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RELATO DE CASO

HYPERBARIC OXYGEN THERAPY IN THE ADJUVANT TREATMENT OF CUTANEOUS MANIFESTATIONS IN DERMATOMYOSITIS: A CASE REPORT

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Abstract

Cutaneous manifestations of dermatomyositis are unusual and difficult to treat. This study aimed to report a case of cutaneous manifestations of dermatomyositis treated with hyperbaric oxygen. We present a case of dermatomyositis in a 44-year-old female with pain ulcers in her left leg for 17 months, refractory to an exclusive clinical treatment, who underwent a hyperbaric oxygen therapy (HBOT) breathing O2 100%, 90 minute sessions, six days a week, at 2.4 ATA. HBOT therapy proved to be highly efficacious in wound healing in this case and HBOT should be considered as a treatment in the assistance given to such patients.
Keywords: Autoimmune diseases. Connective tissue diseases. Dermatomyositis. Hyperbaric oxygen therapy.

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OXIGENIOTERAPIA HIPERBÁRICA ADJUVANTE AO TRATAMENTO DA MANIFESTAÇÃO CUTÂNEA DA DERMATOMIOSITE: RELATO DE CASO

Resumo

Manifestações cutâneas da dermatomiosite são raras e difíceis de ser tratadas. O objetivo deste estudo é relatar um caso de manifestações cutâneas da dermatomiosite tratadas com oxigenioterapia hiperbárica, ocorrido em uma paciente de 44 anos, sexo feminino, com úlceras dolorosas em seu membro inferior esquerdo por 17 meses. O caso foi refratário ao tratamento clínico exclusivo e a paciente submetida a tratamento de oxigenioterapia hiperbárica (HBOT), respirando oxigênio a 100%, em sessões de noventa minutos, seis dias por semana, a 2,4 ATA. O HBOT mostrou ser altamente eficaz na cicatrização da lesão neste caso e deve ser um tratamento considerado no cuidado desses pacientes.

Palavras-chave: doenças autoimunes. Doenças do tecido conjuntivo. Dermatomiosite. Oxigenoterapia hiperbárica.

LA OXIGENOTERAPIA HIPERBÁRICA EN EL TRATAMIENTO ADYUVANTE DE LAS MANIFESTACIONES CUTÁNEAS EN LA DERMATOMIOSITIS: REPORTE DE UN CASO

Resumen

Las manifestaciones cutáneas de la dermatomiositis son inusuales y difíciles de tratar. El objetivo de este estudio fue reportar un caso de manifestaciones cutáneas de dermatomiositis tratadas con oxigenoterapia hiperbárica. Presentamos un caso de dermatomiositis en una mujer de 44 años con úlceras dolorosas en su pierna izquierda durante 17 meses, refractaria a un tratamiento clínico exclusivo, que se sometió a oxigenoterapia hiperbárica (HBOT) respirando O2 100%, sesiones de 90 minutos, seis días a la semana, a 2,4 ATA. La terapia con HBOT demostró ser muy eficaz en la cicatrización de heridas en este caso y la HBOT debe considerarse como un tratamiento en la asistencia brindada a estos pacientes.

Palabras clave: Enfermedades autoinmunes. Enfermedades del tejido conectivo. Dermatomiositis. Oxigenoterapia hiperbárica.

