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CASE REPORT

Successful treatment of a Morbihan's disease patient after a therapeutic challenge: A case report and comprehensive literature review

Afsaneh Sadeghzadeh Bazargan MD[1] | Ali Zare Dehnavi MD[2] | Abbas Dehghani MD[1] | Kambiz Kamyab Hesari MD[3] | Paria Jafari MD[1] | Azadeh Goodarzi MD[1]

[1]Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences (IUMS), Tehran, Iran

[2]Tehran University of Medical Sciences, Tehran, Iran

[3]Department of Dermatopathology, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran

Correspondence
Azadeh Goodarzi and Abbas Dehghani, Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences (IUMS), Niayesh Street, Sattar Khan Avenue, Tehran 1445613131, Iran.
Email: goodarzi.a@iums.ac.ir; azadeh_goodarzi1984@yahoo.com and dehghani.aba@iums.ac.ir; dehghani.abs@gmail.com

Abstract

Morbihan's disease is a rare condition characterized by chronic facial edema. While its exact cause is unknown, it is thought to involve local cutaneous vascularization and lymphatic drainage imbalance. Traditional treatment options are often ineffective, and no established efficient treatment exists. We present a case study of a 17-year-old male with Morbihan's syndrome who showed resistance to traditional treatments but responded well to a combination of cromolyn sodium nasal spray and oral montelukast after histopathology revealed hyperplasia of plasma cells and mast cells. This combination has not been used before for Morbihan's syndrome. Our review of the literature also provides insight for clinicians seeking to manage this condition.

KEYWORDS
adult's Morbihan disease, cromolyn sodium, mast cell, montelukast, Morbihan syndrome

1 | INTRODUCTION

Morbihan's disease (MD) is a rare condition characterized by persistent, nonpitting, nontender, and symmetrical lymphedema over the upper half of the face.[1] As a result of the lack of specific laboratory or pathologic findings, the diagnosis is mainly made according to the patient's clinical presentation and exclusion of another differential diagnosis.[1]

In respect of histopathology, dilated lymphatic arteries, dermal edema, perivascular and perifollicular infiltrates of lymphocytes, neutrophils, and in certain cases, mast cells as well as perilymphatic granulomas, have all been reported.[2] All of them, on their own, can be detected in a variety of cutaneous illnesses and therefore are considered somewhat unspecific.[2] Since its physiopathology is unknown, treatment management is challenging and no treatment guideline has been defined yet.[3]

Various topical and systemic medications have been used, generally with poor outcomes. In this study, we report an MD case that was not responsive to classic treatment options and finally was treated based on biopsy findings after a therapeutic challenge.

2 | CASE REPORT

A 17-year-old boy was referred with a history of intermittent, painless, and bilateral facial edema on the upper and midface from 1 year ago, which has recently become more severe and persistent. He had a history of acne vulgaris (Figure 1A). The patient did not mention a history

