Reticular rash on the lower extremities

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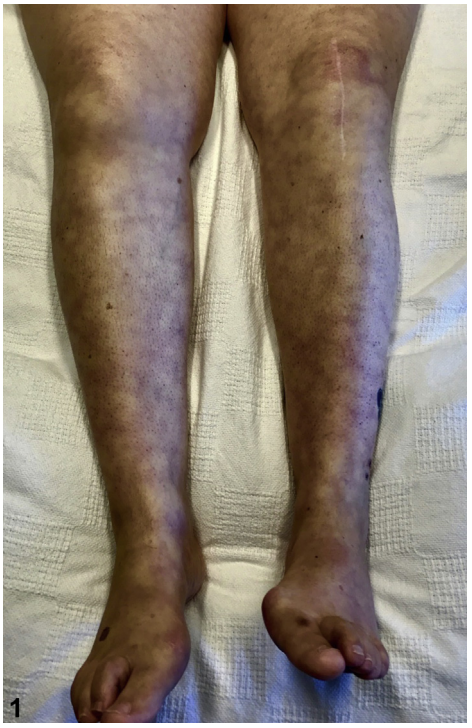

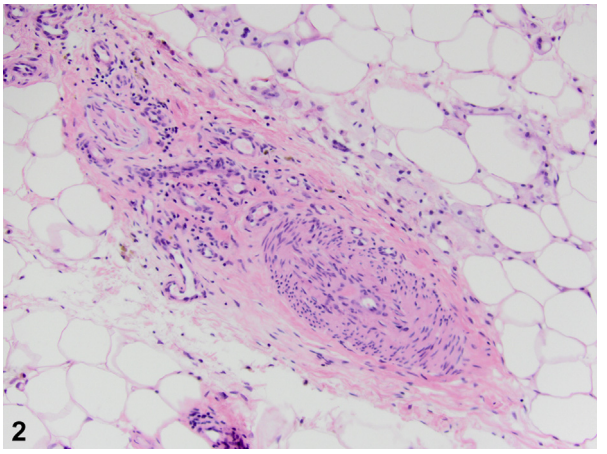

A 62-year-old woman presented with numbness, tingling, and an asymptomatic rash on the bilateral lower extremities. She had a history of recently diagnosed untreated multiple myeloma. Physical examination found decreased sensation over the bilateral feet and symmetric, violaceous, reticular patches over the bilateral lower extremities (Fig 1). Laboratory studies found a monoclonal IgG κ gammopathy and elevated serum viscosity elevation to 2.0 centipoises. Rheumatoid factor, antinuclear antibody, antineutrophil cytoplasmic antibody, antiphospholipid antibodies, and hepatitis serologies were negative. Skin biopsy found subcuticular vessels with intimal hyperplasia, increased reactive small vessels, and hemosiderin deposition suggestive of prior vascular thrombosis and no associated vasculitis (Fig 2).

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Question 1. What is the most likely diagnosis?

A. Classic polyarteritis nodosa

B. Rheumatoid vasculitis

C. Type I cryoglobulinemia

D. Mixed cryoglobulinemia

E. Antiphospholipid syndrome

Answers:

A. Classic polyarteritis nodosa — Incorrect. Cutaneous polyarteritis nodosa is characterized by palpable purpura, but livedo racemosa and retiform purpura can also be seen. Systemic signs include weight loss, fever, arthralgias, and renal failure. Histology findings show vasculitis rather than vascular thrombosis.

B. Rheumatoid vasculitis — Incorrect. Rheumatoid vasculitis occurs in less than 5% of rheumatoid arthritis patients and can involve the skin, nervous system, heart, and kidneys. Because rheumatoid vasculitis can affect small or medium-sized vessels, cutaneous findings range from palpable purpura to acral ulcerations and infarcts. A skin biopsy would most likely show vasculitis and not vascular occlusion.

