Dermatomyositis recalcitrant to treatment associated with occult malignancy

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INTRODUCTION

The incidence of malignancy in patients with dermatomyositis is about 5 to 7 times greater than that of the general population.[1] The most common malignancies associated with dermatomyositis include adenocarcinomas of the lung, ovaries, cervix, pancreas, and stomach.[1-4] Several factors have been reported as possible predictors of paraneoplastic disease, which include older age at diagnosis, male sex, autoantibodies to transcription intermediary factor 1-γ, nuclear matrix protein-2, elevated erythrocyte sedimentation rate, cutaneous necrosis, and antinuclear antibody negativity.[3-7]

In our practice, we noticed that dermatomyositis recalcitrant to therapy may be an additional predictor of underlying malignancy. We classified recalcitrant dermatomyositis as having both cutaneous and muscle disease resistant to appropriate treatment, with the exception of resistant skin disease only in an amyopathic case. Here we report 3 cases.

Abbreviation used:

CT: computed tomography

CASE REPORTS

Patient 1

Patient 1 is a 61-year-old man with amyopathic dermatomyositis. He had classic periungual erythema, red papules symmetrically distributed over the extensor metacarpophalangeal and interphalangeal joints, and erythema of the upper back in a shawl distribution with a mildly elevated serum creatinine kinase but no muscle weakness (Fig 1, *A* and *B*). His symptoms were only marginally controlled on methotrexate, folic acid, hydroxychloroquine, and prednisone. Malignancy screening tests at the time of diagnosis, including prostate-specific antigen, colonoscopy, and computerized tomography (CT) scan of the chest, were negative. He also underwent several other diagnostic imaging studies at that time including CT scan of head and neck, all of which were unremarkable. The patient underwent a repeat CT scan about 2 years after dermatomyositis diagnosis revealing a mass of the left tonsil. A tonsillectomy and fine-needle aspiration of 2 lymph nodes was performed, which confirmed squamous cell carcinoma. He was treated with weekly cisplatin and radiation therapy. After completion of chemo-radiation, his rash improved remarkably. Currently, his disease continues to be well controlled with hydroxychloroquine. He has routine follow-up with the oncology and dermatology departments and has not experienced any dermatomyositis flares for the last 18 months.

Patient 2

Patient 2 is a 68 year-old woman who presented initially with proximal muscle weakness and elevated serum creatinine kinase and aldolase levels; she had biopsy-proven inflammatory myositis. After 1 year, her dermatomyositis diagnosis was made when classic cutaneous manifestations presented including photoexacerbated erythema on the neck and chest (V sign), shoulders, back, dorsal arms, and hands and ragged cuticles with dilated capillary loops on the proximal nail folds. A skin biopsy of

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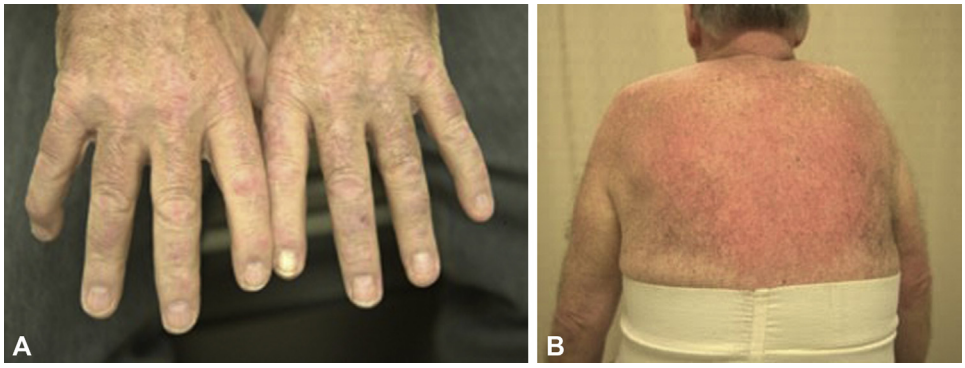

Fig 1. A, Periungual erythema and red papules symmetrically distributed over the extensor metacarpophalangeal and interphalangeal joints. **B**, Diffuse erythema of the upper back in a shawl distribution.

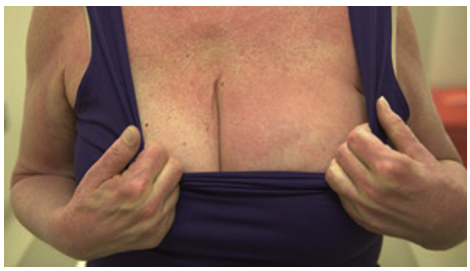

Fig 2. Edematous left breast and confluent areas of erythema on the V of the neck, shoulders, and dorsal arms and hands.

the mid-back showed findings consistent with connective tissue disease. She was started on a prolonged prednisone taper and transitioned to mycophenolate mofetil; however, neither muscle weakness nor rash improved. At this time, all malignancy screenings (mammography, pelvic ultrasound scan, colonoscopy, and CT chest/abdomen/pelvis) were up to date. One month later, her skin disease and muscle weakness were still present when acute enlargement of the left breast developed (Fig 2). Repeat mammography, ultrasound scan and MRI were negative. She subsequently underwent needle biopsy of the left axilla, which revealed angioimmunoblastic T-cell lymphoma. She had a repeat lymph node and bone marrow biopsy, results of which were all consistent with the diagnosis. Dermatomyositis therapy was discontinued. She completed 6 rounds of chemotherapy and underwent autologous bone marrow transplant. One month after bone marrow transplant, her skin cleared completely, muscle weakness significantly improved, and serum creatinine kinase level normalized. A few months later, she had recurrence of erythema on her chest, hands, and back, but repeat positron emission tomography/CT was negative. She restarted hydroxychloroquine and her disease has been well controlled for the last 2 years.

