Morbihan disease: a therapeutic challenge*

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Abstract: Morbihan disease is a rare condition characterized by chronic and persistent erythematous solid edema localized on the face. It is believed to be a complication of rosacea and may occur at any stage of the disease. Features of this condition include variable therapeutic response and great refractoriness. We report a case of a 61-year-old man with rosacea history diagnosed with Morbihan disease, who showed excellent therapeutic response with the combination of deflazacort and oral isotretinoin but developed recurrence after corticosteroid discontinuation. We believe that in severe cases of lymphedema of the face this combination is effective and corticosteroid suspension should be done slowly and gradually.
Keywords: Glucocorticoids; Isotretinoin; Lymphedema; Rosacea

INTRODUCTION

Morbihan disease is a rare entity with only a few cases reported in the literature. It is characterized by a chronic and recurrent pattern of erythema and symmetrical facial edema, mainly located in the middle and upper thirds of the face (malar regions, nose, glabella, eyelids, and forehead). The evolution of the condition results in deformity of facial contours and even in visual changes.[1]

CASE REPORT

A 61-year-old Caucasian man reported a 20-year history of rosacea, which evolved over the past two years to erythematous, with painless and persistent edema on the face (Figure 1). He complained of a hot sensation on his face and was unhappy with the cosmetic aspect. He reported no visual complaints. He had previously been treated with oral isotretinoin for six months (he was not able to inform the dose he used), with partial response during use and relapse after drug suspension. Laboratory tests were normal. Histopathological examination is shown in Figure 2. The patient started on isotretinoin (20mg – 0.3mg/kg) and deflazacort (30mg) with excellent therapeutic response after one month (Figure 3). Isotretinoin was maintained, and the corticosteroid was discontinued after one month of use, with recurrence occurring within a few days. Topical metronidazole and later oral metronidazole were then associated, but we observed no improvement. We increased the dose of isotretinoin to 40mg (0.5mg/kg), but with no improvement either. Finally, we reintroduced the systemic corticosteroid (deflazacort 30mg/daily) and maintained isotretinoin (20mg/daily), with significant improvement of the erythema and lymphedema of the face, recommending that a slow and gradual withdrawal of the medication should be done.

DISCUSSION

Morbihan disease affects Caucasian adults of both genders and is considered by most authors as a clinical variety or complication of acne or rosacea. However, it is unclear whether it is a distinct disease and may occur in patients without clinical manifestations of rosacea.[2,3] The term "Morbihan" refers to a district of France where the first French patient was observed by Robert Degos in 1957.[1]

Other nomenclatures include rosacea lymphoedema, solid

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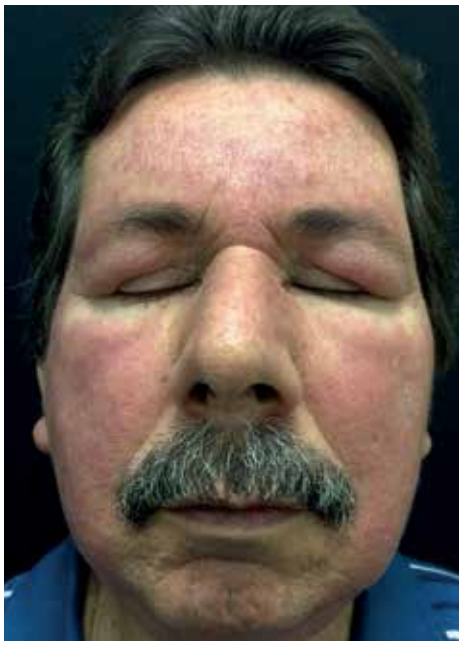

Figure 1A: Facial fixed erythema and edema, altering facial contours, and telagiectasias, before starting treatment

