Comparing cases of type I cryoglobulinemia with histopathologic findings of vasculitis

To the Editor: We read with interest the recent manuscript "Multiple myeloma presenting as cyroglobulinemic vasculitis" by Runge et al[1] and present 2 additional cases of patients with type I cryoglobulinemia with similar clinical and histopathologic findings.

CASE 1

A 53-year-old woman with a history of recent acute anterior aspect of the right side of the cerebral artery infarct presented with necrotic digits (Fig 1) and painful ulcerations on the bilateral lower extremities, which had worsened over 18 months. Physical examination revealed retiform purpura on both cheeks, helices, chest, and upper and lower extremities.

Punch biopsy demonstrated leukocytoclastic vasculitis without prominent fibrin thrombi in initial sections reviewed (Fig 2); however, deeper levels highlighted the focal presence of thrombi. Blood and tissue cultures for bacteria, fungi, and atypical mycobacteria were negative. Laboratory workup was significant for a positive cryoglobulin screen but negative urine drug screen, rheumatoid factor, antineutrophil cytoplasmic antibody, and antiphospholipid antibody panel, as well as normal C4. These laboratory findings supported a diagnosis of type I cryoglobulinemia. Serum protein electrophoresis with immunofixation revealed a faint band of IgG κ suspicious for an early monoclonal protein. Serum light chain testing demonstrated an elevated IgG κ at 25.14 mg/dL (normal range, 0.33-1.94 mg/dL). Bone marrow biopsy was performed and demonstrated 15% plasma cells with κ light chain restriction, consistent with multiple myeloma. Given the presence of limb-threatening disease, treatment with methylprednisolone 125 mg intravenously 3 times per day and plasmapheresis was initiated, with subsequent transition to dexamethasone 40 mg weekly. Eight sessions of plasmapheresis were completed with a plan to pursue outpatient treatment with bortezomib.

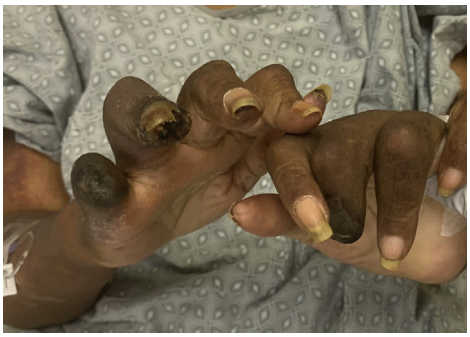

Fig 1. Digital ischemia with gangrene and partial autoamputation in a patient with type I cryoglobulinemia due to multiple myeloma.

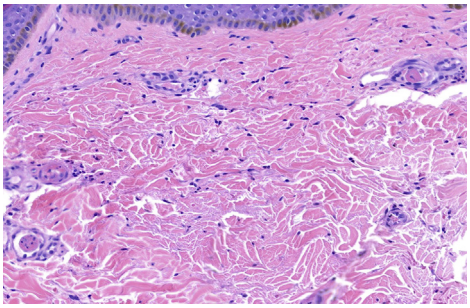

Fig 2. Perivascular and interstitial neutrophils with evidence of leukocytoclasia. There are also small fibrin thrombi within capillaries. This mixed pattern can be interpreted as a late lesion of leukocytoclastic vasculitis, in which fibrin thrombi follow more classic changes of vasculitis (Hematoxylin-eosin stain; original magnification: ×200).

CASE 2

A 62-year-old woman with history of seronegative arthritis presented with a 1-week history of an asymptomatic eruption on both lower extremities. Review of systems was remarkable for 60-pound weight loss and night sweats. Physical examination revealed stellate/retiform purpura on the thighs, knees, and lower portion of the legs (Fig 3). Initial skin biopsy demonstrated leukocytoclastic vasculitis with negative direct immunofluorescence. The rash progressed over a month to involve the lower portion of the abdomen. Several weeks later, the patient was hospitalized for progressive skin findings associated with tenderness. Examination revealed retiform purpura on the trunk and extremities, along with left side supraclavicular and axillary lymphadenopathy. Repeat skin biopsies demonstrated thrombi within small-caliber vessels along with leukocytoclastic vasculitis (Fig 4). Laboratory workup demonstrated elevated cryoglobulins (qualitative). Hepatitis

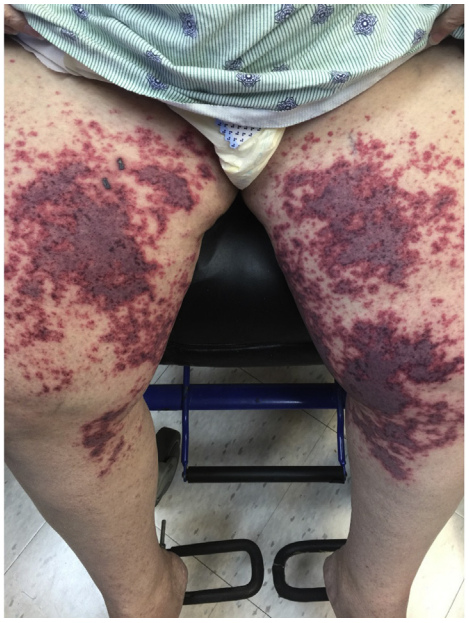

Fig 3. Retiform or stellate purpura on the thighs of a patient with type I cryoglobulinemia due to small lymphocytic lymphoma.

C antibody, anti-cardiolipin antibodies, rheumatoid factor, and antineutrophil cytoplasmic antibody were negative. Serum protein electrophoresis and immunofixation demonstrated an IgG κ M-spike. An excisional biopsy of a cervical lymph node confirmed the diagnosis of small lymphocytic lymphoma. Bone marrow biopsy demonstrated extranodal involvement, resulting in TNM stage IV disease. Bendamustine and rituximab were initiated, and the patient completed 3 cycles of therapy. At followup 5 years later, the patient remained in remission, and there was no recurrence of skin findings.

DISCUSSION

Along with the case presented by Runge et al,[1] these presentations expand the spectrum of histopathologic findings seen in type I cryoglobulinemia. In all 3 cases, clinical findings of thrombotic vasculopathy and laboratory findings were all consistent with type I cryoglobulinemia. However, both vasculopathic and vasculitic patterns were identified on histopathology. Small-vessel vasculitis, a hallmark finding traditionally associated with mixed cryoglobulinemia rather than type I cryoglobulinemia,[2] should not preclude or delay diagnostic workup for underlying hematolymphoid dyscrasia in a patient with retiform purpura, ischemia, and elevated cryoglobulins.

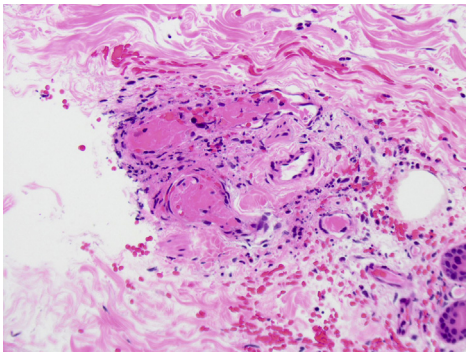

Fig 4. Thrombotic vasculitis: Fibrin thrombi in small-caliber vessels along with prominent perivascular neutrophils and karyorrhexis (Hematoxylin-eosin stain; original magnification: ×200).

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Conflicts of interest

None disclosed.

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