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A rare case of erythema elevatum diutinum presenting as diffuse neuropathy.

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A rare case of erythema elevatum diutinum presenting as diffuse neuropathy

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INTRODUCTION

Erythema elevatum diutinum (EED) is a rare skin disease characterized by indolent red-to-purple papules and nodules, usually occurring symmetrically on extensor surfaces and dorsal joints.[1] Histologic characteristics include leukocytoclastic vasculitis of the mid and papillary dermal vessels with fibrinoid necrosis and a dense dermal infiltrate characterized predominantly by neutrophils, with fibrosis in older lesions. A review of the literature described EED associated with a wide range of clinical illnesses, including hematologic abnormalities (most commonly IgA gammopathies), recurrent infections, human immunodeficiency virus infection, cancer, and several autoimmune diseases.[2-5] Although EED has been seen in association with many autoimmune disorders, the precise etiology is poorly understood. With respect to this underlying aberrant immune response, symptomatology improves with therapies like dapsone.[6] Here, we describe a case of EED associated with diffuse neuropathy, a diagnostic puzzle until biopsy found features characteristic of EED.

CASE REPORT

An otherwise healthy 56-year-old white woman presented in 2000 with extreme nausea attacks followed by cold sweats and shivering of 6 months' duration. An extensive gastrointestinal workup had normal results. Several months later, she reported seeing the muscles of her extremities contracting tightly during nausea attacks, with extremity pain on standing and sitting. Over the next few years, she slowly lost mobility in her arms and legs. She visited many doctors without a clear diagnosis.

Abbreviation used:

EED: erythema elevatum diutinum

In 2006, she reported discrete lumps at locations of pressure, mostly her fingers and soles, worse in the evening and associated with shooting pain and numbness of her hands and feet. She presented to the neurology department where she received a diagnosis of bilateral carpal tunnel syndrome. Electromyography found a diffuse neuropathy of unknown etiology.

The patient was lost to follow up between 2007 and 2012. In the interim, she experienced a 50-pound weight loss accompanied by deformity of her hands and feet. The previously intermittent lesions on her hands became persistent. On evaluation by orthopedic surgeons and rheumatologists, multiple laboratory and radiograph studies found no insight into the etiology of her symptoms. Serum protein electrophoresis findings were normal. Rheumatologic workup found positive antinuclear antibody by enzyme-linked immunosorbent assay, with anti-Sjögren's syndrome—related antigen A/B, antichromatin, anti-Smith, anti-ribonucleoprotein, anti-centromere, anti—Jo-1, anti—Scl-70, anti-dsDNA, and RF all within normal limits.

On presentation to the dermatology department, a generalized bluish and purplish color of her hands and feet was noted, with symmetrical soft, baggy and redundant skin of her toes. There were symmetric, moderately firm, nontender purple papules on her hands and feet, particularly over the dorsal joints of

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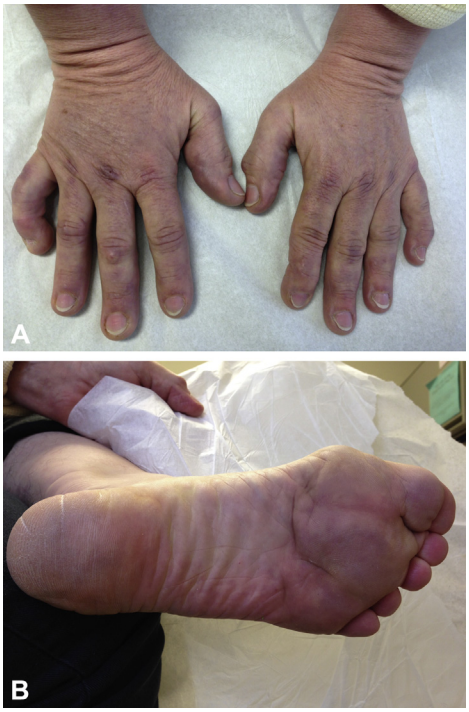

Fig 1. A, Generalized bluish and purplish color of the hands with purple papules and nodules observed over the dorsal joints. **B**, Soft, baggy, and redundant skin with purple nodules coalescing into plaques on the sole of the foot.

her hands (Fig 1, *A*), with some coalescing into plaques on her palms and soles (Fig 1, *B*). Discrete subcutaneous nodules were felt on deep palpation of the bilateral hands, most noticeable the thumbs and index fingers. Additionally, she had tan soft papules on the bilateral antihelices of her ears and on the columella of her nose. Neurologically, she had loss of temperature and sensation of the distal bilateral hands and feet, with preserved vibration and proprioception. Reflexes were hypoactive. Motor function was limited. Phalen and Tinel signs were positive bilaterally. Weakness of grip strength was present, right greater than left, with prominent thenar muscle atrophy bilaterally.

