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THERAPEUTIC HOTLINE

Improvement of ulcerative pyoderma gangrenosum with hyperbaric oxygen therapy

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ABSTRACT: Pyoderma gangrenosum (PG) is a rare noninfectious destructive neutrophilic dermatosis of unknown origin affecting the skin and occasionally the subcutaneous fat. In this report, we present the results of intensive hyperbaric oxygen (HBO) therapy in a 62-year-old Greek woman who had been diagnosed with ulcerative PG two years ago, but had been resistant to other therapies.

KEYWORDS: hyperbaric oxygen, pyoderma gangrenosum, ulcers

Pyoderma gangrenosum (PG), first described by Brunsting et al. in 1930 (1), is a rare noninfectious destructive neutrophilic dermatosis affecting the skin and occasionally the subcutaneous fat (2,3). It is characterized by single or multiple, chronic, and recurrent painful cutaneous ulcerations with mucopurulent or hemorrhagic exudates (2). PG occurs most commonly on the lower legs with preference for the pretibial area, and in many cases is associated with inflammatory bowel disease, rheumatic or haematological diseases, and malignancies (2,3). Diagnosis of PG is based on history of an underlying disease, typical clinical presentation, histopathology (non-specific), and exclusion of other diseases that would lead to a similar appearance (2). Although etiology has not been clearly determined yet, the current accepted theory is that PG is an immunologic-based phenomenon (2,3). Several therapies have been used to control PG, with limited success, including systemic therapy, topical therapy, and surgical therapy (2–4). Hyperbaric oxygen (HBO) therapy had been explored and reported as successful in some patients whose disease had been resistant to other methods of treatment (3,4).

Here, we present the results of intensive HBO therapy in a woman with ulcerative PG resistant to previous therapy.

A 62-year-old Greek woman was admitted to Naval Hospital of Crete for programmed HBO therapy because of resistance to previous therapies for two painful PG ulcers, located on the anterior (PG Ulcer 1, FIG. 1A) and posterior (PG Ulcer 2, FIG. 2A) surfaces of her left lower leg, respectively. A final diagnosis of ulcerative PG without an

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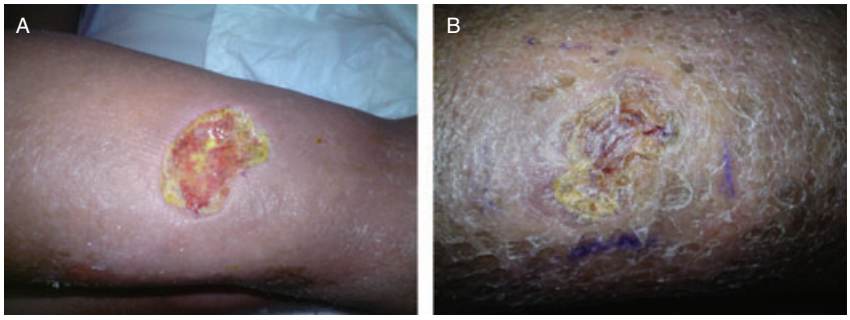

FIG. 1. **(A) PG Ulcer 1 before HBO treatment. (B) PG Ulcer 1 six weeks after HBO treatment.**

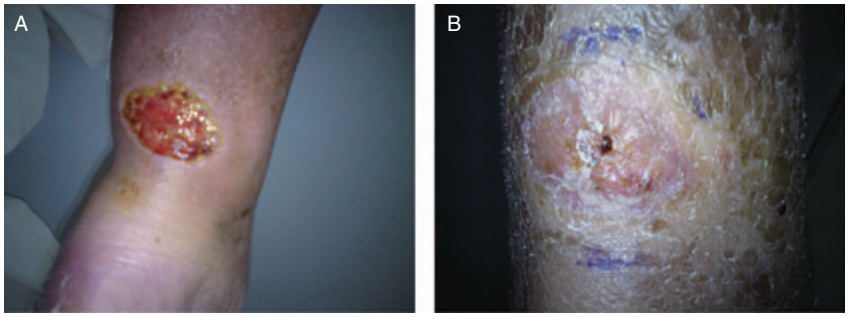

FIG. 2. **(A) PG Ulcer 2 before HBO treatment. (B) PG Ulcer 2 six weeks after HBO treatment.**

