Hyperbaric oxygen treatment in three cases of necrotizing infection of the neck

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Abstract

Necrotizing infections of the head and neck are rare conditions in our hospital. Clinical and microbiological characteristics of three consecutive cases treated in Haukeland University Hospital in western Norway in the year 2010 are described. Two cases of Lemierre’s syndrome and one case with a descending necrotizing mediastinitis (DNM) were diagnosed. All three cases were treated with broad spectrum antibiotics and in two cases surgery was possible. Hyperbaric oxygen treatment (HBOT) with intensive care facilities began recently available at our hospital, and this treatment was used in all these patients regardless of surgery. In one case we describe the use of HBOT on the basis of strong clinical suspicion of anaerobic infection only. Bacterial identification by partial sequencing of the 16S rDNA gene proved to be a useful supplement to conventional culture techniques. All the cases all demonstrated a significant clinical improvement after introduction of HBOT. When HBOT is available, it should be considered as adjunctive treatment in extensive infections with anaerobes.

Case Report #1

A 67-year-old man in previously good condition, experienced a sore throat and dysphagia for 5 days. On admission to hospital he appeared acutely ill. Temperature was 38.1°C, heart rate (HR) 125/min, blood pressure (BP) 110/59 mm Hg, respiratory rate (RR) 30/min, and SaO2 87% with 12 l 02/min supplement via a non-rebreather mask. On clinical examination the neck was asymmetric with an enlarged mass on the left side, and crepitus was felt by palpation. Laboratory studies revealed a white blood cell count of 34.1 x 109/L with 98% neutrophils. Other laboratory data are given in Figure 1. A CT-scan demonstrated soft tissue swelling, subcutaneous gas (Figure 2), and a muscle abscess in the neck. Antibiotic treatment was initiated, and he had to undergo immediate surgery with drainage of the abscess. Mixed anaerobic microbes were identified (Table 1). Due to the foci of infection, gas-production in the tissue and positive cultures for anaerobic bacteria, it was decided to start with hyperbaric oxygen treatment (HBOT) for 90 min sequences at 3 ATA and positive cultures for anaerobic bacteria, it was decided to start with hyperbaric oxygen treatment (HBOT) for 90 min sequences at 3 ATA was chosen based on the recommendation for treatment of clostridial myonecrosis from Undersea and Hyperbaric Medical Society (UHMS). A total of 5 HBOT were performed in the next 2.5 days, the first starting a few hours after the initial surgery. Already after 3 HBOTs the surgeon had to undergo immediate surgery with drainage of the abscess. Mixed anaerobic microbes were identified (Table 1). Due to the foci of infection, gas-production in the tissue and positive cultures for anaerobic bacteria, it was decided to start with hyperbaric oxygen treatment (HBOT) for 90 min sequences at 3 atmospheres absolute (ATA). HBOT at 3 ATA was chosen based on the recommendation for treatment of clostridial myonecrosis from Undersea and Hyperbaric Medical Society (UHMS). A total of 5 HBOT were performed in the next 2.5 days, the first starting a few hours after the initial surgery. Already after 3 HBOTs the surgeon reported a halt of the ongoing necrotizing infection in the area. After 5 HBOTs the patients condition was reported to be under control and stabilized, and HBOT was discontinued. During HBOT-treatment the Sequential Organ Failure Assessment (SOFA) score decreased from 12 to 5, and vasopressor was ceased (Figure 1). Although the condition improved, another CT-scan of the neck and chest demonstrated thrombosis of the left jugular vein and an additional abscess in the upper mediastinum. Treatment with low molecular weight heparin (LMHW) was introduced. The abscess was removed by thoracoscopy and mediastinotomy. Eight teeth were extracted upon discovery of infection. After 27 days in the ICU, the patient was transferred to the medical ward, were he stayed another 36 days before he was discharged from hospital to home. He is suffering of a minor sequela in is upper right extremity.