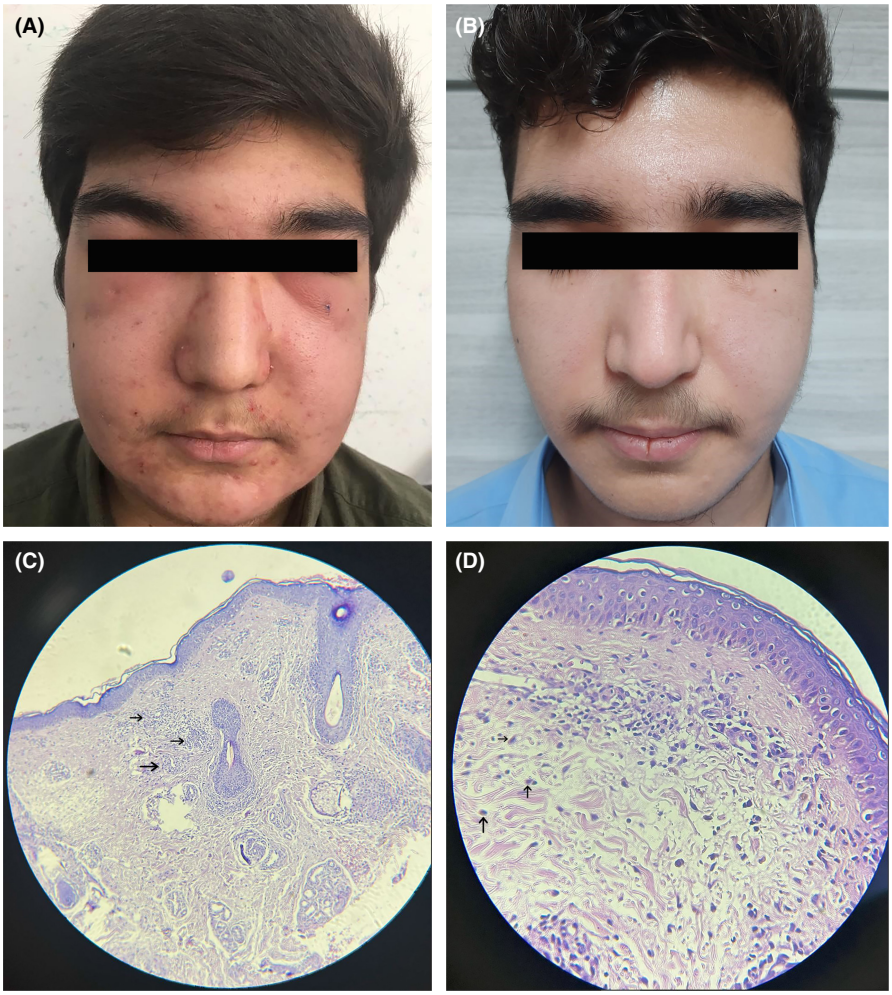

FIGURE 1 (A) Edema of the face especially eyelids with visual impairment, also sparse papules and pustules. (B) A dramatic response after adding cromolyn sodium nasal spray and oral montelukast. (C) Low power (10×) magnification shows edema with variable fibrosis, loose granuloma, and perivascular lymphocytic (arrows) infiltration in upper to deep dermis. (D) High power (40×) magnification shows mast cells (arrow), plasma cells, and polymorphonuclear cells hyperplasia is seen.

of facial erythema against heat, flushing attacks, and symptoms related to rosacea disease. Also, he did not have any history of alcohol consumption. He was otherwise healthy and did not take any medication. Examination showed prominent erythematous, firm, and non-tender edema of the face especially eyelids with visual impairment.

Laboratory tests especially for collagen vascular disorders and imaging (orbital MRI and chest X-ray) were normal. Before any treatments, the patient underwent a 3 millimeters punch biopsy with suspected MD from about 2 cm below the lower eyelid of the left eye. The clinical diagnosis was confirmed by histopathology that revealed edema with variable fibrosis, loose granuloma, and perivascular infiltration of lymphocytes with hyperplasia of plasma cells and mast cells (Figure 1C,D).

The patient started on isotretinoin (20 mg every other day) and prednisolone (25 mg daily) but because of elevated triglycerides level, the dose of isotretinoin was reduced to 20 mg weekly, and clofibrate 500 mg daily was started. As the clinical condition improved, the dose of prednisolone tapered within 2 months, but with 10 mg per day, the edema increased gradually.

Therefore, along with isotretinoin 20 mg weekly and prednisolone 10 mg daily, we administered colchicine 1 mg once daily, as well as microneedling and intralesional injection (4 mg/mL) with triamcinolone monthly. Triamcinolone 40 mg/mL was diluted with lidocaine 2% 1:10; 1 cc of the solution was injected intradermally into the lesion, and 1 cc of this solution was used in microneedling the lesion. At first, facial edema decreased relatively but despite these treatments, the disease recurred after 3 months significantly, so the protocol of treatment changed.

The patient was treated with cromolyn sodium nasal 2% spray twice a day and oral montelukast (10 mg daily), so a dramatic reduction was seen in the facial edema after 3 weeks of the treatment (Figure 1B). We could discontinue prednisolone over 2 months and isotretinoin was maintained. No recurrence occurred for the patient during the 1 year follow-up. Since the biopsy site was on the face, the patient refused to allow us to do a second biopsy after healing. As a result, the treatment was assessed based on the patient's clinical response rather than comparing the amount of mast cells on pathology slides.

