Prominent dyspigmentation in a patient with dermatomyositis and TIF1-γ autoantibodies

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INTRODUCTION

Dermatomyositis (DM) is an inflammatory myositis that commonly presents with a characteristic skin eruption, which can occur even in the absence of muscle inflammation. Cutaneous manifestations tend to be more severe in a recently described DM-specific autoantibody subtype, transcription intermediary factor 1-γ (TIF1-γ) DM.[1] As DM has the potential to cause significant pruritus, photosensitivity, and dyspigmentation, TIF1-γ-associated DM may be psychologically distressing to patients and have a negative effect on overall quality of life. Herein, we present the case of a 46-year-old man who presented with significant dyspigmentation in the setting of TIF1-γ DM and improved after treatment with methotrexate despite failing rituximab. We highlight the importance of early disease detection with dyspigmentation as a potential presenting cutaneous finding in darker-skinned individuals.

Abbreviations used:

DM: dermatomyositis
TIF1-γ: transcription intermediary factor 1-gamma

CASE REPORT

A 46-year-old man with classic DM and TIF1-γ autoantibodies presented for evaluation of widespread areas of dyspigmentation progressing over the preceding 6 months after being treated by his rheumatologist with 200 mg hydroxychloroquine twice daily, oral glucocorticoids, and 3 infusions of rituximab over a 19-month period. Despite this therapy, cutaneous involvement progressed with notable pruritus and only slight improvement in proximal muscle weakness.

On physical examination, there were many hypopigmented and depigmented patches on the face, trunk, and back with notable sparing of follicular ostia (Fig 1). Many of these patches also demonstrated slight erythema. The depigmented patches without erythema enhanced with wood's lamp evaluation. Mucosal examination was unremarkable. Nailfold capillary dilatation was noted. Sclerodactyly, digital tuft pits, and matted telangiectasias were absent. Additional laboratory evaluation was undertaken to evaluate for development of new-onset vitiligo or overlapping autoimmune connective tissue disease with systemic sclerosis in this patient.

An antinuclear autoantibody test by immunofixation was positive with a titer of 1:320 in a diffuse, speckled pattern. A test for TIF1-γ autoantibodies was positive. Tests for U1RNP, SSA-52/60, Jo1, MI2, Pl-7, Pl-12, EJ, KU, U2-snRNP, U3RNP, OJ, SAE1, NXP-2, MDA5, dsDNA, Scl-70, RNA-Polymerase 3, centromere, signal recognition particle, and p- and c-antineutrophil cytoplasmic autoantibodies were negative.

A lesional punch biopsy of the upper portion of the left arm revealed a superficial perivascular lymphocytic infiltrate with many dermal melanophages. Lymphocytes were also present at the dermoepidermal junction in a vacuolar-interface pattern with necrotic keratinocytes and a thickened basement membrane. Increased connective tissue mucin was present throughout the papillary and reticular dermis.

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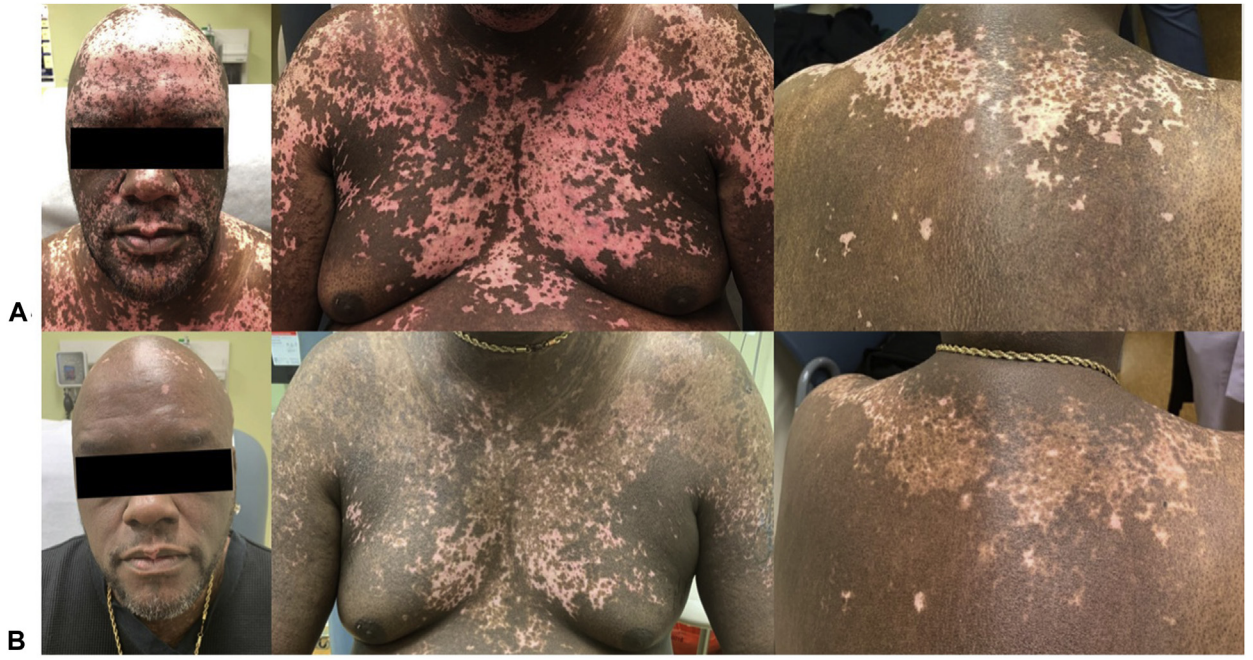

Fig 1. Transcription intermediary factor 1-gamma (TIF1-γ)-associated dermatomyositis (DM). Clinical images of the face, chest, and upper back, demonstrating initial presentation (**A**) and repigmentation at 3-month follow up of treatment with methotrexate (**B**). *DM*, Dermatomyositis; *TIF1-γ*, factor 1-gamma.

