Case report

A rare case of NXP-2 positive dermatomyositis

Nariman Khan*[,1], Zehra Hasan Kazmi[1], Rahaf Alkhateb[2]

[1]Department of Internal Medicine, University of Texas Health Science Center San Antonio, Joe R. and Terry Lozano Long School of Medicine, San Antonio, TX, USA; [2]Department of Pathology and Laboratory Medicine, University of Texas, San Antonio, TX, USA

Abstract

Dermatomyositis is an idiopathic inflammatory myopathy with variable cutaneous manifestations. Several autoantibodies each with distinct clinical phenotypes are associated with the disease. Here we present the case of a 36-year-old Laotian woman with hypothyroidism who presented with severe proximal and distal muscle weakness, dysphagia, diffuse rash, and anasarca that was diagnosed with NXP-2 (nuclear matrix protein 2) antibody positive dermatomyositis. The patient's hospitalization was complicated by disease resistant to conventional therapy.

Keywords: *rheumatology; hypothyroidism; dermatomyositis; NXP-2*

Introduction

Dermatomyositis (DM) is a systemic disease that presents with progressive and symmetric proximal muscle weakness with variable cutaneous manifestations. Several autoantibodies each with distinct clinical phenotypes can be associated with the disease, including one against nuclear matrix protein 2 or NXP-2. Individuals with the NXP-2 autoantibody tend to present with severe muscle weakness, calcinosis, dysphagia, and peripheral edema [1]. Here we present the case of a 36-year-old woman with treatment resistant NXP-2 antibody positive dermatomyositis.

Received: January 2021; Accepted after review: March 2021; Published: March 2021.

*Corresponding author: Nariman Khan, UT Health San Antonio, Joe R. and Terry Lozano Long School of Medicine, Department of Internal Medicine, 7703 Floyd Curl Dr, San Antonio, TX 78229, USA
Email: khan_nariman@yahoo.com

Case presentation

A 36-year-old Laotian woman with hypothyroidism and recent Percutaneous Endoscopic Gastrostomy (PEG) tube placement for dysphagia presented to the emergency department with a two-month history of progressively worsening anasarca, difficulty controlling respiratory secretions, proximal and distal muscle weakness, and a diffuse erythematous macular rash. The patient was pan-scanned with computed tomography of the chest, abdomen, and pelvis but no acute pathology was found. Electromyography was performed on the patient's right upper and lower limbs and revealed a generalized, necrotizing, myopathic process concerning for an autoimmune disease. The patient was started on prednisone at 1 mg/kg/day for her diffuse weakness but had minimal improvement in symptoms so was started on IVIG at 0.4 g/kg for five days for severe treatment-resistant disease. However, she also showed poor response to this therapy as determined by continued inability to raise her head, arms, and legs against gravity. Left deltoid muscle biopsy

was performed and revealed perivascular inflammation along with acute and chronic denervation of myofibers suggestive of vasculitis versus connective tissue disease. Shave biopsy of a proximal arm skin lesion revealed interface dermatitis with a sparse perivascular lymphocytic infiltrate with edema and mucin in the dermis concerning for dermatomyositis (Figure 1). Creatine kinase (CK) was found to be elevated to 790 U/L and aldolase to 17.8 U/L. Antibodies including ANA, DsDNA, RF, CCP, anti-cardiolipin, B2GP, Aquaporin 4 receptor, Jo-1, and the Mayo clinic paraneoplastic antibody panel proved to be negative. Myositis panel was performed and revealed a highly positive NXP-2 antibody.

The patient was diagnosed with NXP-2 dermatomyositis. Malignancy workup was performed with positron emission tomography scan and whole body computed tomography and magnetic resonance imaging scans, but all imaging proved unremarkable. Her hospital course was complicated by disease resistant to pulse dose steroids, plasma exchange treatments, rituximab, and tofacitinib. Eventually the patient developed hypercapnic respiratory failure requiring tracheostomy. After a seven month long hospitalization with multiple secondary complications, the patient's condition remained minimally improved from admission and she was discharged with a steroid taper. She remained trach and PEG tube dependent but has had moderate improvement in her weakness after chronically remaining on treatment with methyl-prednisolone 8 mg/daily as evidenced by her ability to walk several steps independently. She is currently receiving physical and speech therapy services to help her with strength, speech, and swallowing.