3 | DISCUSSION

MD is an illness that is rarely documented and it is still considered as a diagnosis of exclusion with a wide spectrum of differential diagnoses. MD's pathophysiology is also yet unclear[2] and was discussed about it in the File S1.

TABLE 1 Successful treatments of Morbihan's disease patients from 2014 to 2021 by literature review.

Author	Year	Sex	Age	Histopathology	Treatment	Duration	Recurrence
Hattori, Y. et al.	2021	M	32	NA	Surgical Lymphaticovenous anastomosis	–	No recurrence after 1 year of follow-up
Donthi, D. et al.	2021	M	67	Mild spongiosis with periadnexal mixed infiltrate and dermal edema. The dermis showed perivascular and perifollicular lymphoplasmacytic inflammation, solar elastosis, and superficial dermal telangiectasia. No granulomata were observed	2 cases with a combination of 2.5% hydrocortisone cream, brimonidine 0.33% gel, metronidazole gel, and doxycycline	3 months	No recurrence after 1 year of follow-up
		M	50	Dermis with perivascular and perifollicular lymphoplasmacytic inflammation, solar elastosis, and superficial dermal telangiectasias. No granulomata were observed			
Cinar, G.N. et al.	2021	M	18	NA	Complete decongestive therapy for 24 sessions	8 weeks	NA
Yvon, C. et al.	2020	M: 8 F: 2	Mean age: 67	Features of inflammation and vascular dysfunction, are highly suggestive of a rosacea histological picture complicated by chronic lymphoedema	Ten cases: the most effective treatments included oral isotretinoin, intralesional triamcinolone, and debulking surgery	NA	NA
Welsch, K. et al.	2020	M: 2 F: 2	Mean age: 63	NA	Four cases with ultralow dose isotretinoin (10 mg daily) and antihistamines	Mean: 14 months	NA
Pflibsen, L.R. et al.	2020	M	55	Chronic inflammation, some granulomas, and histiocytes	Surgical resection	–	Contralateral involvement after 3 years
Kutlay, S. et al.	2019	F: 2	51, 45	NA	Two cases with complete decongestive therapy for 10–15 sessions	NA	NA
Olvera, V. et al.	2019	M: 3	51	Granulomatous blepharitis	Three cases with high-dose isotretinoin	1 year	No recurrence after 1 year of follow-up
			62	Superficial perivascular dermatitis, dermal edema, and chronic lymphoplasmacytic perifolliculitis			
			29	Superficial and deep periadnexal dermatitis with lymphocytic infiltration			
Kim, J.E. et al.	2019	NA	NA	Various extents of perivascular and perifollicular inflammation and dermal edema	Six cases with surgical eyelid reduction	–	NA
Kafi, P. et al.	2019	F	65	Non-specific inflammation consistent with rosacea	Omalizumab 450 mg	Monthly for 5 months	NA

TABLE 1 (Continued)

