Etiologic role of *Borrelia burgdorferi* in morphea: A case report

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Abstract. Morphea is an inflammatory skin disease with self-limited evolution, presenting as localized sclerosis of the skin and/or underlying tissues. The incidence is not exactly known; the disease occurs more frequently in women, and there is no sex prevalence. Pathogenesis of morphea remains still controversial. Several theories exist and the *Borrelia burgdorferi* infection is not yet elucidated. The aim of this report is to present the main mechanisms involved in the etiophatogenesis of morphea and also the thepapeutic options. A case of a 60-year-old woman is presented, who was referred to the clinic for an erythematous-violaceus, asymptomatic eruption, located on the trunk and legs, for appoximately 2 months. The patient's medical history revealed an infection with *Borrelia* 1 year previously. After diagnosis of morphea was established, and with systemic therapy (corticosteroids and methotrexate), the evolution was favorable.

Introduction

Mophea, also known as localized scleroderma (LSc) or circumscribed scleroderma, is an inflammatory cutaneous condition, characterized by localized sclerosis of the skin (1). Morphea presents as single or multiple inflammatory or sclerotic plaques, which are usually active for 3-6 years (2). This skin condition presents in several clinical forms: plaque (circumscribed), generalized, linear (en coup de sabre) and deep morphea. Also, we can classify morphea in: superficial (primarily dermal) or deep (involving the deep dermis plus the subcutis, fascia, and/or bone) (3). In most cases, the diagnosis of morphea is clinical. Sometimes, the histopathological examination may be useful (4). The treatment depends on the stage and extension of morphea (5).

Case report

A case of a 60 year-old woman is presented, who was referred to the Dermatology Clinic for an evaluation of erythematous-violaceus, asymptomatic eruption, located on the trunk and legs, in evolution for 2 months. Her medical history revealed an infection with *Borrelia burgdorferi* (1 year previously) (Fig. 1), and dyslipidemia. The patient was informed of the study and written informed consent was obtained from the patient.

Physical examination showed grade II obesity. Clinical examination revelead numerous erythematous-purple plaques, indurated, relatively well delimited, with irregular edges, with central atrophy, diameter 2-7 cm, disseminated at the level of the trunk and lower limbs (Fig. 2).

Routine laboratory tests revealed inflammatory syndrome and dyslipidemia. Radiological examination and abdominal-pelvic ultrasound were within normal limits. Because a form of morphea was suspected, several autoantibodies were evaluated and antinuclear antibody serum levels were elevated; anti-single-stranded DNA (ssDNA), anti-double-stranded DNA (dsDNA), antihistone, anti-topoisomerase IIα and antiphospholipid antibodies were negative. The medical history of our patient revealed infection with *Borrelia*, which is known as an etiologic factor of morphea.

Generalized morphea was suspected, so a skin biopsy from a lesion was prelevated, and the histopathological examination revealed moderate orthokeratosis and minimal epidermal basal pigmentation; at the dermal level, areas of fibrosis were identified, which focally compressed the attached structures (ducts and sweat glands); minimal inflammatory lymphocyte inflitrate, predominantly perinaexial or perivascular; papillary

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Abbreviations: LSc, localized scleroderma; ssDNA, anti-single-stranded DNA; dsDNA, anti-double-stranded DNA

Key words: morphea, *Borrelia burgdorferi*, corticosteroids, methotrexate

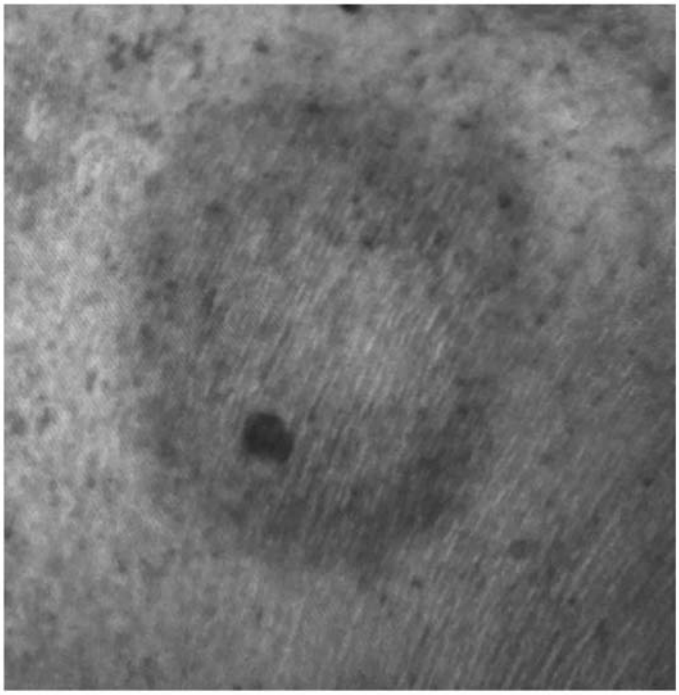

Figure 1. Infection with *Borrelia* (erythema migrans).

