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Morbihan Disease: A Rare Case of Periorbital Bilateral Edema with Histopathological Findings of Chronic Inflammation and Demodex Localization

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Patient: Male, 61-year-old
Final Diagnosis: Morbihan disease
Symptoms: Discomfort in the periocular region
Clinical Procedure: —
Specialty: Dermatology • Laboratory Diagnostics • Ophthalmology

Objective: Unknown etiology

Background: Morbihan disease, also known as Morbihan syndrome, is a rare medical condition characterized by chronic facial edema predominantly affecting the upper two-thirds of the face. Despite being recognized in medical literature for decades, its true prevalence and underlying pathophysiology remain poorly understood. Various hypotheses, including impaired lymphatic drainage, abnormal vascular permeability, immune dysregulation, and inflammatory reactions to demodex infestation, have been proposed to explain the etiology.

Case Report: We present a case of a 61-year-old man with organized periocular edema of the upper third of the face, ultimately leading to Morbihan disease diagnosis. The patient underwent a midface lift, allowing for tissue retrieval for histopathological examination of the eyelid edematous skin, which revealed chronic inflammation, ectasia of small lymphatic vessels, and features of demodex intrafollicular localization. These findings were not specific, but consistent with the diagnostic hypothesis. The patient was referred to a rheumatologist for further evaluation and treatment. He did not respond well to systemic corticosteroids and immunosuppressive therapy. Rather, this resulted in extension of the edema to the upper eyelid. The patient opted not to undergo further treatment.

Conclusions: Morbihan disease is often misdiagnosed due to its rarity and overlapping clinical features with other facial conditions. Its management is challenging and can require a combination of medical and surgical interventions. Systemic corticosteroids, immunosuppressive agents, and topical treatments have had varying success. Surgical procedures, such as blepharoplasty or laser therapy, can be considered in severe cases. Early recognition and appropriate management are crucial to improving patient outcomes and quality of life.

Keywords: Edema • Dermatitis, Perioral • Skin Diseases

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Introduction

Morbihan disease, also known as Morbihan syndrome, is a rare medical condition characterized by persistent, chronic edema predominantly affecting the upper two-thirds of the face, particularly around the periorbital region, forehead, and cheeks in patients in their 40s to 60s [1,2]. This condition takes its name from the Morbihan region of Brittany, France, where the first case series was described [3,4]. First reported in 1957 by Degos and Chevron, it is believed to be a rare condition, with only a small number of cases reported in the literature [2,4-10].

The exact etiology of Morbihan disease remains elusive, and it is currently considered a clinical syndrome associated with chronic inflammation of facial tissues [1]. The chronicity and persistence of the edema suggest a potential role of inflammatory mediators in its pathogenesis. However, no etiology has been conclusively proven. Diagnosis of Morbihan disease can be challenging due to its rarity and the overlap of inflammatory and granulomatous clinical features with other facial conditions, such as angioedema, rosacea, or cutaneous lupus erythematosus, and foreign body granulomata [2,11]. The lack of specific diagnostic criteria further contributes to the difficulties in identifying and distinguishing Morbihan disease from other similar entities.

This article presents the case of a 61-year-old man affected by organized periocular edema of the upper third of the face, ultimately leading to the diagnosis of Morbihan disease. Herein, we describe the clinical approach that we used to diagnose and treat the patient.

Case Report

A 61-year-old White male patient presented to the Ophthalmology Department of the Humanitas Research Hospital in Rozzano, Milan, Italy, with recurrent and persistent lower eyelid swelling in both eyes that began 4 years earlier and steadily progressed. He denied any history of trauma, contact with chemicals, insect bites, previous surgeries to the area, and symptoms of neuropathy. He had a history of acne in his youth, and the slight thickening of the skin around his nose could have indicated an early stage of rhinophyma. Moreover, he had a history of 9-year non-insulin dependent diabetes mellitus and chronic obstructive pulmonary disease. There were no significant ophthalmic conditions in his past medical history.

Visual acuity and ocular motility were normal, and there were no signs of proptosis or diplopia. Intraocular pressure was within the normal range. The patient reported that the edema was initially mild and unilateral but gradually worsened, to involve both periorbital regions. Bilateral edema was particularly pronounced in the lower eyelid region. The skin overlying the affected areas was hard, and a slight erythematous discoloration was noted (**Figure 1**).

