

# Successful Hyperbaric Oxygen Treatment of Gangrenous Lesions due to Systemic Lupus Erythematosus

## Sistemik Lupus Eritematozusa Bağlı Gelişen Gangrenin Hiperbarik Oksijen ile Başarılı Tedavisi

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**ABSTRACT** Necrotizing vasculopathy is a relatively uncommon and life-threatening condition in children. Raynaud phenomenon and digital ischemia are the most common symptoms. Although immunosuppressive treatments in combination with vasodilators are the first chosen therapies, hyperbaric oxygen therapy is also used as primary or adjuvant therapy. Herein, we present an adolescent female patient who has had gangrenous lesions at bilateral feet phalanges diagnosed with necrotizing vasculitis due to systemic lupus erythematosus. Effective treatment by hyperbaric oxygen therapy in combination with immunosuppressive and vasodilator drugs led to significant improvement without amputation. Adjunctive hyperbaric oxygen therapy should be considered in cases with progressive gangrenous lesions due to vasculopathies.

**Keywords:** Lupus erythematosus, systemic; hyperbaric oxygenation; vasculitis

**ÖZET** Nekrotizan vaskülopati çocukluk çağında oldukça nadir görülür ve hayatı tehdit eder. Raynaud fenomeni ve parmaklarda iskemi en sık görülen semptomlardır. Vazodilatör tedaviler ile beraber kullanılan immünespresif tedaviler ilk tedavi seçeneği olmasına rağmen hiperbarik oksijen tedavisi de birincil tedavi seçeneği olarak veya tedavilere ek olarak kullanılabilir. Bu makalede, her iki ayak parmaklarında gangren ile başvuran ve sistemik lupus eritematozus tanısı alan adölesan bir kız olgu sunulmuştur. İmmünespresif ve vazodilatör tedavilere ek hiperbarik oksijen tedavisi uygulanmış ve amputasyona gerek kalmadan lezyonlarda düzelme görülmüştür. Nekrotizan vaskülopatilere bağlı gelişen ilerleyici gangrenöz lezyonu olan olgularda tedavilere ek olarak hiperbarik oksijen tedavisi uygulanması akılda tutulmalıdır.

**Anahtar Kelimeler:** Lupus eritematozus, sistemik; hiperbarik oksijenasyon; vaskülit

Vasculitis is the inflammation of blood vessels of any type and size and can be seen as a primary disorder or clinical manifestation of various conditions. Systemic necrotizing vasculitis is a rare condition especially in children and its clinical manifestations include Raynaud phenomenon and digital ischemia.<sup>1</sup> Immunosuppressive treatment along with vasodilator therapy is the first chosen therapy method. In case of failure, rituximab, bosentan, and iloprost have been found effective.<sup>2-4</sup> Hyperbaric oxygen therapy (HBOT) is also used as primary or adjuvant therapy in such cases.

We report a case with refractory digital gangrene responding to HBOT used in combination with immunosuppressive and vasodilator agents, with

supporting therapies consisting of high dose vitamin C and omega-3 fatty acids.

## CASE REPORT

A 15 year-old girl admitted to rheumatology clinic with complaints of paleness and color change from white, purple, then to black of feet phalanges in two weeks. She had history of recurrent oral ulcers and photosensitivity without any medication and vaccination history. Family history revealed maternal type 1 diabetes mellitus.

On admission, she was complaining from pain assisting ischemic lesions at the distal part of the feet phalanges. She was 38 kg (<3<sup>rd</sup> percentile) and 151 cm (3<sup>rd</sup>-10<sup>th</sup> percentile). Physical examination revealed erythematous raised patches on her cheeks, dark bluish/purple discoloration of the feet phalanges without arterial pulsation on bilateral posterior tibial and dorsalis pedis arteries. There was no evidence of active cutaneous vasculitic lesion (Figure 1). The touch and pain sensations on distal phalanges of left foot were completely lost while sensory assessment of the right foot was normal. Muscle weakness was not noted. Systemic examination findings were normal.

Laboratory findings showed coombs negative mild anemia (hemoglobin level: 11 g/dL), leukopenia (3.800/mm<sup>3</sup>) and lymphopenia (1000/mm<sup>3</sup>). Thrombocyte count (255.000/mm<sup>3</sup>), serum biochemical and urine analyses, complement levels were normal. Laboratory examinations for evaluation of antibodies re-



FIGURE 1: The gangrenous lesions of phalanges.

vealed strongly elevated anti-dsDNA antibody and lupus anticoagulant. Viral serology and syphilis screening tests were negative. Thrombosis panel, osmotic fragility test and hemoglobin electrophoresis were normal. Chest X-ray, abdominal ultrasound, echocardiography ruled out the presence of serositis or other complications of the disease. Doppler ultrasonography and angiography showed complete occlusion and severe stenosis of bilateral lower extremity arteries behind tibial arteries.

She was diagnosed with systemic lupus erythematosus by American College of Rheumatology (ACR) classification criteria. Thrombolytic and anticoagulant therapies were initiated with immunosuppressants as corticosteroids, hydroxychloroquine and azathioprine.