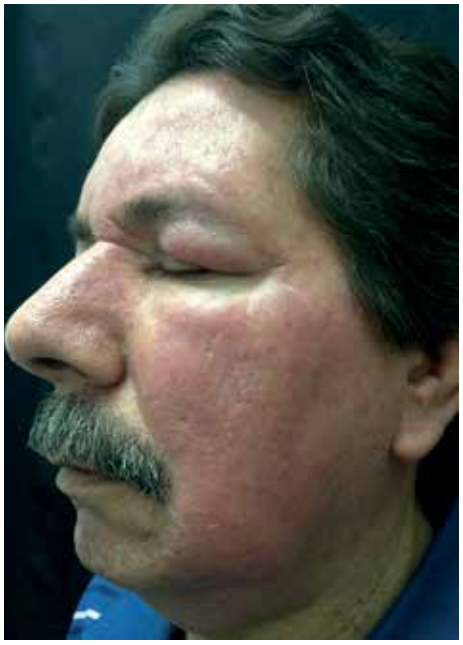

Figure 1B: Side view of the face before starting treatment

persistent facial edema, and morbus Morbihan.[2,4] The typical finding of Morbihan's disease is non-depressive edema of the upper two thirds of the face, with no tendency for spontaneous regression.[5] However, pitting edema may be evident in its early stages and the typical solid edema appears after fibrotic induration that occurs due to recurrent inflammation.[2,6] The facial erythema is described as poorly defined or as discrete patches or isolated plaques.[2] Its evolution is initially fluctuating but becomes permanent with time, leading to disfigurement of facial contours.[7] Eye involvement with rosacea is common, especially in the form of blepharitis and conjunctivitis. Al-

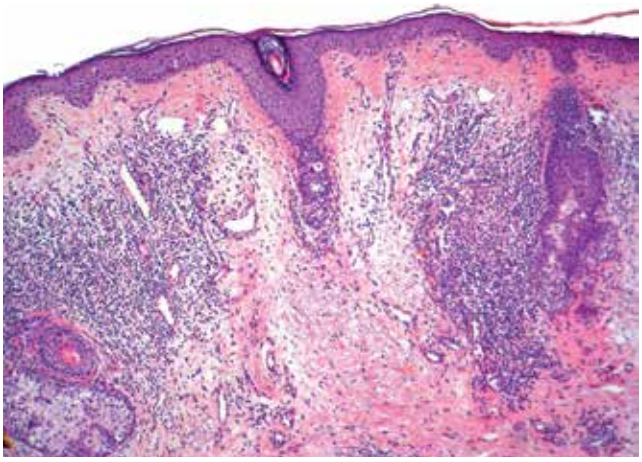

Figure 2A: Preserved epidermis; dermis with edema between collagen fibers, dilated vessels with telangiectasias and lymphocytic infiltrate (Hematoxylin & eosin, X40)

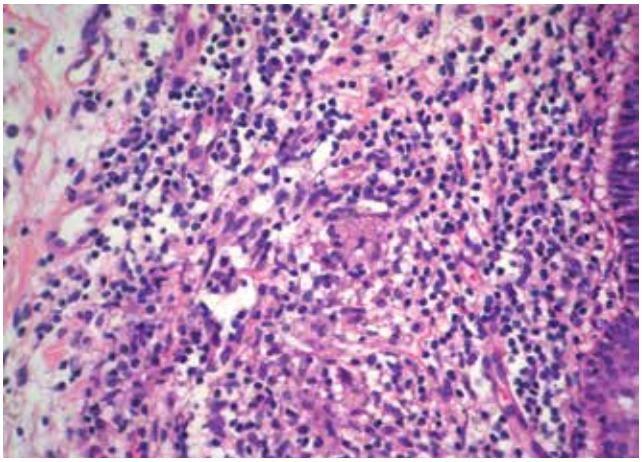

Figure 2B: Lymphocytic infiltrate in the dermis with few plasma cells, mast cells and granulomas, as well as Langhans giant cells (Hematoxylin & eosin, X400)

though reported, lymphedema of the eyelids is a rare complication.[8]

The etiology of Morbihan disease is uncertain. Clinical manifestations are presumably caused by derangement of local cutaneous vascularization and disbalance between lymphatic production and drainage.[3,9] There are indications of the association between Morbihan disease and rosacea. Vasodilation and chronic inflammation accompanying rosacea can lead to the destruction of collagen and elastic fibers around the blood vessels in the dermis, resulting in increased vessel permeability and fluid transudation. With chronic evolution, permanent obstruction of lymphatic vessels or fibrosis in the dermis induced by mast cells leads to lymphedema of the underlying tissue.[2,5,6,8-10] Histochemical and immunohistochemical studies show that more than one-third of dilated vessels in lymphedematous skin are lymphatic vessels. Recently, findings such as the increase in D2-40 expression in the lymphatic endothelium of the skin affected by rosacea suggest that the lymphangiogenesis process