Case Report #2

A healthy 53 year old man with psoriatic disease experienced 6 days of sore throat. Due to sudden onset of chest pain a coronary event was suspected. On admittance to hospital he was in reduced general state with a temperature of 37 °C, HR 90/min, RR 28/min, and hypoxia was noted (PaO2 8 kPa). The patient had redness in the pharynx, but no obvious clinical tonsillitis. A CT-scan of neck and chest showed inflammation of the upper and lower mediastinum, involving the pericardium, and gas was seen in deep tissue layers. He was diagnosed with tonsillitis and mediastinitis (Figure 3). After start of antibiotics, surgical treatment with sternotomy and mediastinotomy was done. Fat tissue in the mediastinum was found...
infected and/or necrotic. Mixed anaerobic bacteria were identified (Table 1). It was decided to treat the surgical wound with vacuum assisted closure (VAC), and initially not by HBOT. However, over the next 5 days his condition did not improve, a CT-scan demonstrated bilateral empyema, significant inflammation in soft tissue of the neck and mediastinum, and gas surrounding the heart. Due to the foci of infection, gas-production in the tissue and identification of anaerobic pathogens, HBOT then was started. He underwent a total of 5 HBO-treatments the next 3 days, as described in case 1. Upon HBOT, the patient improved, vasopressors were ceased, and CRP decreased from 285 to 116 mg/L (Figure 4). Four days after the last HBO-treatment his sternum was closed. After a total of 21 days in ICU he was discharged to the ear-nose-and throat ward (ENT). He stayed another 25 days in hospital before he could go home. He is not suffering from any sequela.

**Case Report #3**

A previously healthy woman, age 22, had a history of 6 days with progressive dysphagia. She was admitted to the local hospital due to increasing systemic signs of infection, accompanied by tenderness of the neck and chest pain. A CT-thorax demonstrated an abscess of the upper mediastinum. She received treatment with antibiotics for one day, before she was transferred to the regional hospital. She then had a temperature of 38.3°C and HR 100/min. At clinical examination, distinct tenderness on the left side of the neck was found, as well as discrete oedema. Crepitus in left supraclavicular space was suspected. On inspection of the oropharynx, slight elevation of the left side of the lateral pharyngeal wall was seen. Laboratory results are given in Figure 5. A new CT-scan and an MRI confirmed the findings of inflammatory changes in the neck as well as an mediastinal abscess, together with thromboses of the left jugular and subclavian veins. The abscess was not suited for surgical drainage due to difficult access; small volume and density measured by CT. Blood cultures and other bacteriological investigations were negative. She was treated with antibiotics and LMWH in the infectious diseases ward. In an attempt to reduce further progression of inflammation and pus formation, HBOT was started (3 ATA, 90 min) whereby the patient’s condition improved shortly after this treatment was introduced (Figure 5). Three days after discontinuation of HBOT she was transferred to her local hospital for further conservative measures. After two weeks she was discharged from the local hospital, where treatment was continued with antibiotics for another 2 weeks and anticoagulation for 3 months. She is now back at school, suffering no sequela.
Discussion

In each of these three cases we diagnosed the patient with an extensive soft-tissue infection of the neck and mediastinum. Patient #1 and #3 met the criteria for Lemierre’s syndrome, and patient #2 had findings consistent with DNM. In patient #1 and #2 several bacteria were identified with an oropharyngeal origin. Both anaerobic and aerobic bacteria were probably involved in the disease of these two patients. Anaerobic involvement was probably also the case in patient #3, as crepitations in the skin were found under clinical examination. The contribution of HBOT to the recovery of each patient will be discussed in the following.

Descending necrotizing infections of the head and neck are rare and the case fatality rate is high. Severe infections of the head and neck often start with symptoms from the source of infection. In Lemierre’s syndrome sore throat and neck pain may be early symptoms, followed by signs of a neck mass.11 The origin is often a pharyngotonsillitis or a peritonsillar abscess. In CNF, dysphagia and a sore throat are also common. A dental infection is often the primary source of infection. In DNM, pharyngeal infection is most often the primary source.3 In our three cases, all presented with a history of sore throat and dysphagia. Chest pain, pain when swallowing and swelling of the neck were reported. The two patients with Lemierre’s syndrome both had oropharyngeal infections with downward spread to the mediastinum. In Lemierre’s syndrome the spread is usually metastatic from the thrombophlebitis of the affected vein. The patient with DNM had tonsillitis and an early spread to the mediastinum. In DNM the spread is probably facilitated by gravity, breathing and negative intrathoracic pressure.12 The systemic effects predominated when the mediastinum becomes more involved; capillary leak, possible respiratory distress syndrome (ARDS) and empyema.

