

Hyperbaric oxygen therapy in necrotizing soft tissue infections caused by *Vibrio* species from the Baltic Sea – three clinical cases

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We read with great interest the report on the presence of *Vibrio* spp in the Gulf of Gdansk, Baltic Sea, Poland by Kurpas et al. [1]. So far, the vast majority of identifications of *Vibrio* spp in open waters concerned the subtropical zone. In an analysis of 19 publications describing 2,227 patients with NSTI caused by *Vibrio vulnificus*, 95% of cases concerned such subtropical zones [2]. However, there are also reports describing the changing location of *Vibrio*, mainly due to the gradual increase in open water temperature [3]. The identification of *Vibrio* spp in the climatic zone of the Baltic Sea is a new observation that is of great importance not only from the microbiological point of view but also for clinical reasons.

Vibrio is one of the more common bacteria in tropical or subtropical waters. It is a gram-negative rod that can cause necrotizing soft tissue infection (NSTI), which also includes necrotizing fasciitis, and often leads to septic shock and an immediate threat to life. From the aetiology point of view, NSTI most often has a polymicrobial aetiology, often described as type I, or monomicrobial, usually described as type II (most often caused by group A beta-haemolytic streptococci, e.g. *Streptococcus pyogenes*), sometimes in combination with *Staphylococcus aureus* [4, 5]. According to the same classification, infections caused by *Vibrio* spp are referred to as type III related to other less common causative agents (e.g., *Clostridium* spp, *Aeromonas* spp, *Vibrio* spp). Type IV describes fungal infections (e.g., *Candida* spp, *Zygomycetes*). Regardless of aetiology, the treatment of any form of NSTI is multimodal and includes surgery, antibiotic therapy, and haemodynamic sepsis management [4–8]. In the case of *Vibrio* NSTI, the importance of surgical

interventions is emphasized [9]. Most of the recommendations also suggest using hyperbaric oxygen therapy (HBOT). In the literature, one can find descriptions of clinical cases successfully treated with HBOT, but in most of those reports the infections came from sub-tropical waters of the United States or Japan [10, 11].

An interesting coincidence is a fact that at almost the same time as the publication by Kurpas et al. [1] on the occurrence of *Vibrio* spp in the Gulf of Gdansk, a clinical case report of a 68-year-old patient with NSTI caused by *Vibrio vulnificus*, most probably from the south-western part of the Baltic Sea, treated with adjunctive HBOT in our department was published [12]. In summary, after injuring while swimming in Baltic seawater, the patient developed NSTI of the lower extremity. *Vibrio vulnificus* was identified in blood. Initially, this patient was treated in a local municipal hospital. However, due to the progression of NSTI confirmed in computed tomography scan, with increasing inflammatory markers and general deterioration with sepsis, the patient was transferred to our department, where he underwent surgical debridement with general care using antibiotics (ceftriaxone, ciprofloxacin, doxycycline), septic shock management and adjunctive HBOT. After 5 days of treatment in our department, where 10 HBOT sessions were performed, the general and local condition improved. Control cultures were negative and inflammation markers decreased: white blood cell (WBC) count from 13.93 G/L to 8.58 G/L; C-reactive protein (CRP) from 137.9 mg/L to 36.9 mg/dL, procalcitonin (PCT) from 8.52 ng/mL to 1.3 ng/mL. After this treatment, the patient was transported back to the referring unit for further treatment.

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Figure 1. A. Before hyperbaric oxygen therapy; B. After hyperbaric oxygen therapy

Although this clinical case was published as the first report of NSTI with *Vibrio vulnificus* originating from the Baltic Sea, it was not the first clinical case of *Vibrio* infection treated with HBOT in our department. In fact, we treated at least two similar cases of *Vibrio* infection also from the waters of the Baltic Sea.

In an earlier case from 2019, the disease occurred in a 60-year-old man admitted to the local general hospital with a purulent infection of the lower limb in the severe clinical condition of septic shock with multiorgan failure, cardiac arrest occurred during disease with successful cardiopulmonary resuscitation. *Vibrio cholerae* was identified in the wound tissue samples and this was confirmed by the independent governmental central laboratory using the polymerase chain reaction test. The source of the infection has never been documented, but according to information from the family, the patient with venous ulcerations of the lower limbs submerged in the waters of the central-southern part of the Baltic. Because of the clinical features of NSTI and the progress of the compartment syndrome, the patient was transferred to our department to extend the treatment with HBOT. General surgery, intensive therapy with mechanical ventilation, continuous veno-venous haemodiafiltration, antibiotics (ciprofloxacin, imipenem-cilastatin, linezolid), septic management, and adjunctive HBOT were used in the treat-

ment. Within 5 days, 10 HBOT sessions were performed, resulting in improvement of the general condition and local tissues (Fig. 1A, B), resolution of septic shock, and reduction of inflammatory parameters: WBC from 22.19 G/L to 20.54 G/L; CRP from 264 mg/L to 65.1 mg/L; PCT from over 100 ng/mL to 3.16 ng/mL. After the end of HBOT, he was transferred to the referring hospital for further treatment.

