Anti-MDA5 antibody-positive dermatomyositis presenting as unilateral eyelid edema

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Key words: anti-MDA5 antibody; dermatomyositis; rapidly progressive interstitial lung disease.

INTRODUCTION

Dermatomyositis (DM) is an idiopathic inflammatory myopathy with diverse cutaneous manifestations that may or may not parallel the severity or timing of systemic symptoms.[1] DM is associated with more than 15 myositis-specific autoantibodies, including anti-MDA5 antibody (anti-MDA5ab). Anti-MDA5ab is associated amyopathic dermatomyositis with rapidly progressive interstitial lung disease (RP-ILD). We report a case of anti-MDA5ab DM that presented with a unilateral edematous eyelid for months before developing the clinical manifestations associated with this phenotype.

Abbreviations used:

Anti-MDA5ab:	anti-MDA5 antibody
CT:	computed tomography
DM:	dermatomyositis
ILD:	interstitial lung disease
MMF:	mycophenolate mofetil
PFTs:	pulmonary function tests
RP-ILD:	rapidly progressive interstitial lung disease

CASE REPORT

A 48-year-old woman with no medical history presented to the emergency department complaining of an expanding, painless, and edematous left eyelid for 6 weeks (Fig 1). She denied any fever, chills, night sweats, vision change, myalgia, arthralgia, rashes, fatigue, or recent illnesses. She was admitted for workup of suspected preseptal cellulitis. Physical examination found exuberant edema on the left upper and lower eyelid with overlying ill-defined erythema. Computed tomography (CT) of the orbits found nonspecific edema. Because of suspicion for lymphoma, CT scans of the chest, abdomen, and pelvis were performed, finding only mild ground glass opacities at the bilateral lung bases. Laboratory evaluation was notable for low hemoglobin (10.9), anti-nuclear antibody titer of 1:640, and positive titers to anti-Sjogren syndrome antibody A (>8), and anti-Sjogren syndrome antibody B (>8). HIV, viral hepatitis panel, and tuberculosis screening were all negative. Punch biopsy of the left upper lid showed a granulomatous blepharitis with a lymphocytic infiltrate and dermal mucin deposition. A second eyelid biopsy performed during outpatient clinic follow-up found a lichenoid lymphoplasmocytic infiltration with focal basal vacuolar changes.

After initial clinical suspicion for cutaneous lupus versus dermatomyositis, eyelid edema showed moderate slow improvement on prednisone taper and hydroxychloroquine. One month later, the patient reported progressive joint pains in the hands, wrists, and knees with prominent morning stiffness. She also noted new 1- to 2-mm nontender papules on dorsal hands with scaling and fissuring of distal fingertips (Fig 2). Biopsy result of hand papules was consistent with lichenoid lymphohistiocytic vasculitis. At her initial evaluation by the rheumatology department, which was 2 months after initial hospital presentation, she complained of new proximal leg weakness, dyspnea on exertion, and difficulty with deep inspiration. Pulmonary function tests (PFTs) found restrictive pattern (72% of predicted) and decreased diffusing capacity of the lung for carbon monoxide. The patient was re-admitted to the hospital for dyspnea at rest, dry cough, fever,

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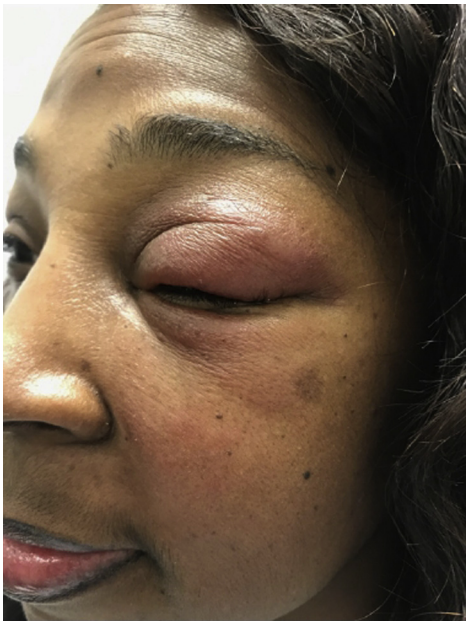

Fig 1. Anti-MDA5ab DM. Initial presentation of unilateral eyelid swelling with overlying erythema.