Microbiology

The necrotizing infections described herein are typically polymicrobial, and anaerobic microbes normally harboured in the oral cavity are usually involved. The pathogens identified in these patients are considered apathogenic or of low virulence. Still, all or some have caused progressive infection, even during antimicrobial therapy. All the tested bacteria were sensitive to penicillin G and are considered sensitive to the initial empiric therapy. However, the suboptimal effect of antibiotics observed was most likely caused by local factors as impaired perfusion, oxygen depletion, impaired immunofunction or bacterial community mediated antibiotic tolerance mechanisms.13

The detection of microbes in a polymicrobial setting is difficult. Strictly anaerobic microbes are easily killed during specimen transport and handling if anaerobic conditions are not maintained. Fusobacterium spp., often considered the main bacteria causing Lemierre’s syndrome,11 are extremely sensitive to O2, and can be missed by traditional culture methods. Some microbes require enriched media, special environmental conditions and prolonged incubation for growth. These microbes are therefore most likely not detected by conventional culture techniques. The usefulness of alternative techniques is illustrated in case 1, where 16SrDNA detection identified in total 6 species that were not identified by conventional culture. 16SrDNA sequencing in mixed infections gives mixed chromatograms where overlying sequences make it difficult to identify which nucleic acid belong to which microbe. This was overcame by using the newly developed software RipSeq that identified 2 microbes (Porphyromonas gingivalis and Bacteroides spp.).14 The 16SrDNA sequencing, in this study targeted either or both of the variable gene regions V1-V3 and V3-V4. Using group specific primers and RipSeq we were able to identify an additional 4 microbes. Such detection methods based on genus/species specific nucleic acids are particularly useful in infections caused by fastidious and oxygen sensitive bacteria. Earlier only infections caused by a single bacterial species could be detected by 16 rDNA sequencing, but by using group specific primers and Rip Seq software this can be accomplished also for polymicrobial infections, even after antimicrobial therapy is started, as illustrated in this case report. Susceptibility testing is however, not possible when molecular methods are used.

Treatment of our patients

All three patients received early and targeted antimicrobial treatment. Surgical therapy was needed in two of the cases. Patient #1 and #2 were treated in a multiplace-chamber due their need of intensive care and respirator (Haux-Quadro 2500-2200). In patient #1, an improvement in the clinical condition was objectively observed after three HBOTs. He received two additional treatments, and his clinical condition further improved, objectively observed by marked reduction of the SOFA-score (Figure 1).
However, his condition worsened a few days later, and an abscess in the mediastinum was found and removed by drainage. One might argue a need for additional HBOT in this patient, but this was not done. Studies on NF advocate a treatment protocol of at least ten sessions. Patient #2 was early suspected with an anaerobic infection. HBOT was considered at first, but not started as Clostridium ssp. was not detected during the first surgery. However, his clinical condition worsened and it was not until the start of HBOT at day 5 one was able to get control over his infection and his condition stabilized. Patient #3 did not have an infection suitable for surgery. Instead we started aggressive treatment with antibiotics and HBOT. This patient was treated in a monoplace-chamber (Baramed Hyperbaric Chambers, ETC).

The use of HBOT in conjunction with surgical debridement, antibiotic therapy and maximal critical-care therapy for severe soft tissue infections is widely accepted, but the efficacy of HBO remains unproven. In soft tissue infections, an area of hypoxia develops. The hypoxia impairs phagocytosis, and the drop in pH creates a milieu for growth of anaerobic organisms. The local hypoxia again causes tissue necrosis that may contribute gas production. Gas is frequently seen in crepitant necrotizing infections that may illustrate its therapeutic potential. In all the cases, HBOT provides oxygenation to otherwise ischemic areas, and reduces the impact of hypoxia on leukocyte function. The oxygenation of tissue thereby limits the spread and progression of infection. HBOT of infections also occurs via HBO acting as a bactericide or as a bacteriostatic agent to some microorganisms, and through an additive and/or synergistic effect on some antimicrobial drugs. In patient #1 the surgeon reported *vital tissue only* in the affected area, shortly after start of HBOT which may illustrate its therapeutic potential. In all the cases, a clinical improvement was seen after the start of HBOT, but the specific role of HBOT in this improvement is difficult to estimate.

**Conclusions**

The incidence of cervical necrotizing infections is low also in our hospital. Data on HBOT of such infections are scarce and not conclusive, but somewhat in support of this. Recent availability of HBOT with intensive care facilities at our hospital has led to three HBO treated cases all demonstrating a significant clinical improvement. We also show that HBOT may be used on the basis of only strong clinical suspicion of anaerobic infection. The cases demonstrate that use of polymerase chain reaction is especially useful in the diagnostics of anaerobic infections. When HBOT is available, it should be considered as an adjunctive treatment in extensive infections with anaerobes, but more studies are needed to evaluate the effect.

**References**