A female with subcutaneous nodules and livedo racemosa

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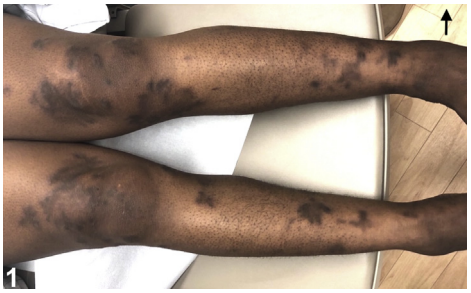

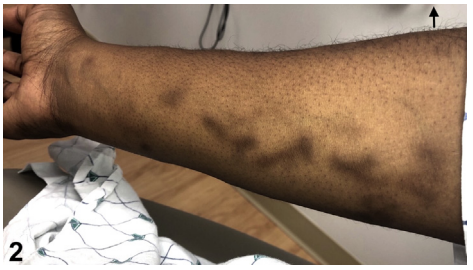

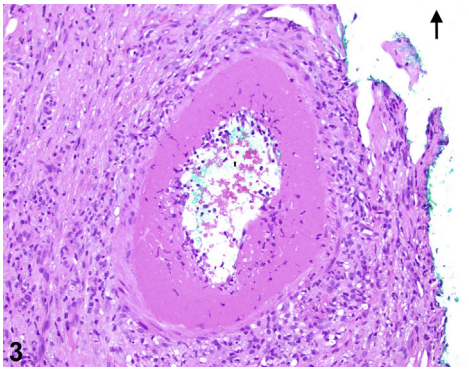

INTRODUCTION

A 23-year-old female presented with painful upper and lower extremity lesions and fatigue. She denied neurologic, pulmonary, cardiac, renal, gastrointestinal, and musculoskeletal symptoms during a review of the systems. Clinical examination revealed bilateral lower extremity tender subcutaneous nodules (Fig 1) and upper extremity livedo racemosa (Fig 2). Punch biopsy revealed a perivascular lymphohistiocytic infiltrate, extravasated red blood cells, and a necrotic blood vessel at the dermal-subcutaneous junction (Fig 3). The vitals were within normal limits, and laboratory investigations, including renal and hepatic function, antinuclear and antineutrophil cytoplasmic antibodies, cryoglobulins, rheumatoid factor, hypercoagulability workup, and angiography, were unremarkable, except for an elevated erythrocyte sedimentation rate.

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Question 1: What is the most likely diagnosis?

A. Sneddon syndrome

B. Cutaneous polyarteritis nodosa (c-PAN)

C. Erythema nodosum

D. Granulomatosis with polyangiitis

E. Erythema induratum

Answers:

A. Sneddon syndrome—Incorrect. Sneddon syndrome may present with livedo racemosa, although typically widespread, as well as hypertension and central nervous system disease. Subcutaneous nodules are not a characteristic feature. A biopsy may show endothelial inflammation, myointimal hyperplasia, and occlusion of the arterioles.[1] It is often caused by antiphospholipid antibodies in adults and adenosine deaminase 2 deficiency in children.[1] Testing for an adults and adenosine deaminase 2 gene mutation in this patient yielded negative results.

B. c-PAN—Correct. Tender subcutaneous nodules, livedo racemosa, and the biopsy demonstrating the necrotic blood vessel at the deeper, dermal-subcutaneous junction suggest medium-vessel vasculitis. The perivascular lymphohistiocytic infiltrate and concentric layers of fibrosis signify that the lesion is more than 48 hours old and in the reparative stage.[2,3] Fatigue, weight loss, fever, arthralgias, and neuropathy can be present in both c-PAN and systemic polyarteritis nodosa; however, c-PAN lacks multiorgan-system involvement, including hypertension, abdominal pain, renal failure, as well as hematuria and microaneurysms upon laboratory studies and imaging, respectively.[2]

C. Erythema nodosum—Incorrect. A biopsy of erythema nodosum reveals septal panniculitis with radial (Miescher) granulomas without vasculitis.[4] Livedo racemosa suggests a vascular etiology.[5]

D. Granulomatosis with polyangiitis—Incorrect. Granulomatosis with polyangiitis may present with subcutaneous nodules and livedo racemosa; however, the absence of upper respiratory tract, pulmonary, and renal involvement makes this diagnosis unlikely.[1]

E. Erythema induratum—Incorrect. Erythema induratum presents with tender nodules, often on the calves; livedo racemosa is not a characteristic feature. Histology shows septal panniculitis and vasculitis in the connective tissue septa and venules of fat lobules.[1]

Question 2: Which of the following is most commonly associated with this condition?

A. Levamisole

B. Coccidiomycosis

C. *Mycobacterium tuberculosis*

D. Group A *Streptococcus*

E. Irritable bowel syndrome

Answers:

A. Levamisole—Incorrect. Levamisole is a common adulterant in cocaine in the United States and can cause a vasculitic or vasculopathic syndrome with acral lesions involving the digits, ears, and nose. It is one of the few conditions that can cause both p- and c-ANCA positivity. Minocycline is a well-known trigger of c-PAN, and drug-induced vasculitis is often associated with p-ANCA positivity.[2]

B. Coccidiomycosis—Incorrect. Coccidiomycosis is associated with erythema nodosum.[1] However, there is no strong association of c-PAN with coccidiomycosis.

C. *M tuberculosis*—Incorrect. *M tuberculosis* is an associated trigger of erythema induratum, not c-PAN.[1]

D. Group A *Streptococcus*—Correct. Group A *Streptococcus* is the most commonly associated entity, with many patients having a preceding Group A *Streptococcus*-induced upper respiratory infection.[2] Other upper respiratory infections, such as parvovirus B19, have also been reported to cause c-PAN.[2]

E. Irritable bowel syndrome—Incorrect. c-PAN has been associated with inflammatory bowel disease.[2]

Question 3: Which of the following is the best treatment option for this patient?

A. Oral corticosteroids

B. Narrow band ultraviolet B

C. Minocycline

D. Plasmapheresis

E. Warfarin

Answers:

A. Oral corticosteroids—Correct. Oral corticosteroids may be used for acute flares of c-PAN, particularly when there are extracutaneous symptoms present.[1,2] Additional agents, including hydroxychloroquine, azathioprine, methotrexate, and cyclophosphamide, may be used in conjunction with corticosteroids or following corticosteroid tapering in patients with refractory or more severe disease.[2] For mild cases, nonsteroidal anti-inflammatory drugs, colchicine, and topical or intralesional steroids may also be effective.[2] If an underlying cause is identified, such as a streptococcal infection, this should be treated.[1,2]

B. Narrow band ultraviolet B—Incorrect. Narrow band ultraviolet B does not play a role in c-PAN treatment.

C. Minocycline—Incorrect. Minocycline is a known trigger of c-PAN.[2]

D. Plasmapheresis—Incorrect. Plasmapheresis may be considered in the initial treatment of PAN, not c-PAN.[1]

E. Warfarin—Incorrect. Anticoagulation may be warranted in c-PAN with the presence of antiphospholipid antibodies.[1]

Abbreviation used:

c-PAN: cutaneous polyarteritis nodosa

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