Toxic epidermal necrolysis–like dermatomyositis associated with antimelanoma differentiation antigen 5

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INTRODUCTION

Patients with dermatomyositis (DM) and autoantibodies against melanoma differentiation–associated protein 5 (MDA5) are likely to subsequently have clinically amyopathic dermatomyositis and interstitial lung disease (ILD).[1-3] These patients characteristically present classical cutaneous manifestations of DM in addition to specific findings such as palmar papules and skin ulceration, especially at the digital pulp.[1-3] We present a patient with anti-MDA5–positive DM with toxic epidermal necrolysis (TEN)-like eruption.

Abbreviations used:

DM:	dermatomyositis
ILD:	interstitial lung disease
MDA5:	melanoma differentiation–associated protein 5
TEN:	toxic epidermal necrolysis

REPORT OF A CASE

A woman in her 30s of Arab ethnicity, was referred to our department with a 2-month history of a generalized pruritic rash over her face, trunk, and extremities, accompanied by fatigue and weight loss, she denied joint pain or respiratory difficulties. Physical examination found heliotrope rash, Gottron sign, and poikilodermic patches over the lateral thighs. Eroded violaceous papules and plaques covered by scale and crust were spread over the palmar joint creases and digital tips (Fig 1). Muscle strength was preserved. Laboratory investigation found anemia (hemoglobin, 9.9 g/dL), leukopenia (3.5 k/μL), elevated erythrocyte sedimentation rate (100 mm/h) and mildly elevated aldolase levels (15.2 U/L). Electromyography and muscle biopsy found no sign of myositis. Skin biopsy from a violaceous plaque exhibited interface dermatitis and a biopsy from the palmar ulcer edge found fibrinoid necrosis involving small-to-medium vessels in the reticular dermis and subcutis. Rheumatology blood panel was positive for MDA5 and Ro52 antibodies. Considering the latter, pulmonary evaluation found moderately reduced (43%) diffusing capacity of the lungs for carbon monoxide and bilateral ground glass opacities on high-resolution computed tomography—findings compatible with ILD. Occult malignancy was ruled out. A diagnosis of anti-MDA5–positive clinically amyopathic dermatomyositis with ILD was

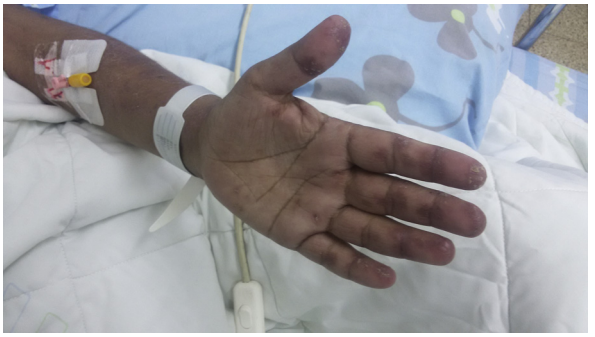

Fig 1. Anti-MDA5–associated DM. Eroded violaceous papules and plaques covered by scale and crust over the palmar joint creases and digital tips.

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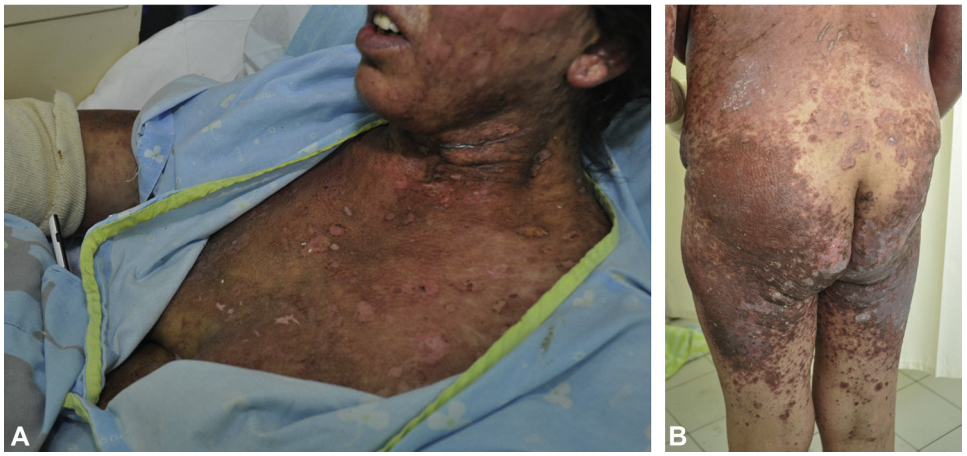