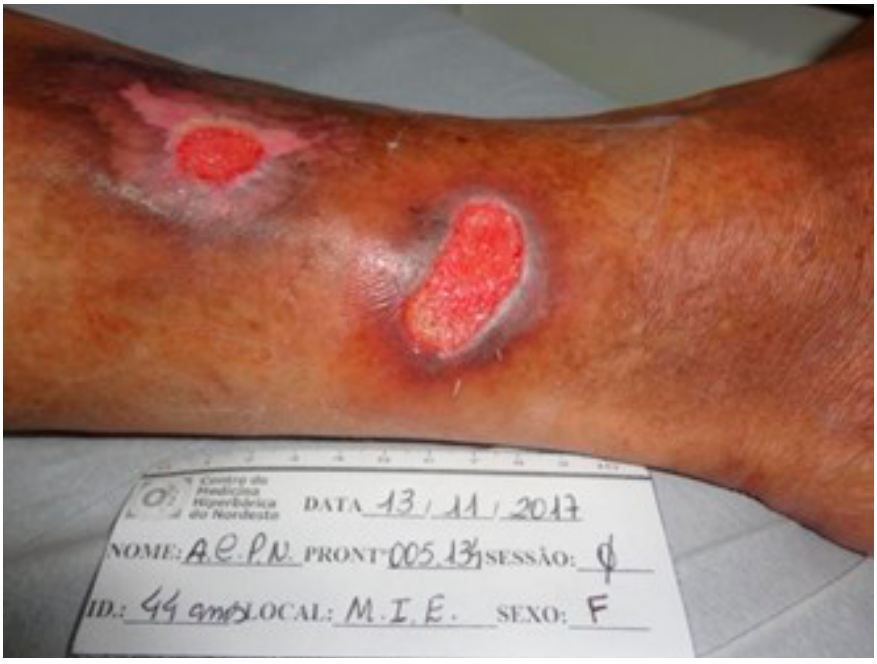
INTRODUCTION

Dermatomyositis is a chronic idiopathic inflammatory disorder that affects skeletal muscles, the skin, and other organs. Bohan and Peter[1] established the diagnostic criteria, and the patients may be classified into five groups: juvenile dermatomyositis, primary dermatomyositis, amyopathic dermatomyositis, dermatomyositis associated with malignancies and with other connective tissue disorders. It affects predominantly women, and the mean age of diagnosis is 40 years. Skin manifestations are observed in all patients. Loss of proximal strength is the most common systemic alteration, and lung involvement is normally found as interstitial pneumopathy. Neoplasms may be detected during the course of the disease, especially in patients older than 60 years. Lactic dehydrogenase serum levels are altered in the majority of cases, and diagnosis can be established on the basis of skin and muscle biopsies or electroneuromyography. Corticosteroids are the first-line drugs. For the treatment of refractory vasculitis skin ulcers the use of prednisone combined with other drugs such as methotrexate, azathioprine, cyclophosphamide or chloroquine is often recommended.

CASE REPORT

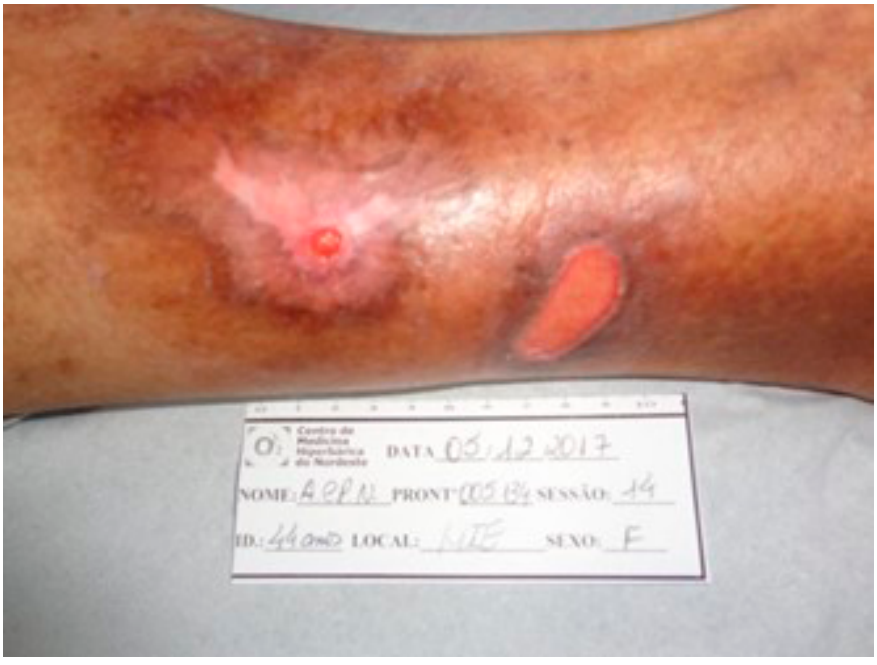
We report on a 44-year-old female with a history of dermatomyositis in 2013 with a violet-colored or dusky red rash on her face, eyelids, knuckles, elbows, knees, and with elevated levels of muscle creatine kinase (CK). Muscle biopsy revealed inflammation. During the mainstay treatment, prednisone, associated with azathioprine and chloroquine, was used until the myositis decreased clinically. In 2017 she had diabetes mellitus and cutaneous manifestations - ulcers in the left leg for 17 months refractory to exclusive clinical treatment with prednisone, diltiazem and methotrexate, without any improvement regarding the pain or wound healing in regular follow-up at the vascular department of Hospital Geral Roberto Santos, Salvador, Bahia, Brazil. At admission, the patient had two ulcers in the *lower* third of the *medial surface* of the left *leg*. The ulcers measured 5x4 cm and 4x3 cm with full thickness loss, involving damage of subcutaneous tissue and irregular borders (**Figure 1**). She was treated with hyperbaric oxygen therapy at the Centro de Medicina Hiperbárica do Nordeste (Center for Hyperbaric Medicine in Northeast Region), Salvador, Bahia, Brazil, breathing O2 100% at 2.4 atmospheres absolute (ATA). Treatment sessions lasted for 90 minutes each, six days a week (**Figure 2**). Pain relief was observed in the initial sessions. After two weeks the most proximal was wound healing. After 52 sessions the healing process of both wounds was complete (**Figure 3**).