Four deep excisional biopsies were performed of the purple papules on her hands. Results of 3 biopsies of the right thumb, proximal small finger, and distal small fingers were similar, finding diffuse neutrophilic infiltrates in the skin, subcutis, and synovial tissue (Fig 2, *A*). The epidermis was largely uninvolved. The inflammatory infiltrates consisted of primarily neutrophils, with scattered eosinophils, histiocytes, and lymphocytes. Leukocytoclasis, endothelial swelling, and focal necrosis were noted (Fig 2, *B*). Special stains were negative for fungal organisms (Grocott's methenamine silver

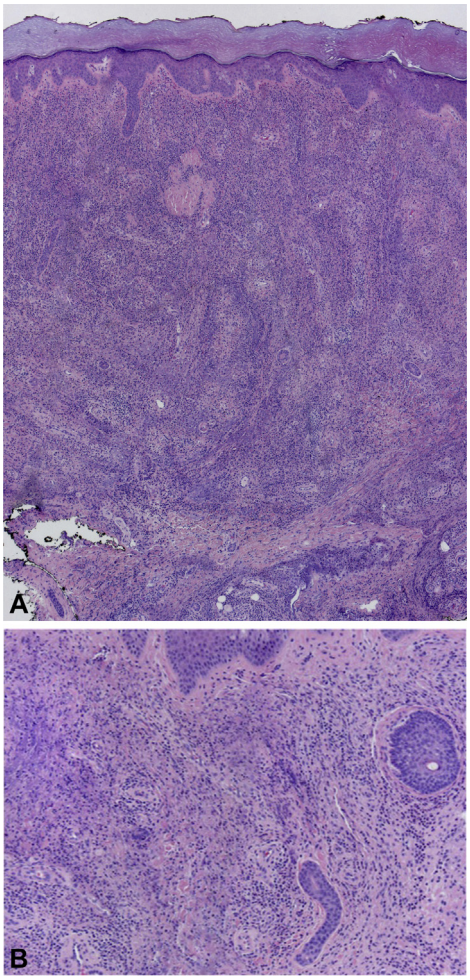

Fig 2. A, The epidermis is rather normal, with the inflammatory infiltrates consisting of primarily neutrophils. Scattered eosinophils, histiocytes, and lymphocytes are also present. **B**, Leukocytoclasis, endothelial swelling and focal necrosis are noted. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×4; **B**, ×10.)

stain), bacteria (Gram stain), and acid-fast bacilli (acid-fast bacillus stain). These aforesaid features were clinically and histologically consistent with erythema elevatum diutinum.

We noticed a remarkable response, as both the skin lesions and neuropathy improved with dapsone, 50 mg daily. Repeat electromyography found no evidence of generalized polyneuropathy. Later, when the patient decided to take her dapsone on an as-needed basis rather than daily, her dermatologic symptoms and neuropathy worsened.

DISCUSSION

Our patient presented with progressive neuropathy, a rare presentation of EED. Results of skin biopsies were characteristic of EED with leukocytoclastic vasculitis and prominent neutrophils.

Although EED often presents as red-to-purple cutaneous nodules on the extensor surfaces, vesicular, bullous, and ulcerative types have also been reported.[7] The lesions are generally asymptomatic but might be tender, pruritic, or painful. Lesions are initially soft and become more firm and indurated over time.[8] Constitutional symptoms, including fever and arthralgias, are often seen. The disease course is chronic with frequent relapses.[8] Our patient's clinical presentation and history were consistent.

The etiology of EED is not well understood but is thought to be related to deposition of circulating immune complexes in perivascular spaces secondary to infections or hematologic or autoimmune disease, thereby inducing an inflammatory cascade leading to damaged vessel walls. The evolution of lesions is apparent both clinically and histopathologically. Early lesions have a classical presentation of leukocytoclastic vasculitis, histopathologically presenting with leukocytoclasis, fibrin deposition, and endothelial swelling in the papillary and mid dermis. Older lesions show dermal clusters of perivascular fibrosis, intracellular lipid deposition, and capillary proliferation.[9] None of these findings are pathognomonic for EED, with differential diagnosis including Kaposi sarcoma, Sweet syndrome, leukocytoclastic vasculitis, neutrophilic dermatoses, sclerosing hemangioma, dermatitis herpetiformis, and granuloma annulare.[9,10]

Among the various treatment options for EED—tetracyclines, niacinamide, colchicine, topical, intralesional, and systemic glucocorticoids, sulfapyridine, and chloroquine—dapsone (50−200 mg/d) is considered the treatment of choice.[1,6]

Although several diseases are associated with EED, the diffuse neuropathy observed in our patient was unique among previous reports. Regarding her neuropathy and muscle pain, we theorize that nerve atrophy possibly happened as the result of direct (autoimmune infiltrative neurologic disorder involving small fibers) or indirect injury (chronic or intermittent swelling leading to nerve compression or entrapment). These constellations help explain the symptoms this patient observed, with pain, loss of sensation, and rigidity in all extremities. Awareness of this unusual presentation of EED helps to avoid misdiagnosis and to initiate treatment early.

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