underlying disorder had been made two years after an extensive investigation in a dermatologic clinic. The disease started as painless multiple (four) small ulcers following skin trauma on the left and right legs, which progressively developed into painful and clinically apparent PG ulcers. Of the four PG ulcers, the clinical appearance of two (FIGS 1A and 2A) remained almost unchanged over the two years despite multiple therapeutic interventions, which included antibiotics, corticosteroids (continuous administration of prednisolone during the two years; 15 mg/day during the last 16 months) with prophylactic medication for osteoporosis (aledronate sodium and calcium carbonate), immunosuppressive drug (cyclosporine, 125 mg/day for the first three months and 75 mg/day for the following five months), tumor-necrosis factor alpha antagonist (etanercept, 100 mg/week during the last 16 months), and local/topical therapies. The remaining two PG ulcers (anterior surfaces of left crural and right tibia) improved during the previous therapies. The patient was not taking any medications at the time of presentation. The clinical examination, laboratory tests, and instrumental investigations prior to the HBO therapy showed no underlying disorder or extracutaneous involvement. An electrocardiogram, chest and foot radiography, spirometry, gastroscopy, colonoscopy, and abdominal and neck ultrasound scans were normal. A tuberculin skin test, immunological (antineutrophil cytoplasm auto-antibodies or ANCA and other auto-antibodies) and serological tests, such as tests for viruses, all proved negative. The antistreptolysin (ASTO) level, protein electrophoresis, coagulation panel, renal, liver and thyroid function tests gave results within the normal range, and multiple wound cultures were repeatedly negative for aerobic and anaerobic microbial agents. The patient herself discontinued receiving the combined medical therapy of oral methylprednisolone and etanercept two months prior to the initiation of the HBO treatment. Using the University of Texas Wound Classification System (5,6), which uses a matrix of wound grade (depth) and wound stage (infection and/or ischemia), the classification of our patient's ulcer was grade 2 (wound penetrating to tendon and capsule) and stage C (ischemic noninfected wound). The HBO treatment protocol consisted of 32 sessions over a period of six weeks with the administration of 100% oxygen for 90 minutes at 1.8 ATA (Atmosphere Absolute) for the first 22 sessions and then at 2 ATA for the remaining 10 sessions. The therapy had no side effects, and the patient tolerated the protocol very well. After the 32 sessions, an overall healing of the two ulcers was observed (FIGS 1B and 2B). So, our patient's new ulcers classification after HBO treatment was grade

1 (superficial wound through the epidermis or epidermis and dermis that did not penetrate to tendon, capsule, or bone) and stage A (clean wound). The patient did not receive any other medical treatment during HBO therapy. There was no recurrence at follow-up six months later.

HBO therapy is increasingly used in a number of areas of medical practice (7). The mechanism of action of hyperbaric treatments is attributed to the immediate direct physical effects of oxygen and other gases under pressure and to the delayed secondary physiological and biochemical effects that are set into motion with each hyperbaric treatment (7). HBO treatment can be used as an adjuvant therapy for patients with ischemic ulcers because of its double therapeutic action which is altering the hypoxia environment and promoting the oxygen-dependent steps of wound healing (3,6,7). It is known that wounds that fail to heal are typically hypoxic and angiogenesis occurs in response to high oxygen concentration (7). Fibroblast proliferation and collagen synthesis are oxygen dependent (3,7), and collagen is the foundational matrix for angiogenesis. In addition, HBO therapy is likely to stimulate growth factors involving angiogenesis and other mediators of the wound healing process (7). HBO also has been shown to have direct and indirect antimicrobial activity (8), such as anti-inflammatory and immunosuppressive properties (9). A review of medical bibliography reveals a beneficial role of HBO treatment in several PG case studies (3,10). However, the limited availability, expense, and time are relevant problems that must be undertaken by the patients.

Our patient had received medical agents in various combinations during the chronic course of PG. However, the HBO therapy was the only treatment that showed a quick improvement without any side effects against the established resistant PG ulcers. When considering the cost effectiveness of HBO therapy, we should compare it to both the high cost of other long-term treatments for the management of severe cases of PG, and to the patient in terms of suffering numerous side effects caused by the other treatments. The lack of major side effects and the relatively low cost of HBO therapy make this treatment beneficial for patients with nonhealing PG skin ulcers.

In conclusion, HBO treatment can be an efficacious and safe therapy for selected patients with PG ulcers resistant to the use of other therapies. Further clinical studies are needed to prove the real benefits of HBO therapy on PG and to develop a standardized treatment protocol.

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