C. Type I cryoglobulinemia — Correct. Type I cryoglobulinemia represents a thrombotic vasculopathy caused by monoclonal immunoglobulin occlusion of vessels in patients with hematologic malignancy, such as multiple myeloma, and can be associated with elevated serum viscosity. Cutaneous findings range from livedo reticularis to necrotic ulcerations and may be accompanied by neuropathy, arthralgias, and renal disease.[1,2]

D. Mixed cryoglobulinemia — Incorrect. Mixed cryoglobulinemia describes both type II and type III cryoglobulinemia in which cryoglobulins are polyclonal immunoglobulins. Unlike type I cryoglobulinemia, mixed cryoglobulinemia results in vasculitis of the small and medium-sized vessels and is associated with underlying infection (most commonly hepatitis C), connective tissue disease, and, less frequently, lymphoproliferative disorders.

E. Antiphospholipid syndrome — Incorrect. Antiphospholipid syndrome is a systemic disorder of coagulation resulting in arterial or venous thrombosis. Dermatologic findings include livedo reticularis, ulceration, retiform purpura, livedoid vasculitis, and splinter hemorrhages. Diagnosis requires two positive antiphospholipid antibody tests at least 12 weeks apart.

Question 2. What complication can occur in this disease?

A. Hyperviscosity syndrome

B. Periarticular bony erosions

C. Recurrent spontaneous abortions

D. Cirrhosis

E. Gastrointestinal bleeding

A. Hyperviscosity syndrome — Correct. Hyperviscosity syndrome is caused by aggregation of light chains and resultant increased blood viscosity in type I cryoglobulinemia.[3] Symptoms of hyperviscosity syndrome include bleeding, blurry vision, headache, peripheral neuropathy, and heart failure and generally appear when the blood viscosity is greater than 4.0 centipoises.[4]

B. Periarticular bony erosions — Incorrect. Periarticular bony erosions are seen in 45% of patients with early rheumatoid arthritis but are not associated with cryoglobulinemia.

C. Recurrent spontaneous abortions — Incorrect. Consecutive spontaneous abortions are a clinical criterion for the diagnosis of antiphospholipid syndrome and are not characteristic of cryoglobulinemia.

D. Cirrhosis — Incorrect. In mixed cryoglobulinemia, cirrhosis can occur in the setting of chronic hepatitis C infection. It is not a complication of type I cryoglobulinemia.

E. Gastrointestinal bleeding — Incorrect. Gastrointestinal bleeding caused by mesenteric ischemia is a poor prognostic sign in patients with polyarteritis nodosa. It is not a common symptom of cryoglobulinemia.

Question 3. What is the preferred method of treatment?

A. Systemic steroids alone

B. Plasma exchange with cytoreductive therapy

C. Cyclophosphamide and systemic steroids

D. Anticoagulation

E. Conservative management with cold exposure avoidance

A. Systemic steroids alone — Incorrect. Systemic steroids alone are not recommended in treatment of type I cryoglobulinemia, as it does not treat the underlying disorder. High-dose steroids are often used in conjunction with cytoreductive therapy in the treatment of multiple myeloma.

B. Plasma exchange with cytoreductive therapy — Correct. In the setting of progressive disease or symptomatic hyperviscosity, plasma exchange with cytoreductive therapy is the first line treatment for type I cryoglobulinemia caused by multiple myeloma.[5] This patient was treated with plasma exchange, lenalidomide, daratumumab, and dexamethasone with improvement in her neurologic and cutaneous symptoms over 1 month.

C. Cyclophosphamide and systemic steroids — Incorrect. Cyclophosphamide and systemic steroids are used in the treatment of moderate and severe polyarteritis nodosa but not in the treatment of cryoglobulinemia.

D. Anticoagulation — Incorrect. The mainstay of treatment for antiphospholipid syndrome is anticoagulation.

E. Conservative management with cold exposure avoidance — Incorrect. Because this patient is symptomatic, conservative management is not appropriate.

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