He underwent an ear-nose-throat examination to rule out disease to the paranasal sinuses, and magnetic resonance imaging of the orbits was negative for compressive masses. Given the persistent and progressive nature of the periocular edema, we decided to perform a midface lift to relieve the pressure caused by the edema and to obtain tissue for histopathological examination.

On histological examination, the periorbital skin samples were mainly characterized by mild to moderate edema, predominantly affecting the dermis and associated with ectasias of small lymphatic vessels and sometimes capillaries.

The associated inflammatory infiltrates were multifocal, mixed in cell nature, mainly chronic, localized in correspondence of hair infundibles, and often occupied by demodex follicolorum. Moreover, they had follicolytic aspects. Interstitial infiltrates were less frequent.

Immunohistochemical staining with inflammatory cell line markers CD163 (histiocytes), CD138 (plasma cells), CD20 (B

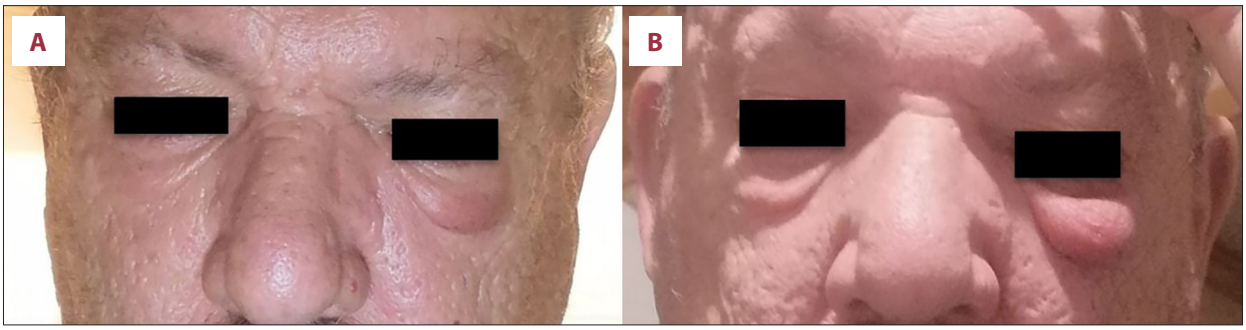

Figure 1. (**A**) Patient's photograph dated from approximately 3 years earlier. The predominantly unilateral edema collected in the lower portion of the periorbital region is evident. (**B**) Photograph taken 1 year later, in which the edema is now clearly bilateral, even if asymmetric, and appears to have worsened. The skin overlying the region seemed hardened, with a slight reddish discoloration.

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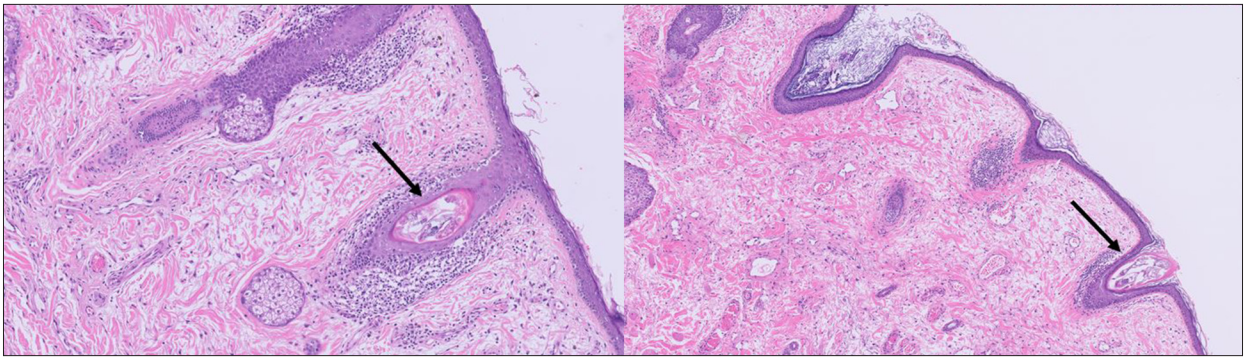

Figure 2. Hematoxylin and eosin staining, 5× magnification. Histological preparations of eyelid skin characterized by marked dermal edema, with some ectasia predominantly affecting the superficial lymphatic capillaries. Hair follicles, sometimes occupied by demodex (arrow), present associated foci of predominantly chronic periinfundibular inflammatory infiltrate, in the absence of a significant eosinophilic or granulomatous component.