Patient 3

Patient 3 is a 50-year-old woman with dermatomyositis diagnosed after presenting with heliotrope rash and violaceous erythema of the chest, upper back, and arms accompanied by symmetric proximal muscle weakness with elevated serum creatinine kinase and aldolase levels. She was initially treated with hydroxychloroquine, methotrexate, and prednisone; however, her disease was minimally responsive to therapy. Fig 3, *A* and *B* show persistent involvement of the upper back, chest, and arms. Routine malignancy screening was up to date and negative. About 6 months after dermatomyositis diagnosis, despite a recent normal mammogram, she noticed a lump on self—breast exam, and subsequent workup confirmed invasive ductal breast carcinoma. Dermatomyositis treatment was discontinued. She underwent a double mastectomy followed by chemotherapy and radiation. Following chemo-radiation, her skin was completely clear. She remained symptom free for about 2 years; however, she then presented with an itchy rash on her face and upper back and myalgia of the shoulder and pelvic girdle muscles. Complete metastatic workup was negative for recurrent breast cancer. She was given a steroid taper and subsequently resumed hydroxychloroquine. She has been doing well for the last 3 years.

DISCUSSION

We present 3 patients with dermatomyositis whose symptoms were relatively recalcitrant to systemic therapy. See Table I for a complete diagnostic work-up for each case. All had a negative initial malignancy evaluation and were subsequently found to have an occult malignancy.

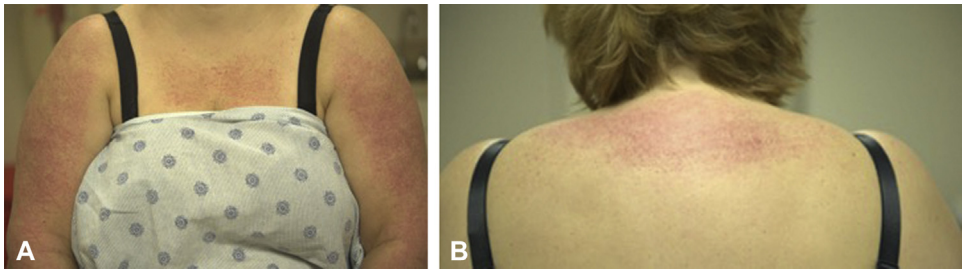

Fig 3. **A** and **B**, Violaceous erythema on the chest, dorsal arms, and upper back.

Table I. Patient work-up and diagnostic summary

	Patient 1	Patient 2	Patient 3
Diagnostic workup	Clinical diagnosis based on classic cutaneous findings Mildly elevated CK although no muscle weakness Anti-Jo1$^-$; no other myositis markers obtained ANA not obtained	Positive muscle biopsy Positive skin biopsy Elevated serum skeletal muscle enzymes (CK/aldolase) Anti-Jo1$^-$; no other myositis markers obtained ANA positive (1:5120 speckled)	Clinical diagnosis based on classic cutaneous findings Elevated serum skeletal muscle enzymes (CK/aldolase) Anti-Jo1$^-$ Comprehensive myositis panel negative including PL-7, PL-12, Mi-2, Ku, EJ, OJ, SRP ANA weakly positive (1:80 speckled)

ANA, antinuclear antibody; *CK*, creatinine kinase.

Based on our experience, recalcitrant dermatomyositis may be indicative of malignancy, even in those whose initial malignancy screening was unremarkable. Because baseline malignancy screening may be negative,[8-10] patients with intractable disease should be closely monitored for any abnormal signs or symptoms, and additional, more frequent screening should be considered.

Two of the 3 patients we described had malignancies not typically associated with dermatomyositis, in particular, angioimmunoblastic T-cell lymphoma, which is a mature CD4$^+$ T-cell lymphoma and may present as edema, ascites, arthritis, and pruritic skin rash.[11] Although there are previous reports of angioimmunoblastic T-cell lymphoma mimicking the rash of dermatomyositis,[12] our patient also had muscle involvement and continued to have the classic rash after successful treatment of her underlying malignancy. As such, to our knowledge, this is the first reported case of paraneoplastic dermatomyositis caused by angioimmunoblastic T-cell lymphoma.

A recent study that examined factors associated with clinical remission in dermatomyositis found malignancy-associated dermatomyositis to have higher rates of clinical remission (odds ratio, 14.46; 95% confidence interval, 2.18-96.07; P = .01).[13] Although all 3 of our patients achieved clinical remission after treatment of the underlying malignancy, 2 had subsequent relapse of dermatomyositis symptoms. However, their skin disease was more responsive to systemic therapy compared with that before the occult malignancies were found and treated.

We propose that clinicians should have a high level of suspicion for occult malignancy in patients with recalcitrant dermatomyositis and should consider more extensive and frequent malignancy screening for these patients.

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