Skin discoloration was reduced and there was a better demarcation border of viable and necrotic tissue after the first month of therapy. Control lower extremity color Doppler USG revealed biphasic flow pattern and decreased velocity at anterior-posterior tibial and dorsalis pedis arteries on the left side without thrombosed segments. The right lower extremity arteries and other arteries of the left lower extremity showed normal blood flow pattern and velocity. After that, anticoagulant therapy at prophylactic dosage, immunosuppressive therapy and anti-aggregating platelet therapy were continued. Intravenous high dose vitamin C (5 g/day) and omega-3 fatty acid (2 g/day) treatments as potent antioxidant and anti-inflammatory agents and nifedipine as a potent vasodilator were also added.

Both cardiovascular and plastic surgeons recommended amputation of gangrenous foot phalanges. To preserve phalanges, adjunctive HBOT was added to medical treatment. HBOT was administered in multiplace chamber, with sessions at 2.4 ATA, for 120 min, once a day, 5 days a week. After 15<sup>th</sup> session of HBOT, the edema and hyperemia around gangrenous lesions, demarcation line and the ischemic ulcer were completely resolved. Pain was significantly reduced. She was discharged with oral prednisone, hydroxychloroquine, azathioprine, acetyl salicylic acid, enoxaparin, nifedipine, oral omega-3, and vitamin C therapies. A total of 34 sessions of HBOT were applied in 7 weeks.

After 7 weeks course and total of 34 sessions, HBOT was well tolerated with no side effects and her phalanges exhibited marked improvement without amputation. At her last outpatient clinic control, the symptoms and clinical findings showed nearly complete recovery and she had gained weight (Figure 2). Her inflammatory indexes, blood count and complement levels are within normal limits and there have been no new attack of the disease so far.

Written informed consent was obtained from patient's family for publishing this case.

## DISCUSSION

Systemic lupus erythematosus is a multisystemic autoimmune disease. It is characterized with presence of antibodies and clinical manifestations with a relapsing and remitting course.<sup>5</sup>

Necrotizing vasculopathy is a rare life-threatening condition. The standard therapy includes systemic immunosuppressive and vasodilator drugs. Combination therapies are recommended for refractory cases. Although further studies are needed, some therapeutic options such as Rituximab, Bosentan, and Iloprost were found worth to try.<sup>2-4</sup> Acute administration of high dosages of vitamin C and omega-3 fatty acids are beneficial. The administration of hyperbaric oxygen is an effective and safe therapeutic option as an adjunctive therapy.<sup>6</sup>



FIGURE 2: The phalanges after treatment.

We present an adolescent diagnosed with lupus vasculitis that represented with refractory gangrenous lesions at feet phalanges. Although lesions improved under medical treatment, digital amputation was recommended. In order to prevent irreversible consequences of amputation, we added HBOT to medical therapy.

Undersea and Hyperbaric Medical Society defines HBOT as a treatment method in which a patient intermittently breathes 100% oxygen while the treatment chamber is pressured to a pressure greater than the sea level. The therapeutic principle of HBOT relies on increased partial pressure of oxygen in tissues when the oxygen is breathed under pressure. Treatment of decompression sickness with recompression therapy, fastening nitrogen washout and anti-hypoxic effects take an important role in the development of HBOT. There are more than 10 indications accepted worldwide at the development of HBOT.<sup>7</sup> HBOT had been successfully used for treatment of refractory vasculitic ulcers.<sup>2,6</sup>

Hyperbaric oxygen treatment restores neutrophil mediated killing of bacteria by increasing free radicals with bactericidal, bacteriostatic effects and increases effects of some antibiotics improving their oxygen dependent transport. These effects are useful in treating some severe aerobic and anaerobic infections such as chronic refractory osteomyelitis, necrotizing fasciitis and gas gangrene. It can provide adequate oxygen tension in hypoxic tissues essential for the formation of collagen matrix and angiogenesis in wound healing. It inhibits post-ischemic vasoconstriction and increases microcirculation.<sup>8,9</sup> It promotes healing in wounds with ischemic diabetic ulcers, nonhealing vasculitic ulcers and radionecrosis. It is generally safe and well-tolerated. Possible side effects are rarely seen and most of them are mild and reversible, such as air or sinus barotrauma, reversible myopia, and claustrophobia.<sup>10</sup>

In our patient, a total 34 sessions of HBOT in 7 weeks provided additional impact on resolution of the digital gangrene without amputation need.

Hyperbaric oxygen therapy as a safe treatment modality has an additive potential role in the man-

agement of hypoxic lesions in case of vasculitis. It may be considered as an adjunctive therapy when tissue hypoxia is a part of the problem.

### Conflict of Interest

Authors declared no conflict of interest or financial support.

### Authorship Contributions

**Concept:** Çiğdem Aktuğlu Zeybek, Ertuğrul Kıyıkım, Pınar Özge Avar Aydın; **Design:** Pınar Özge Avar Aydın, Ertuğrul

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