Figure 1. At admission, the ulcers. Salvador, Bahia – 2017



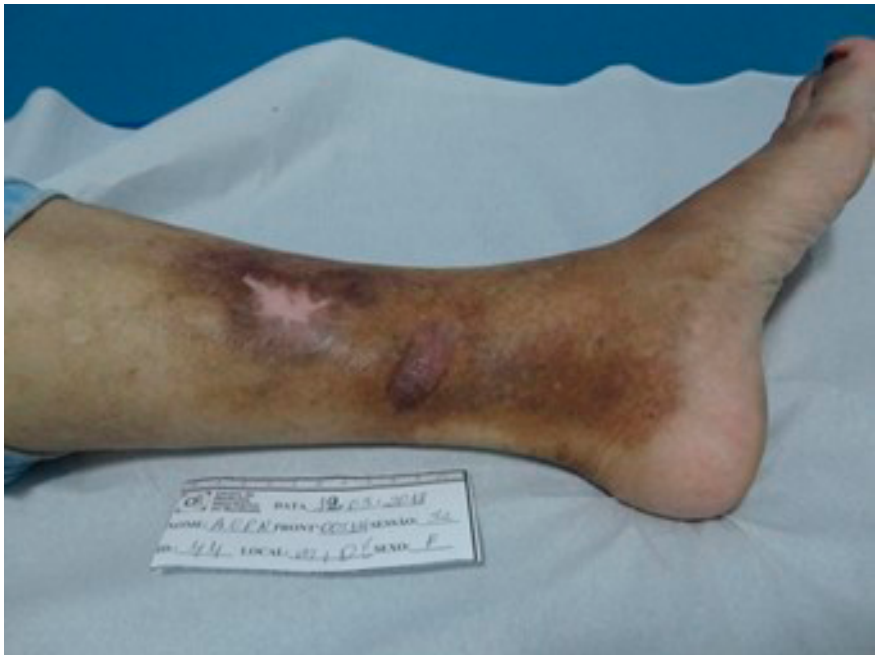
Source: Author's own elaboration.

Figure 2. After 2 weeks. Salvador, Bahia – 2017



Source: Author's own elaboration.

Figure 3. Fifty-two sessions: the ulcers healed. Salvador, Bahia – 2017



Source: Author's own elaboration.

DISCUSSION

Ulcerations in dermatomyositis are painful and difficult to treat. Manifestations of connective tissue diseases may have etiology of histocompatibility antigens, viruses, drugs and autoimmune. They are initially treated with oral steroid and immunosuppressive drug therapy and usually heal with oral treatment. For the treatment of vasculitis refractory, methotrexate, azathioprine, cyclophosphamide and chloroquine are recommended. HBOT therapy has been used for vasculitis refractory to clinical treatment[2,3].

Hyperbaric oxygen therapy breathing O2 100% at 2-3 ATA increases the oxygen level, thus altering the ischemic effect by reducing the local hypoxia, also increasing diffusion distance, reducing edema and modulating nitric oxide production. Repetitive treatments increase the vascularization of the lesion, increase both receptors of growth factors and growth factors, modulate the cytokines, have antibiotic effect by oxidative mechanism. It promotes cell proliferation, accelerates the deposition of collagen, stimulates the growth and folding of capillaries and modulates the response of the immune system as well. We used HBOT to promote the healing process in this situation since exclusive oral and topical treatment failed.

HBOT has been used in the treatment of critical leg ulcers to help throughout the healing process.