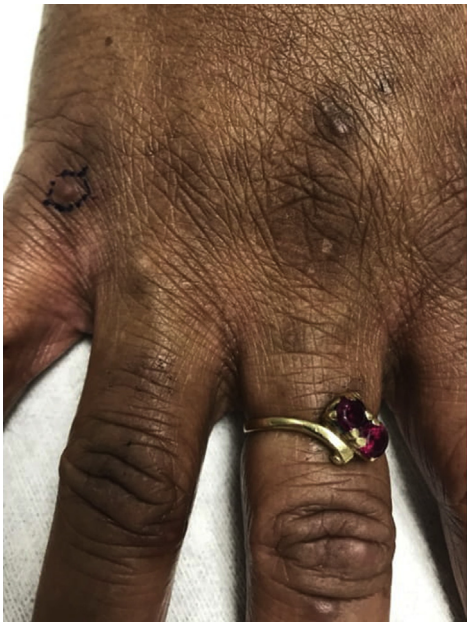

Fig 2. Anti-MDA5ab DM. Scattered 1- to 2-mm skin-colored papules on the dorsal hands.

night sweats, synovitis, and dactylitis. Repeat chest CT found worsening ground glass opacities bilaterally in the middle and lower lobes. Creatine kinase and aldolase were normal. Myositis panel showed positive anti-MDA5ab. The patient's eyelid edema and pulmonary symptoms improved on combination therapy with prednisone, hydroxychloroquine, and mycophenolate mofetil (MMF).

DISCUSSION

Anti-MDA5ab DM is difficult to detect in the absence of characteristic dermatologic findings and CT findings. This case is an atypical presentation of a patient who presented initially with unilateral eyelid swelling for months before having arthralgias, mechanic's hands, and RP-ILD. It is likely that early initiation of hydroxychloroquine and prednisone influenced the course of the disease. This case underscores the importance of re-assessing clinical findings to recognize the evolution of this variant of DM.

Anti-MDA5ab DM was first described in 2005 within a Japanese cohort and has only recently been described in non-Asian populations.[2] Its incidence of 10% to 30% within DM is most frequently seen in Asian patients and is most importantly associated with RP-ILD. Prevalence of interstitial lung disease (ILD) in anti-MDA5 DM is estimated to be 42% to 100% and those who test positive for anti-MDA5ab have 20-fold higher odds of having RP-ILD compared with those who test negative.[3,4] Other risk factors for RP-ILD include elderly age, decreased PaO_2/F_iO_2 ratio and elevated levels of serum ferritin.[5] RP-ILD has a 6-month mortality of approximately 59% and a median survival duration of 2 months.[4,5] Serum ferritin levels are found to negatively correlate with pulmonary function and are associated with the mechanism of RP-ILD in anti-MDA5ab DM.[6] Baseline ferritin concentrations can predict prognosis of RP-ILD, with a cut-off value greater than 1600 ng/mL as the best indicator of mortality.[5,6] Anti-MDA5ab titers, ferritin, and interleukin-18 are useful for evaluating response to treatment and predicting disease relapse.[5] High-resolution CT of the chest is the preferred imaging modality because of its high sensitivity for detecting ILD.[3] Initial screening can be done with PFTs, and abnormal results are confirmed with high-resolution CT with repeat screening every 3 to 6 months for the first year after diagnosis.[3]

Anti-MDA5ab DM can present with unique cutaneous findings such as mucocutaneous ulceration, painful palmar papules, and panniculitis.[1] Ulcerations found in the digital pulp or periungual area correlate with anti-MDA5ab.[3] Most anti-MDA5ab DM patients have circulating anti-SSA (Ro52/60) autoantibodies.[2] Histopathology of affected skin can vary, characterized by a heterogeneous group of findings including epidermal atrophy, vacuolar interface dermatitis, dermal edema, pigmentary incontinence, mucin deposition, vasculopathy, and vasculitis.[1,7] This case is unusual in that there were multiple histologic

patterns seen on skin biopsy. The unilateral eyelid edema may have been secondary to lymphatic obstruction from the granulomatous inflammation present in the skin.

Currently, there are no evidence-based guidelines for the treatment of anti-MDA5ab DM.[8] Historically, corticosteroids have been the gold standard of DM-related myopathy; however, they are not recommended as monotherapy or for amyopathic patients.[9] Algorithms emphasize hydroxychloroquine as a first-line systemic agent for cutaneous lesions and MMF for ILD.[8] MMF has been shown to normalize PFTs and resolve dyspnea with reduction in prednisone dose.[1] In cases in which corticosteroids and oral immunosuppressants fail, rituximab is an appropriate next step.[9] Rituximab with corticosteroids is also used as first-line treatment for adults with anti-MDA5ab and severe or recalcitrant pulmonary disease.[3,9] Rituximab use is reported to improve respiratory symptoms, decrease LFTs, and improve chest imaging.[8] Third-line options include intravenous immunoglobulin and calcineurin inhibitors.[10] Additionally, anti-MDA5ab DM is rarely associated with an increased risk of malignancy, therefore, no additional screening is recommended other than that which is age appropriate.[1]

The clinical presentation of anti-MDA5ab DM differs considerably from standard cutaneous DM, which can lead to a delay in diagnosis and treatment. A high level of suspicion is necessary to recognize the distinct clinical characteristics of anti-MDA5ab DM patients, and eyelid edema may be an important initial sign of this systemic disease.

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