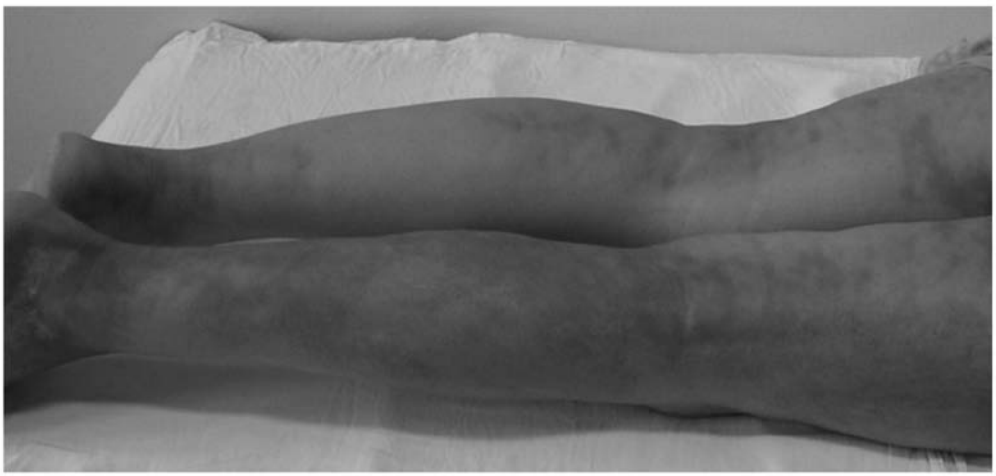

Figure 2. Multiple indurated plaques, on the lower limbs.

dermis with homogenized appearance and turgid capillaries. The histopathological findings supported the clinical diagnosis of morphea. Corroborating the clinical, paraclinical data and histopathological examination, the final diagnosis of generalized morphea was establised.

The patient was hospitalized, and systemic treatment initiated with corticosteroids (prednisolone 1 mg/kg per day, slowly decreasing), associated with gastric protection and methotrexate 15 mg/week, administered subcutaneously. This treatment was chosen because there were multiple, indurated, and disseminated lesions. As local treatment, the patient applied tacrolimus 0.1% ointment. During hospitalization, the evolution was favorable, with improvement of lesions. Upon discharge, continuation of prednisolone in decreasing doses, with gastric protection, continuation of the same dose of methotrexate, and local treatment were recommended.

Four weeks after discharge, our patient presented to evaluation, the evolution was favorable, with improvement of injuries and induration. Moreover, there was no more inflammation of the lesions. The recommendations were: continuing the cortizonic treatment, with decreasing doses as in the initial scheme, under gastric protection; keeping the same dose of methotrexate and local treatment.

Discussion

The etiopathogenesis of morphea is not well understood. Drugs, local trauma, environmental toxins or infections may be involved in the pathogenesis. There are two processes that trigger the disease: abnormal fibroblast function and immune dysfunction resulting in autoimmunity (6). The possible mechanism involved in pathogenesis of morphea, also in

our patient, may be the infection with *Borrelia burgdorferi*. According to some authors, increased levels of antibodies against this organism, was higher in patients with morphea compared with controls. They also identified *Borrelia* DNA in skin biopsies of patients with morphea, using polymerase chain reaction (7-9). This theory is quite controversial, because other studies did not show any association between morphea and *Borrelia* (10). A review concluded that *Borrelia* infection may not be involved in triggering morphea, or that only some species of *Borrelia* that live in few countries in Europe and Asia may lead to developing this skin condition (11). However, this subject remains to be further studied: some authors suggested that *Borrelia* may be responsable for morphea, as they reported a case of a patient with morphea and this infection (12).

In some cases of morphea, the diagnosis of certainty is established by histopathological examination. A skin biopsy can be taken from the inflammatory margin or from the central sclerosis. It is always important to take the biopsy with subcutaneous fat, because the changes are seen at the border between the dermis and subcutaneous fat. At the inflammatory border, interstitial and perivascular inflammatory cell infiltrate is found (lymphocytes, plasma cells, eosinophils, mast cells, macrophages). In contrast, the atrophic phase reveals loss of inflammatory cell infiltrate, less sclerosis and absence of appendageal structures. Some authors suggested that patients with a histopathological pattern of sclerosis were associated with pain more often than others (4).

The treatment of morphea varies depending on the severity of the disease. Circumscribed lesions respond well to low-concentration dermatocorticoids, intralesional corticosteroids, topical tacrolimus or topical calcipotrione (13). In moderate-to-severe disease (for example, generalized morphea), first line therapy is represented by methotrexate, with or without corticosteroids (14). In non-responsive patients, other systemic treatments may be beneficial: mycofenolate mofetil, colchicine or cyclosporine (15). Infliximab, an anti-TNF-α agent, is a human-murine chimeric drug, composed by a constant human region and a variable mouse region (16,17). Althought a report of a clinical case responding to this biologic agent exists, there are not enought data to support the efficacy of this drug (18).

Patients need to be educated on their comorbidities. In case of our patient, who had associated dyslipidemia and obesity, it was important to inform her of the risks of visceral fat level (especially when treatment with methotrexate was administered) (19).

Morphea is a chronic disorder, with periods of exacerbations and remissions. It is important to follow up the patients with morphea: every 2-4 months during the first year. After the disease is under control, one visit each 6 months is sufficient. Followed by one control per year, for clinical evaluation should be enough. Whereas, if the disease is getting worse, the patient should immediately present to examination (20).

In conclusion, the etiophatogenesis of morphea is not yet elucidated. Several mechanisms may be involved, and the infection with *Borrelia burgdorferi* may be one of them. This is why the medical history of the patient is very important. The treatment of morphea varies depending on the severity of the disease and follow-up of these patients is required.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

FS was involved in the writing of the manuscript and was responsible for the patient follow up based on clinical and paraclinical examinations. APo was involved in the conception of the case study. APe analyzed the data from literature regarding the etiologic role of *Borrelia burgdorferi* in morphea and was involved in the writing of the manuscript. RGM was responsible for the figures and the final aspect of the manuscript. MMC analyzed the histological characteristics of the lesions and was responsible for the writing of the relevant section of the manuscript. RCP analyzed the main mechanisms involved in the etiophatogenesis of morphea and was responsible for the writing of the relevant section of the manuscript. TC examined the patient and wrote the section regarding the clinical examination of the lesions. MCD was involved in the conception and writing of the manuscript. All authors critically revised the manuscript and approved the final version to be published.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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