Author	Year	Sex	Age	Histopathology	Treatment	Duration	Recurrence
Boparai, R.S. et al.	2019	F	40	Acanthotic epidermis with hypergranulosis and architectural disarray	Two cases with oral isotretinoin and prednisolone	NA	NA
		M	61	Demodex and mild lymphocytic infiltrate in and around the follicles, as well as superficial vascular ectasia and prominent sebaceous glands			
Cabral, F. et al.	2018	M	61	Edema between collagen fibers, dilated vessels with telangiectasias, and lymphocytic infiltrate	Oral isotretinoin and corticosteroid	NA	NA
Tsiogka, A. et al.	2018	M	44	Edema in upper dermis, discrete perivascular and periadnexal lymphocytic infiltrate without granulomatous reaction, and interstitial mast cells	Intralesional triamcinolone	Monthly for 4 months	No recurrence after 8 months of follow-up
Chaidemenos, G. et al.	2018	F	63	Perivascular and periadnexal lymphohistiocytic infiltrate, dermal edema, mild fibrosis, and sebaceous gland hyperplasia. Demodex mites within the follicular openings were also present	Doxycycline	8 months	NA
Yu, X. et al.	2017	M	42	Dermal telangiectasias and lymphocytic infiltration around the pilosebaceous glands	Tripterygium wilfordii	6 weeks	NA
Okubo, A. et al.	2017	NA	NA	Infiltration of mast cells	Four cases with long-term doxycycline	NA	NA
Carruth, B.P. et al.	2017	M: 4 F: 1	Mean age: 62	NA	5 cases, 1: debulking, 2: doxycycline with debulking, 3: bilateral blepharoplasty, 4, 5: intralesional steroid	NA	NA
Kabuto, M. et al.	2015	F	64	Marked edema and perivascular and perifollicular lymphocytic infiltration throughout the dermis	Minocycline 100 mg daily	4 months	NA
Fujimoto, N. et al.	2015	M	74	Marked dermal edema, perivascular and perisebaceous mononuclear cell infiltration, granulomatous reaction in the deep dermis, deep-reaching fibrosis, and numerous mast cells throughout the dermis	Minocycline	4 months	No recurrence after 8 months of follow-up

Abbreviation: NA, not available.

Regarding microscopic findings, evidence of inflammation in favor of rosacea histopathological picture was detected in the majority of previously reported cases,[4–8] which were usually accompanied by perivascular and perifollicular lymphoplasmacytic patterns.[1,9] In addition, non-specific findings such as dermal edema, architectural disarray, and vascular ecstasies were discovered in some patients. Mast cell infiltration was also seen in a few cases.[2]

To date, no treatment guideline for MD is established. As a result, its management is primarily empirical, and pharmaceutical therapy options have primarily consisted of isotretinoin, steroids, antibiotics, and antihistamines (Table 1).[9,10] Clinical response to these treatments has been mainly insufficient and the lack of a clear etiology prevents the development of more targeted treatments.[9] More treatment methods were discussed in the File S1.

Here, we present a 17-year-old male with a history of acne vulgaris who was diagnosed with MD based on histological findings of his facial skin biopsy. What distinguishes this case is its brand new treatment with cromolyn sodium nasal spray and oral montelukast, which is, to our knowledge, the first reported one. He was placed on cromolyn sodium nasal spray and oral montelukast, which resulted in a dramatic response and no recurrence after a 1 year follow-up was observed.

In terms of treatment, conventional treatment options such as isotretinoin, antibiotics, steroids, and antihistamines have been utilized solely or in combination with each other in the majority of previously described cases.[1]

The efficacy of treatment has varied; for instance, Lauren A. et al. successfully treated five cases of Morbihan disease with long-term usage of oral isotretinoin, but according to the literature, it may not be an effective solution in 20% of patients.[7]

Following our observation of mast cells in our patient's histology, we came up with cromolyn sodium, a medicine that suppresses the release of histamine and leukotrienes, as well as mast cell degranulation. Montelukast was also added to the treatment as it is a highly selective leukotriene receptor antagonist.

4 | CONCLUSION

We report an effective treatment of an MD patient with a combination of a mast cell stabilizer and a leukotriene antagonist medication, which demonstrated a dramatic response and no recurrence after a 1 year follow-up.

AUTHOR CONTRIBUTIONS

AS and AG designed the study. AS, AZ, and AD wrote the paper. KK reported the histopathology and immunohistochemistry of the case. AG and PJ edited the manuscript. All authors have read and approved the content of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

DATA AVAILABILITY STATEMENT

All data produced in the present study are available upon reasonable request to the authors.

ETHICS STATEMENT

Ethics approval statement: Due to research protocol at Iran University of Medical Sciences, the ethical committee's approval for case reports is not needed however patient's consent for publication is obtained.

Patient consent statement: Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Clinical trial registration: None.

CONSENT FOR PUBLICATION

The authors obtained consent to publish.

ORCID

Abbas Dehghani https://orcid.org/0000-0001-9277-3606

Azadeh Goodarzi https://orcid.org/0000-0002-1249-4429

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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