendation of Undersea and Hyperbaric Medical Society [25]. One of these patients had a minor otologic barotrauma as a complication of HBO that did not interfere with the treatment. Two out of 3 patients that didn't complete the whole HBO treatment accomplished respectively 10 and 12 HBO sessions; there isn't information registered about the third patient that didn't finish the treatment.

Although there was some follow up clinical information loss once patients referred to our hospital returned to their origin institutions after completing HBO treatment, apparently 8 patients (100%) experienced a clinical and radiological improvement. One of 5 (20%) patients that completed HBO sessions had a full facial paralysis recovery after 6 months of follow up. There is no record of mortality or disease recurrence in a one year follow up period.

Basic data at the time of presentation and results are summarized in Table 2.

Table 2: Statistical description of patients included in study.

Descriptive statiscts	Patients
Age – yr	76 ± 11
Male sex – no. (%)	5 62.5)
Diabetes – no. (%)	8(100)
Insulin-dependent – no. (%)	5(62.5)
Clinical presentation	
Otalgia – no. (%)	5(62.5)
Otorrhea – no. (%)	5(62.5)
Headache – no. (%)	2(25)
Microbiology	
Pseudomonas aeruginosa – no. (%)	4(50)
Aspergillus – no. (%)	1(12.5)
Facial nerve paralysis – no. (%)	4(50)
Antibiotic therapy	8(100)
Ciprofloxacin – no. (%)	6(75)
Third-generation cephalosporins –no. (%)	2(25)
Surgery – no. (%)	3(37.5)
Hyperbaric oxygen therapy (hbo) – no (%).	8(100)
Hbo side effect – no. (%)	1(12.5)
Outcome	
Mortality – no. (%)	0
Recurrence – no. (%)	0
Facial palsy resolution – no. (%)	1 (25)
Clinical improvement – no. (%)	8 (100)

Discussion and Conclusion

Historically, NOE used to be a mortifying disease with a mortality rate that has already been described by Chandler et al. as nearly 50%. It has become a treatable disease with the advent of systemic antibiotics. However, despite the treatment, considerable recurrence and complication rates are still reported and the prognosis worsens once skull base osteomyelitis or other complications develop [17].

The refractory nature of NOE is probably due to association of several factors as the poor immunological function and typical microangiopathy of diabetic patients associated to the necrotizing vasculitis Pseudomonas-induced, which interferes with the tissues oxygenation and antibiotic and other drugs delivery. Because of that, hyperbaric oxygenation has been reported as a valuable adjuvant therapy in NOE cases, particularly those with refractory osteomyelitis. HBO allows elevation of partial pressure of oxygen from hypoxygenation to normal levels or hyperoxygenation, amplifying the oxygen diffusion gradient into the infected and avascular tissues. The accurate tissue oxygenation has been linked with an improvement of leukocytes function and an oxidative killing of bacteria, fibroblastic division, collagen production and angiogenesis, osteoid deposition and higher concentration of antibiotic in infected area.

Although the theoretical advantages of HBO, there aren't identified articles describing randomised controlled trials of HBO in the NOE treatment. The fact that NOE is a rare disease with a poor prognosis and the fact that there isn't a hyperbaric chamber available in every hospital, makes it difficult to build and conduct a randomised study.

We conducted the present study to evaluate the clinical efficacy and safety of HBO in NOE management. However, this is an observational study, no randomised or controlled, with a very small sample and no control group, which makes it impossible to compare a group of patients submitted to HBO and another group treated only with medical therapy. These limitations don't allow to conduct a statistical design or to scientifically state that there is an apparent beneficial effect of HBO in our institution's NOE cases. Bigger samples, use of a control group and randomization of patients are needed to demonstrate the efficacy of HBO when compared to treatment with antibiotics or surgery and to compare rates of complication between the different treatment modalities. However, the fact that none of the patients had major complications, died or presented with infection recurrence for one-year follow-up may be useful predictive factors of therapeutic HBO success.

Despite HBO is an expensive treatment, that requires long periods of time and that can cause some complications as barotraumas, it's described in literature some apparent clinical benefice of HBO on NOE management which is consider an aggressive and potentially fatal disease. Therefore, current recommendations state that HBO should be used whenever a therapeutic pressure chamber is available, even when other treatment measures fail or are contraindicated [12].