Significant postinflammatory pigmentary alteration can confound the diagnoses of cutaneous diseases. In the presence of a clinical background of erythema and with interface dermatitis increased dermal connective tissue mucin seen on histopathologic examination, these findings pointed toward an autoimmune connective tissue disease etiology rather than new-onset vitiligo. While "salt and pepper" dyspigmentation seen in systemic sclerosis could also appear similarly, lack of thickened dermal collagen bundles on histopathology and lack of scleroderma-specific autoantibodies suggested poorly controlled cutaneous DM over an overlap autoimmune condition. The patient was subsequently started on 10 mg methotrexate weekly, with significant repigmentation over the following 3 months (Fig 2).

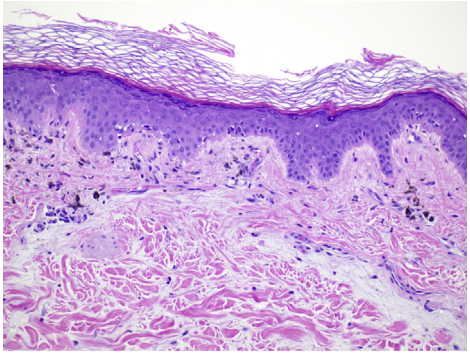

Fig 2. Superficial perivascular lymphocytic infiltrate with many dermal melanophages. Lymphocytes were also present at the dermoepidermal junction in a vacuolar-interface pattern with necrotic keratinocytes and a thickened basement membrane. Increased connective tissue mucin was present throughout the papillary and reticular dermis (H&E staining).

DISCUSSION

DM is an inflammatory myositis typically presenting with a characteristic cutaneous eruption. A relatively recently described DM-specific autoantibody to the 155-kDa nuclear protein termed TIF1-γ has proven useful for disease subclassification.[1] Literature has demonstrated that the presence of TIF1-γ autoantibodies has a 70% sensitivity and 89% specificity for identifying malignancy-associated DM.[2] A new diagnosis of DM may be associated with underlying malignancy, and as such, it is important for patients to undergo malignancy screening. Malignancy workup in our patient was unremarkable in respect to testing with computed tomography of the chest, abdomen, and pelvis; colonoscopy and endoscopy, serum testing for prostate specific antigen, carcinoembryonic antigen, CA19-9, thyroid function tests, as well as urine protein electrophoresis and immunofixation.

Additional specific screening in women only may include mammography, breast ultrasound, transvaginal ultrasound, and pap smears. Individuals with detectable TIF1-γ autoantibodies in DM are less likely to have Raynaud phenomena, interstitial lung disease, and arthralgias.[3] Despite this, cutaneous manifestations tend to be more severe; further, hyperkeratotic palmar and Gottron papules, ovoid hard palatal patches, and psoriasis-like plaques have been described as occurring with increased frequency in patients with TIF1-γ autoantibodies.[2,3] Notably, hypopigmented and telangiectatic (red-on-white) patches have also been described in patients with TIF1-γ autoantibodies, potentially compounding the pigmentary changes seen in this disorder.[3] The case demonstrates that interface dermatitis, especially in darker skin phototypes, can create prominent dyspigmentation arising from poorly controlled inflammation, which can mimic the pigmentary changes seen in conditions like vitiligo or other autoimmune connective tissue diseases, including systemic sclerosis. Early identification of this pattern as representative of cutaneous DM may spare patients of unnecessary, potentially invasive work-up and expedite direct disease-specific management. The development of validated quality of life indices has shed light on the psychological effects of other disorders causing dyspigmentation.[4,5] Thus, the early escalation of care with skin-directed systemic therapies like methotrexate in patients with pigmentary changes in the setting of DM may also improve patient quality of life. Anyanwu et al described a step-wise treatment strategy in cutaneous DM that includes initiating therapy with antimalarials; ie, hydroxychloroquine, and progressing to cytotoxic medications (methotrexate, mycophenolate mofetil, or azathioprine), and finally intravenous immunoglobulin or oral calcineurin inhibitors for refractory disease.[6] Rituximab may be utilized in patients with refractory DM, albeit with variable efficacy, particularly for cutaneous involvement.[7] Notably, the patient presented herein failed initial treatment with previous use of hydroxychloroquine, oral glucocorticoids, and rituximab infusions, and had cutaneous improvement with his described methotrexate regimen. This report highlights that significant dyspigmentation as a clinical clue in darker-skinned individuals may be a presenting cutaneous finding in TIF1-γ-associated DM.

Conflicts of interest

None disclosed.

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