We recently had yet another case of *Vibrio* NSTI from the Baltic Sea. In this case, the disease concerned a 39-year-old man who was admitted to our department from the west coast of Poland. No entry point for bacteria was identified, but the patient's history also revealed a bath in the southern waters of the Baltic Sea (at the western border of Poland). At the local hospital, he was treated for rhabdomyolysis of the lower limb with gas bubbles seen on radiographs. NSTI lesions progressed within a few days, requiring a fasciotomy. Severe septic shock developed with a multiple organ failure. In a microbiological study, *Vibrio vulnificus* was identified. The patient was transported to our department to add HBOT to surgical and intensive care treatment. During the 6-day stay in our department, 10 sessions of intensive care HBOT and multimodal treatment with surgical debridement, antibiotics (ceftriaxone, ciprofloxacin, doxycycline, linezolid, meropenem), septic shock management, and mechanical ventilation were used. There was an improvement both



Figure 2. A. Before hyperbaric oxygen therapy; B. After hyperbaric oxygen therapy

in general condition and at the wound site (Fig. 2A, B); septic shock resolved, and the inflammatory parameters decreased: WBC from max 16.07 G/L to 9.7 G/L; CRP from 296.8 mg/L to 91.6 mg/L; PCT from 50.9 ng/mL to 2.7 ng/mL. The clinical course of the disease was complicated by myocardial infarction. Due to the critical condition the non-invasive treatment was conducted. After HBOT treatment, a reduction in cardiac enzymes was also achieved: troponin from max 2.86 ng/mL to 0.57 ng/mL and creatine kinase myocardial bound (CKMB) from max 4.4 ng/mL to 0.5 ng/mL. After the end of HBOT, he was transferred to the referring hospital for further treatment.

All reported cases shared the common denominator of NSTI with severe clinical course. In all cases, empirical broad-spectrum antibiotic therapy, intensive care management adequate to the patient's condition, surgical interventions and adjunctive HBOT were used.

Hyperbaric oxygen therapy consists of breathing 100% at a pressure exceeding ambient pressure. In most cases, 2.4–2.8 ATA pressure for 60 to 120 minutes is used. For severe NSTI, hyperbaric sessions are performed initially every 8 hours in the first 24-hours and then every 12 hours for a total of approximately ten sessions [13]. In such doses, the influence of oxygen on bacteria and the patient's tissues, vessels, endothelium, cells, and enzymes, is multimodal. High oxygen tension in tissues generates reactive oxygen species (ROS) and reactive nitrogen species (RNS), which are critical mediators of cellular interaction, production of

cytokines and growth factors, bactericidal effect on anaerobic bacteria with degradation of *Clostridium perfringens* exotoxins and modulation of leukocyte activation with enhancement of the killer function of neutrophils and their interaction with the endothelium [14]. It has been suggested that HBOT acts specifically against *Vibrio spp*, taking advantage of its more remarkable inability than other bacteria to tolerate ROS. When HBOT is combined with antibiotics, it exerts a bactericidal effect on *Vibrio spp* while it is only bacteriostatic to most of other bacteria [15–17].

The list of indications for HBOT is determined based on clinical evidence by the European Committee for Hyperbaric Medicine (ECHM), also approved by the European Underwater and Baromedical Society (EUBS) [18]. One of the indications for HBOT is an anaerobic and mixed bacterial infection, which is a general term also including NSTI. In patients with NSTI in severe clinical condition, i.e. septic shock, HBOT sessions should be carried according to the recommendations for hyperbaric intensive care [19].

The clinical cases presented here confirm the threat resulting from the presence of environmental bacteria, such as *Vibrio spp*, which, under optimal development conditions, may lead to NSTI and septic shock, with direct threat to health and life. Rapid diagnosis, empirical antibiotic therapy, decisive surgical procedure adequate to the wound severity and the possible addition of HBOT are the basis of the multimodal treatment.

Conflict of interest: None declared

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