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Flint P, Cummings C, Haughey B, et al. Cummings otolaryngology head & neck surgery, Recherche 2010.
2. Nawas MT, Daruwalla VJ, Spirer D, et al. Complicated necrotizing otitis externa Am J Otolaryngol. 2013;34:706-09.
3. Berenholz L, Katzenell U, Harell M.Evolving resistant pseudomonas to ciprofloxacin in malignant otitis externa. Laryngoscope. 2002;112:1619-22.
4. Franco-Vidal V, Blanchet H, Bebear C, et al. Necrotizing external otitis: a report of 46 cases. Otol Neurotol. 2007;28:771-73.
5. Sreepada GS, Kwartler JA. Skull base osteomyelitis secondary to malignant otitis externa Curr Opin. Otolaryngol. Head Neck Surg.2003;11:316-23.
6. Carfrae MJ, Kesser BW. Malignant otitis externa Otolaryngol Clin North Am. 2008;41:537–49
7. Chandler JR. Malignant external otitis. Laryngoscope. 1968;78:1257-94.
8. Naghibi M, Smith RP, Baltch A.The effect of diabetes mellitus on chemotactic and bactericidal activity of human polymorphonuclear leukocytes. Diabetes Res Clin Pr. 1987;4:27-35.
9. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). FEMS Immunol Med Microbiol. 1999;26:259-65.
10. Driscoll PV, Ramachandrula A, Drezner DA, et al. Characteristics of cerumen in diabetic patients: a key to understanding malignant external otitis? Otolaryngol Head Neck Surg. 1993;109:676-79.
11. Bayardelle P, Jolivet-Granger M, Larochelle D. Staphylococcal malignant external otitis. Can Med Assoc J. 1982;126: 155-56.
12. Coser PL, Stamm AE, Lobo RC, et al. Malignant external otitis in infants. Laryngoscope.1980;90:312-16.
13. Kountakis SE, Kemper JV, Joseph Chang CY, et al. Osteomyelitis of the base of the skull secondary to Aspergillus. Am J Otolaryngol. 1997;18:19-22.

14. Cunningham M, Yu VL, Turner J, et al. Necrotizing otitis externa due to Aspergillus in an immunocompetent patient. Arch Otolaryngol Head Neck Surg. 1988;114:554-56.
15. Amorosa L, Modugno GC, Pirodda A. Malignant external otitis: review and personal experience. Acta Otolaryngol. 1996;521:3-16.
16. Stokkel MPM, Boot ICN, van Eck-Smit BLF. SPECT Gallium Scintigraphy in Malignant External Otitis: Initial Staging and Follow-up. Case Reports. Laryngoscope. 2018;106:338-40.
17. Grandis JR, Curtin HD, Yu VL. Necrotizing (malignant) external otitis: Prospective comparison of CT and MR imaging in diagnosis and follow-up. Radiology. 1995;196:499-04.
18. Slattery WH, Brackmann DE. Skull base osteomyelitis: malignant otitis externa. Otolaryngol Clin North Am. 1996;29:795-06.
19. Murray ME, Britton J. Osteomyelitis of the skull base: the role of high resolution CT in diagnosis. Clin Radiol. 1994;49:408–11.
20. Singh A, Khabori MAl, Hyder MJ. Skull base osteomyelitis: diagnostic and therapeutic challenges in atypical presentation. Otolaryngol Head Neck Surg. 2005;133:121-25.
21. Kimmelman CP, Lucente FE. Use of ceftazidime for malignant external otitis. Ann Otol Rhinol Laryngol. 1989;98:721-25.
22. Narozny W, Kuczkowski J, Stankiewicz C. Value of hyperbaric oxygen in bacterial and fungal malignant external otitis treatment. Eur Arch Otorhinolaryngol. 2006;263:680-84.
23. Shupak A, Greenberg E, Hardoff R, et al. Hyperbaric oxygenation for necrotizing (Malignant) otitis externa. Arch Otolaryngol. Neck Surg. 1989;115:1470-75.
24. Cohen D, Friedman P. The diagnostic criteria of malignant external otitis. J Laryngol Otol. 1987;101:216-21.
25. Weaver LK. Hyperbaric oxygen therapy indications thirteenth edition the hyperbaric oxygen therapy committee report 2014.