Fig 2. TEN like eruption after prednisone cessation. **A**, Multiple erosions accompanied by widespread faint erythema on the chest. **B**, Violaceous plaques over the buttocks and lower limbs.

established. Treatment with prednisone, 1 mg/kg/d, resulted in improvement of fatigue and subsidence of the rash without resolution of the palmar lesions.

One month later, after abrupt cessation of prednisone, the patient was readmitted with worsening of the rash, fever, and painful erythema of the right elbow. She denied new drug initiation. Physical examination found a rash composed of multiple erosions, accompanied by faint erythema, involving the face, neck, and chest (Fig 2), which subsequently spread to involve 70% of her body. Nikolsky sign was negative, and mucous membranes were spared. Histology of skin biopsy disclosed multiple dyskeratotic cells and areas of epidermal necrosis (Fig 3). Direct immunofluorescence examination ruled out immunoglobulin deposition. Under the working diagnosis of severe DM exacerbation, pulse methylprednisolone treatment (500 mg/d for 3 days) was initiated with no improvement, followed by high-dose intravenous immunoglobulin therapy (2 g/kg) with significant improvement. She was further treated for her ILD with cyclophosphamide, cyclosporine, and rituximab with only mild response.

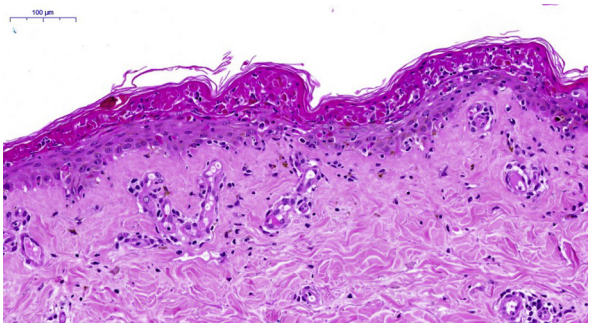

Fig 3. Histology of a cutaneous biopsy taken from TEN-like rash in an anti-MDA5–positive dermatomyositis patient. Biopsy section taken from the edge of a bulla shows multiple dyskeratotic cells and areas of epidermal necrosis. (Hematoxylin-eosin stain; original magnification: ×20.)

DISCUSSION

We present an exceptional manifestation of DM: an acute widespread rash reminiscent of TEN, both clinically and histologically (Figs 2 and 3). However, negative Nikolsky sign, the absence of mucous membrane involvement, and no history of new drug ingestion pointed to severe exacerbation of the underlying disease rather than true TEN. The exacerbation appears to have resulted from abrupt prednisone cessation causing an overt interface reaction manifested by necrotic cells in all levels of the epidermis together with subepidermal blistering.

Interface dermatitis is associated with high levels of type 1 interferons.[4] MDA5 is a component of host immunity against viral genomic particles, which when activated cause transcription of interferon B. Interestingly, germline mutation in STING, another protein in the same pathway that causes a phenotype similar to anti-MDA5 dermatomyositis with palmar ulcers, vasculopathy, and ILD, is associated with increased type 1 interferon levels.[5] Thus, it is possible that the increased levels of interferon in our patient contributed to the severe interface reaction.

TEN-like diseases resulting from causes other than drug hypersensitivity have been described as acute syndrome of apoptotic pan-epidermolysis.[6] We present a case of DM associated with TEN-like eruption, adding to previously described TEN-like forms

of cutaneous lupus erythematosus, including Rowell syndrome, graft-versus-host disease, and pseudoporphyria.

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