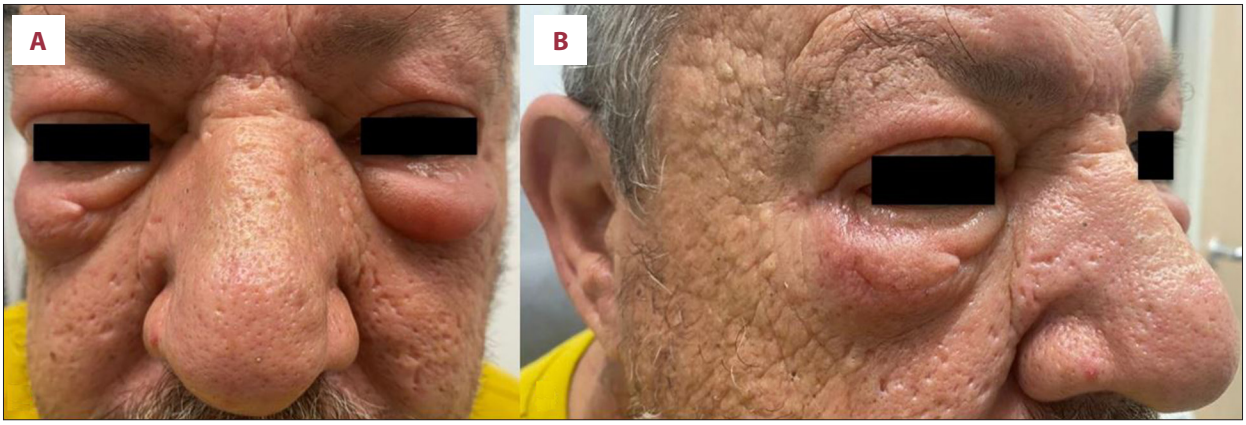

Figure 3. (**A**) Patient's photograph 4 months after inferior blepharoplasty and 2 months after the start of pharmacological treatment. Bilateral edema was still present. (**B**) The involvement of the superior periorbital region could be seen.

lymphocytes), and CD3 (T lymphocytes) was performed to type the cells involved in the inflammatory process and as a visual aid in the search for granulomata.

In addition, PAS and Giemsa histochemical staining was performed to evaluate the mast cell component and basement membrane status and search for fungi, microorganisms, and small parasites.

With the visual aid of immunohistochemical and histochemical staining, the inflammatory infiltrate was shown to consist of cells of chronic inflammation, predominantly T lymphocytes and histiocytes, in the absence of granulomata and an eosinophilic polymorphonuclear component. These histologic findings were nonspecific, but consistent with chronic edematous eyelid skin in the diagnostic hypothesis of Morbihan disease (**Figure 2**).

Hence, the patient was referred to a rheumatologist for further evaluation and treatment. Systemic corticosteroids were promptly started (prednisone 50 mg/day for a month, weekly tapered) and, as initiating dose, dexamethasone 4 mg/mL injectable solution, 2 mL for each side injected twice. Two months later, the patient was reevaluated and still showed a very pronounced bilateral edema, involving the upper eyelid as well (**Figure 3**). The patient was subsequently contacted to schedule a follow-up appointment, but he declined any further therapy.

Discussion

Morbihan disease is a rare and often undiagnosed disorder characterized by persistent edema in the facial region that can begin unilaterally and progress to involve both sides of the face [1]. The etiology of the disease remains unclear, but it is thought to be a type of chronic inflammatory reaction.

Difficulties in diagnosis and treatment can be attributed to poor understanding of the pathophysiology of the disease. Various hypotheses have been proposed, including impaired lymphatic drainage, abnormal vascular permeability, and immune dysregulation. Inflammatory reactions to demodex infestation were also considered.