Mirasoglu et al.[4], in a retrospective analysis of 6 systemic sclerosis (SSc) patients who underwent HBOT for their extremely painful digital and leg ulcers — which were hard to heal, as SSc — used HBOT as an adjuvant therapy for treating chronic wounds as well as for nonhealing SSc wounds, which have a hypoxic nature; the latter may also benefit from it. Three patients had digital ulcers, and the other three had leg ulcers. Three patients (two with leg ulcers and one with a digital ulcer) had bilateral lesions. All of them were treated for at least one and a half months with various modalities. After HBOT was applied, four of the patients' ulcers healed completely and two patients had near-complete healing. In this series of cases, which has the largest number of patients up to now, adjunctive HBOT is shown to probably be helpful in the treatment of SSc ulcers.

Chia and Tang[5] — in a retrospective review on the results of chronic leg ulcers in patients with rheumatic diseases — described the epidemiology, clinical features and outcome of chronic leg ulcers in this group of patients. 29 patients with underlying rheumatological conditions, such as rheumatoid arthritis (15 patients), systemic lupus erythematosus (8 patients), overlap syndromes (3 patients), systemic sclerosis (1 patient) and ankylosing spondylitis(1 patient) were included. The ulcers were mostly around the ankle (55.2%) and calves (37.9%). The predominant etiology of the ulcers, in a decreasing frequency order, was venous disease, multifactorial, vasculitis or vasculopathy, infective, pyoderma gangrenosum, ischemic and iatrogenic microangiopathy. Treatment modalities included aggressive wound bed preparation, compression therapy (17 patients), changes in immunosuppressive therapy (15 patients), hyperbaric oxygen therapy (4 patients) and cellular skin graft (2 patients). Management of chronic kidney ulcers in rheumatological patients is challenging and the importance of careful clinicopathological correlation together with the treatment of the underlying cause cannot be underemphasized.

Systemic vasculitis is a frequent cause of non-healing skin ulcers, which have a significant impact on co-morbidity, mortality, and therapeutic costs. By altering the local hypoxic conditions, HBOT can facilitate wound healing and energy-consuming processes. In addition, hyperoxia has an anti-inflammatory effect on the vessel. HBOT has been used for a long time with antibiotics, debridement and revascularization in the treatment of chronic non-healing wounds associated with diabetes or non-diabetic vascular insufficiency, but its use in conditions such as vasculitis is still poorly reported.

In Canada, Huber et al.[6], a group of The Hospital for Sick Children in Toronto, recommends oral prednisone divided into three daily doses for approximately six weeks for diabetes mellitus treatment (DM). If the goal is not achieved in three months, cyclosporin or

intravenous gamma globulin (GG) is added. Azathioprine and hydroxychloroquine can also be used with a positive response, especially in skin conditions. More recently, good results have been obtained with mycophenolate mofetil. Oral or subcutaneous methotrexate (at the mean dose of 15 mg / m2 / week) or intravenous cyclophosphamide are used as base drugs depending on the initial severity of the case. For more severe and refractory cases, with a predominance of cutaneous ulcers, cyclophosphamide has led to good results, with no evidence of short-term toxicity. Nevertheless, the use of cyclosporine is based on efficacious findings in a series of cases. A comparative study with GG alone and its association with methotrexate or cyclosporine is ongoing. Another series of refractory JMD cases showed a good response to cutaneous manifestations with the use of tacrolimus. Although cutaneous remission was not reached, there was progress regarding myalgia and normalization of muscle enzymes despite no gain in muscle strength, possibly due to severity, chronicity and failure of previous treatment.

Before treatment with prednisone, the mortality rate was 50%. Currently, it has dropped significantly.

In 2006, Efrati et al.[7] published an interesting study on the use of HBOT in 35 patients with vasculitis-induced severe ulcers, which did not heal despite the intense immunosuppressive treatment. The baseline treatment protocol consisted in breathing O2 100% at a pressure of 2 minutes for 90 minutes, five times a week for 4 weeks. Additional sessions were planned in for selected cases. After HBOT, 28 patients (80%) showed complete cure and four showed partial cure; only three of the patients did not respond and none of the patients experienced any HBOT-related side effects. Oxygenation of the ulcer tissue was assessed by measuring transcutaneous oxygen pressure (TcPO2) using a pulse oximeter before and after HBOT. A significant increase in TcPO2 after HBOT was identified, which explains the high response rate. Interestingly, no significant differences in baseline characteristics or tissue oxygenation were observed between non-responders and those patients whose wounds had completely healed. It is, therefore, difficult to predict who will benefit from HBOT, and additional studies are needed for clarification. Hyperbaric oxygenation in 2-2.5 minutes completely oxygenates hemoglobin, and the amount of oxygen dissolved in the plasma increases more than tenfold, thus exceeding the oxygen needs of the tissues. As a result, HBOT generates a positive gradient for the diffusion of oxygen from functional capillaries to sites of ischemic tissue and, by altering local hypoxia conditions, it facilitates the healing of wounds.