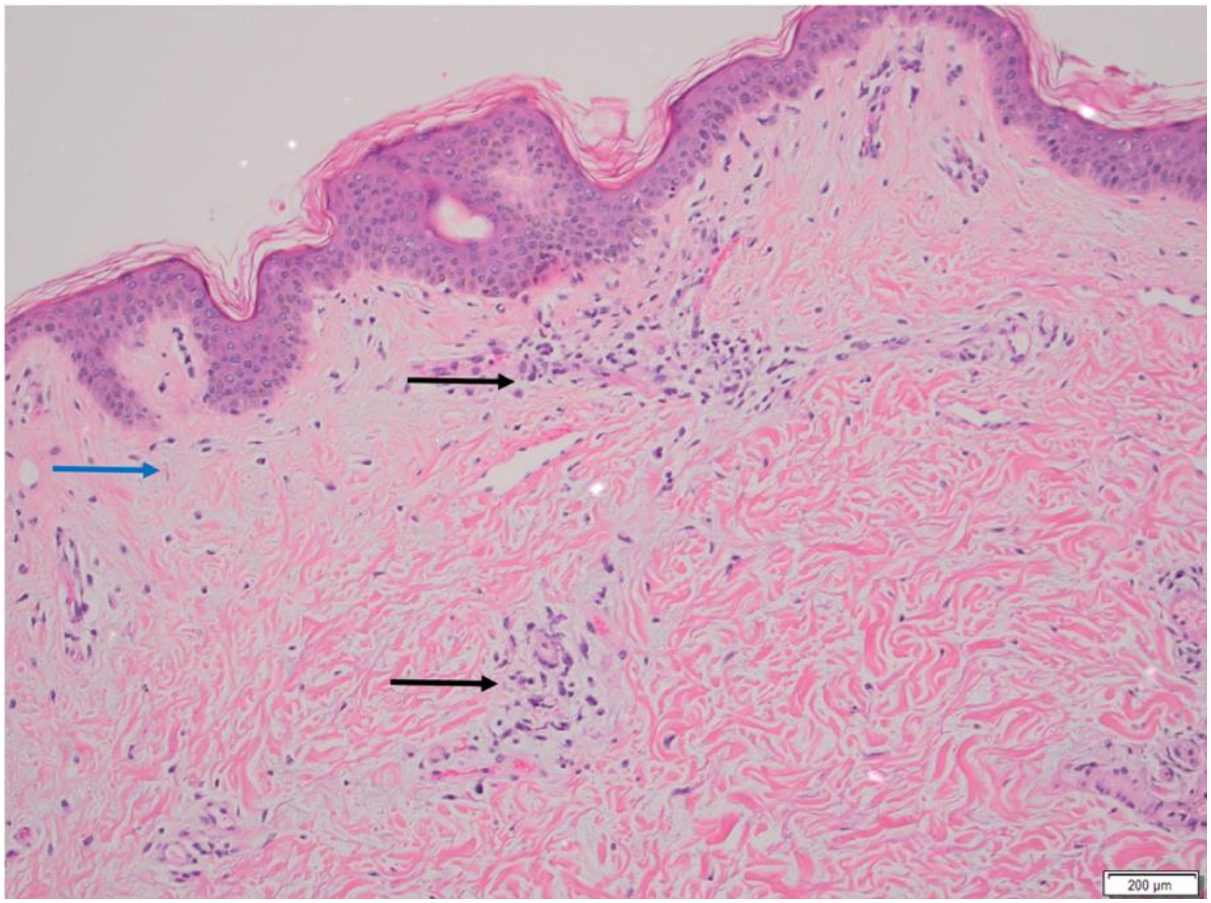

Fig. 1. Dermatomyositis. Perivascular lymphocytic infiltrate (black arrows) and dermal edema with mucus (blue arrow) (HE, x100)

Discussion

Dermatomyositis is an idiopathic inflammatory myopathy with various cutaneous manifestations including heliotrope rash, gottron papules, facial erythema involving the nasolabial folds, and shawl sign. The degree of muscular and skin involvement in DM is highly variable and individuals can have amyopathic disease. Most patients with muscular involvement have elevated CK levels, but up to 15 percent may have normal levels suggesting that the degree of weakness may not always correlate with the degree of CK elevation [2].