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Recent discoveries regarding the pathophysiology of noninsulin-dependent diabetes mellitus have shown that impaired nitric oxide signaling can disrupt lymphatic vascular integrity [5,20].

Overall, it is reasonable that disruptions to the lymphatic system resulting from diabetes mellitus can contribute to the formation of the facial edema that characterizes Morbihan syndrome. Edema has been suggested to result from poor lymphatic flow due to lymphatic obstruction or post-inflammatory dermal fibrosis. Destruction of elastic connective tissue in the perivascular area leads to impaired vascular wall integrity and subsequent exudative edema [21]. Inflammatory reactions to the use of cosmetic products or demodex infestation have been suggested as possible triggers of Morbihan syndrome [4]. More recently, discoveries made in understanding the pathophysiology of noninsulin-dependent diabetes mellitus have shown that impaired nitric oxide signaling can disrupt lymphatic vascular integrity, contributing to the formation of the facial edema characterizing Morbihan syndrome [20].

Diagnosis is based primarily on clinical features, and subsequently, histopathological examination of the affected tissue could help confirm the suspected diagnosis. The typical patient with Morbihan syndrome is middle-aged or elderly male, with a history of acne or rosacea. Moreover, men with Morbihan syndrome have been shown to have a decreased likelihood of the disease resolving with treatment [6,9].

Morbihan disease commonly presents as persistent facial edema. The edema is often diffuse and hard, leading to a stiff, puffy appearance. Erythema and telangiectasia can be present in the affected areas [12]. Over time, the edema can cause skin thickening and fibrosis, leading to a condition similar to "pseudo-cellulitis". Patients may report a history of recurring facial swelling, which does not resolve with conventional treatment modalities [13].

Diagnosing Morbihan disease requires careful consideration of its clinical features and differentiation from other facial conditions that can present with similar symptoms. Some of the major differential diagnoses are angioedema, which, unlike Morbihan disease, is typically transient and resolves within 24 to 48 h [14]; rosacea [15] or cutaneous lupus erythematosus, which is usually accompanied by other skin lesions and systemic manifestations of lupus, such as malar rash and photosensitivity [16]; sarcoidosis, in which swelling of the face can be a rare manifestation [17]; and orbital cellulitis, in which there is typically an absence of pain, fever, and ophthalmological complications seen in orbital cellulitis [18]. Although not mandatory for diagnosis [19], the granulomatous inflammatory component, which is reported to be a histological aspect for Morbihan disease, was researched and, in our case, not found. The absence of evident granulomata might be expected. In fact, it is worth considering that the biopsy sample was taken from the lower eyelids, which are potentially less prone to granulomatous reactions than are other facial areas, like the forehead, zygomatic, or nasal regions.

Given the rarity and complexity of Morbihan disease, a multidisciplinary approach is essential for accurate diagnosis and comprehensive management. Treatment of Morbihan disease is challenging and often requires a combination of medical and surgical interventions [5]. Systemic corticosteroids and immunosuppressive agents, such as methotrexate, azathioprine, and tetracycline-based antibiotic therapies, have been used to manage Morbihan disease [22]. Additionally, antihistamines and diuretics can provide symptomatic relief in some cases. Topical corticosteroids or calcineurin inhibitors can be used to manage localized swelling and inflammation of the facial skin [23]. In cases in which severe fibrosis and skin changes are present, surgeries such as blepharoplasty or laser therapy can be considered to improve the facial appearance and relieve pressure to the affected tissues [7,24]. In cases resistant to the first-line treatments, new therapies including omalizumab can be used [25,26].

Conclusions

Morbihan disease remains a difficult and rare condition, and there is limited understanding of its etiology and pathogenesis. An accurate diagnosis requires a high index of suspicion and a multidisciplinary approach involving dermatologists, ophthalmologists, rheumatologists, plastic surgeons, and pathologists. This report emphasizes the need for correlation between clinical data and the histological result of the biopsy to rule out similar conditions and suggests how recent discoveries in the pathophysiology of diabetes mellitus may contribute to Morbihan syndrome. Early recognition and appropriate management are essential to improve patient outcomes and quality of life. More research and collaboration between specialists are needed to unravel the mysteries surrounding Morbihan disease and develop more effective treatment strategies.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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