Akcali et al.[8] observed cutaneous leukocytoclastic vasculitis (clcv), which is a disorder characterized by the inflammation of the small vessels of the skin, in their study. Clcv may cause recurrent, drug-resistant, non-healing ulcers. They present a patient with

a recalcitrant ulcer caused by clcv who was successfully treated with hyperbaric oxygen therapy and skin grafting. A particular therapy that can heal all type of wounds does not exist. They can achieve better results provided that wound care products and advanced treatments are used at the right time.

In this study, Olivieri et al.[9] show that skin ulcers are a dangerous and uncommon complication of vasculitis. They describe the case of a teenager suffering from systemic lupus erythematosus with digital ulcer resistant to conventional therapy, treated successfully with hyperbaric oxygen therapy. The application of hyperbaric oxygen, which is used for the treatment of ischemic ulcers, is an effective and safe therapeutic option in patients with ischemic vasculitic ulcers, when associated with immunosuppressive drugs. Further studies on hyperbaric oxygen are needed to evaluate its role as a primary therapy for this group of patients.

Rossi et al.[10], at the Rheumatology Unit at Instituto da Criança, Hospital das Clínicas, Medicine School, Universidade de São Paulo, between 1996 and 2002, followed up six patients who underwent hyperbaric oxygen therapy. This therapy was prescribed for the presence of chronic osteomyelitis and tissue ulcer (vasculitis or infection) not responsive to the usual treatment. Two patients presented cutaneous polyarteritis, two others presented recurrent multifocal chronic osteomyelitis, one presented diffuse cutaneous scleroderma and one presented pyoderma gangrenosum. Five patients were girls (aged from 6 to 13.2 years old). The sessions of hyperbaric oxygen therapy were performed under pressures that varied from 2.4 to 2.8 absolute atmospheres and their duration was of two hours. The lowest number of sessions was 18 and the highest was 80. Five patients presented complete resolution of the injuries. The patient with cutaneous scleroderma suspended the treatment after the 18th session because she went back to her hometown with partial improvement of the cutaneous injuries. The hyperbaric oxygen therapy was efficient and well tolerated by the patients with rheumatic diseases and ulcerated injuries by vasculitis, infected injuries or chronic osteomyelitis.

In our case, even though the patient was using prednisone and methotrexate, the ulcer remained open and the adjuvant treatment with HBOT initially caused ease of the pain and then wound healing, which is an excellent result for a long-term ulcer and refractory to the clinical treatment. The mechanisms of hyperbaric oxygen therapy action included proliferation of the epithelium, formation of granulation, stimulation of fibroblasts, increased production of collagen, capillary angiogenesis and alteration of the damaged tissue, thus aiding tissue healing.

We did not observe adverse event during the sessions, either inside the chamber or related to the duration of the session. Spandrel perforation or other adverse events were not observed either. Hyperbaric oxygen therapy proved safe and effective.

CONCLUSION

This case shows that hyperbaric oxygen therapy (HBOT) should be considered in the assistance of such patients. Further research should focus on identifying patients who can benefit from HBOT, also defining the optimal time for the intervention as well as drawing up specific dose-response curves for each condition. The authors state that no conflicts of interest exist in this paper.

PARTICIPATION

1. Project design, analysis and interpretation of data: Cristiane Antequeira Maran, Pollyana Acioli Milazzo and Paulo Sergio Rodrigues de Farias.

2. Writing of the article and critical review of its intellectual content: Cristiane Antequeira Maran and Pollyana Acioli Milazzo.

3. Review and/or approval of the final version to be published: Cristiane Antequeira Maran and Paulo Sergio Rodrigues de Farias.

4. Responsible for all aspects of the study, ensuring accuracy and integrity in any of its sections: Cristiane Antequeira Maran and Paulo Sergio Rodrigues de Farias.

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