DM specific autoantibodies including anti-Mi-2, anti-MDA5, anti-TIF1, anti-NXP-2 also known as anti-MJ, and anti-SAE are useful because they can help guide in predicting which extramuscular manifestations a patient may develop [3]. Our patient possessed the anti-NXP-2 antibody which is strongly associated with malignancy in adults [4]. She also presented with severe proximal and distal muscle weakness, dysphagia, and generalized edema, all characteristics that seem to be more commonly associated with the NXP-2 antibody. This is evident in an article by Albayda et al. who studied 235 DM patients of which 56 were anti-NXP-2 antibody positive. The authors found that patients who possessed this antibody were more likely to present with distal muscle weakness in the arms (35%), legs (25%), and neck (48%), dysphagia (62%), and subcutaneous edema (36%) [4]. Likewise, Espada et al. studied autoantibody patterns in Argentine children with myositis and found that patients that were NXP-2 antibody positive had more severe disease with muscle contractures, atrophy, and diminished functional status [5]. Finally, Rogers et al. performed a retrospective cohort analysis on 178 DM patients of which 20 were NXP-2 antibody positive. The authors found that individuals with this antibody presented with a severe systemic phenotype consisting of myalgias (89%), peripheral edema (35%), and dysphagia (74%) [6].

Dermatomyositis is twice more common in women than in men. The approximate annual incidence of the disease is 9.6 cases per one million people. It tends to affect all age groups but peak incidence in adults occurs from age 40-60 years and in children from age 5-15 years [7]. Individuals with dermatomyositis have a six-fold increased risk for developing malignancy including ovarian, lung, pancreatic, non-Hodgkin lymphoma, stomach, and colorectal cancers particularly within the first two years after diagnosis [8]. Patients that tend to have poorer outcomes include those with delayed initiation of treatment, greater degree of weakness, dysphagia, respiratory muscle weakness, interstitial lung disease, presence of malignancy, and cardiac involvement [9].

The initial therapy for DM is with prednisone at 1 mg/kg per day. In severely ill patients, pulse dose methylprednisolone 1 g/day for three days may be used instead. Some physicians also choose to start treatment with glucocorticoid sparing agents such as azathioprine or methotrexate with glucocorticoids at disease onset [9]. For treatment resistant disease, improvement is usually seen with rituximab followed by IVIG if rituximab fails. Other options include mycophenolate mofetil, calcineurin inhibitors, cyclophosphamide, and janus kinase inhibitors such as tofacitinib which showed efficacy as measured by validated myositis response criteria in a trial of ten patients with treatment refractory dermatomyositis [10, 11]. While most patients respond to corticosteroids and immunosuppressants, approximately one third of patients do not respond or poorly respond to available therapies and remain debilitated such as this patient [12].

Conclusions

DM is a rare condition that can have an uncertain clinical course ranging from mild symptoms to progressive deterioration. Due to the infrequency of this disease, limited clinical trial data is available on optimal therapeutic options. At this time further research in DM is necessary to determine the best treatment type and duration, particularly for patients with disease resistant to conventional therapy.

Acronyms

PEG: Percutaneous Endoscopic Gastrostomy
ANA: Antinuclear antibody
Anti-DsDNA: Anti-double stranded deoxyribonucleic acid
RF: Rheumatoid factor
Anti-CCP: Anti-cyclic citrullinated peptide
Anti-B2GP: Anti-beta 2 glycoprotein
Anti-Jo-1: Anti-histidyl-tRNA synthetase
Anti-MDA5: Anti-melanoma differentiation-associated gene 5
Anti-TIF1: Anti-transcription intermediary factor 1
Anti-SAE: Anti-small ubiquitin-like modifier activating enzyme

Consent

Written informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors declare that they have no competing interests.

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