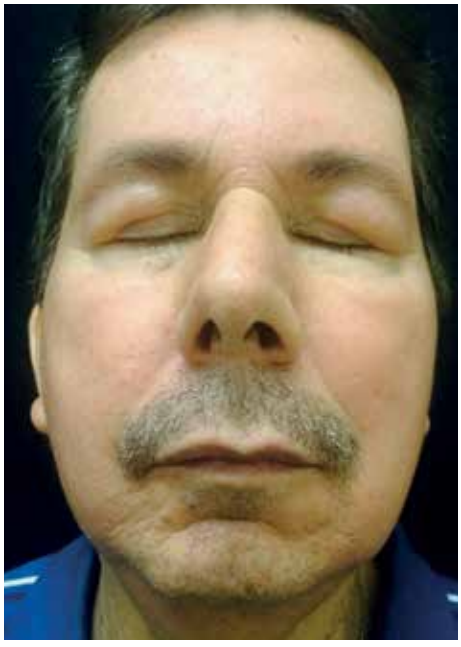

Figure 3A: Excellent improvement of erythema and lymphedema after a month of treatment with isotretinoin and deflazacort

Figure 3B: Side view of the face after the first month of treatment

is early involved in the pathogenesis of rosacea.[6]

Histopathological findings are non-specific and poorly described in the literature. They include edema in the dermis, dilated blood vessels, presence of lymphocytes, neutrophils, and perivascular and perifollicular histiocytes, perifollicular fibrosis, and, rarely, an increase in the number of mast cells.[2,5,7,9] Nagasaka *et al.* also reported the formation of granulomas around dilated lymphatic vessels and luminal obstruction by histiocytic infiltration.[2,9] However, only a few reports reveal granuloma in the dermis. What could explain the absence of granuloma formation in the dermis in previous investigations is the lack of biopsies deep enough to confirm lymphatic involvement and the possibility of Morbihan disease occurring at any stage of rosacea.[5]

Another feature of Morbihan disease is the absence of systemic manifestations and laboratory abnormalities. Clinical history and complete physical examination are important in order to exclude differential diagnoses, which include systemic lupus erythematosus, angioedema, chronic actinic dermatitis, chronic contact dermatitis, dermatomyositis, sarcoidosis, and Melkersson-Rosenthal syndrome.[2,3]

Treatment options for Morbihan disease reported in the literature are isotretinoin, systemic antibiotics (tetracyclines, metronidazole), antihistamines (ketotifen), and systemic corticosteroids (prednisone, prednisolone). Clofazimine and thalidomide are also reported.[1] Although about 20% of patients may not respond to oral isotretinoin, it is considered the first-line of therapy.[1] In 2014 Smith and Cohen showed good results with isotretinoin alone (40mg-80mg/day) for a prolonged period (9-24 months), with no documented recurrence in the five patients reported.[2] Our patient showed no significant improvement with isotretinoin alone. Other studies report the association of isotretinoin with ketotifen or clofazimine, prednisolone with metronidazole and ketotifen, and doxycycline with prednisolone, with variable outcomes.[5,7,9,10] The association of deflazacort with oral isotretinoin, a regimen used in our study, was not found in the literature. Despite the excellent therapeutic response, we observed a relapse after corticosteroid suspension after one month of use. We believe that in severe cases, with significant lymphedema of the face, like that of our patient, corticosteroid withdrawal should be slow and gradual. Surgical procedures, such as blepharoplasty, may be useful in refractive cases.[5]

The pathogenesis of Morbihan disease is still unclear. Only a few therapeutic options are reported with uncertain results and a high index of refractory cases. However, we believe that early diagnosis and treatment are essential to avoid irreversible lymphatic damage. The association of deflazacort with isotretinoin showed to be effective in our patient, but we should monitor him longer to observe possible relapse after the suspension of treatment. ❑

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