Received: 14 September 2023 | Accepted: 28 September 2023

DOI: 10.1002/jha2.810

eJHaem

HAEMATOLOGY IMAGES

Cryoglobulinemic vasculitis with blood schistocytosis and bone marrow vasculitis

Afreen Jasim[1,2] | **Maria E. Vergara-Lluri**[1,2]

[1]Keck School of Medicine of University of Southern California, Los Angeles, California, USA

[2]Los Angeles County + University of Southern California Medical Center, Los Angeles, California, USA

Correspondence
Maria E. Vergara-Lluri, 2011 Zonal Avenue HMR 308, Los Angeles, CA 90033, USA.
Email: maria.vergara-lluri@med.usc.edu

KEYWORDS
haematopathology, infection, rheumatology, vascular disease

A 58-year-old man with hypertension, chronic kidney disease, congestive heart failure, remote polysubstance abuse, and chronic hepatitis C viral (HCV) infection presented with bilateral lower extremity edema and a non-blanching palpable purpuric rash in his lower extremities. No signs or symptoms of hyperviscosity were elicited. Laboratory findings were significant for a complete blood count with moderate anemia (hemoglobin 9.6 g/dL) and mild thrombocytopenia (platelet count 154 $\times$ $10^3/\mu$L). The peripheral blood smear exhibited frequent schistocytes (Figure 1A). His most recent HCV RNA viral load was 79,600 IU/mL. Urinalysis testing was remarkable for nephrotic range proteinuria (urine protein-to-creatinine ratio = 4.95; normal ratio < 0.19) and hematuria (>50 red blood cells per high power field on urine microscopy). Serologic testing for the following antibodies was within the normal range: anti-nuclear antibodies, anti-neutrophilic cytoplasmic antibodies, anti-double stranded DNA, rheumatoid factor, and anti-glomerular basement membrane antibodies. Serum and urine electrophoresis with immunofixation revealed unquantifiable paraprotein typing as immunoglobulin M (IgM) kappa. Further workup demonstrated a positive cryoglobulin screen with a marked cryoprecipitate quantified at 4.09% cryocrit. One IgM kappa protein was

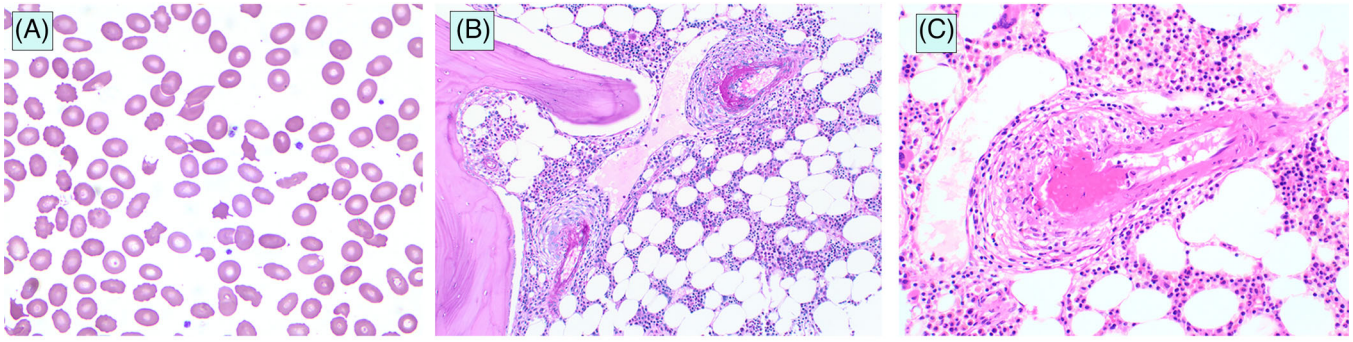

FIGURE 1 (A) Peripheral blood smear exhibiting schistocytes (500× magnification, Wright–Giemsa stain). (B and C) Bone marrow biopsy showcasing medium-sized vessels with striking segmental intravascular and intramural eosinophilic fibrinoid necrosis, as well as overlying vessel wall lamination (i.e., onion skinning): (B) 100× magnification, periodic acid-Schiff (PAS) stain; (C) 400× magnification, hematoxylin and eosin (H&E) stain.

seen on immunofixation of the patient's cryoprecipitate, while immunodiffusion showed IgG, IgA, IgM, kappa, lambda, C3, albumin, and fibrinogen. A skin biopsy of the lower extremity rash was performed, which displayed an evolving leukocytoclastic vasculitis. The differential diagnostic considerations included hematologic malignancies (such as IgM monoclonal gammopathy of undetermined significance [IgM MGUS], multiple myeloma [MM], and lymphoplasmacytic lymphoma [LPL]), prompting performance of a bone marrow biopsy.

The bone marrow biopsy showcased medium-sized vessels with striking segmental intravascular and intramural eosinophilic fibrinoid necrosis, as well as overlying vessel wall lamination (i.e., onion skinning) (Figure 1B,C). In the context of a positive cryoglobulin work-up, these changes are consistent with acute and chronic/healing cryoglobulinemic vasculitis. No clonal population of B cells or plasma cells were uncovered in this normocellular bone marrow with maturing trilineage hematopoiesis. Fluorescence in situ hybridization studies for a myeloma-specific probe set and *MYD88* mutational analysis were negative for abnormalities, further speaking against IgM MGUS, MM, and LPL. No clonal expansion or progression to overt plasma cell neoplasia or lymphoma was observed after 18 months of follow-up.

Type I cryoglobulinemia is associated with hematologic malignancies (such as MGUS, MM, and LPL). In this case, however, in the absence of overt malignancy, the overall findings are supportive of type II mixed cryoglobulinemia related to the patient's chronic HCV infection. Type II "mixed" cryoglobulinemia, observed in up to 90% of patients with HCV infection [1], involves a mixture of monoclonal and polyclonal immunoglobulins, whereby the monoclonal IgM targets the Fc region of the polyclonal IgGs [2].

To our knowledge, no images of bone marrow vasculitis have been previously published in association with cryoglobulinemia. Only rare cases of bone marrow vasculitis have been described with granulomatosis with polyangiitis [3, 4]. Our case highlights an HCV-related cryoglobulinemic vasculitis with a striking illustration of bone marrow involvement with peripheral red blood cell schistocytosis.

AUTHOR CONTRIBUTIONS

Afreen Jasim wrote and revised the initial manuscript drafts, took the photomicrographs, and approved the final manuscript. Maria E. Vergara-Lluri conceived the design of the report and revised and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

FUNDING INFORMATION

The authors received no specific funding for this work.

DATA AVAILABILITY STATEMENT

N/A.

ETHICS STATEMENT

The authors have confirmed ethical approval statement is not needed for this submission.

PATIENT CONSENT STATEMENT

The authors have confirmed patient consent statement is not needed for this submission.

CLINICAL TRIAL REGISTRATION (INCLUDING TRIAL NUMBER)

The authors have confirmed clinical trial registration is not needed for this submission.

ORCID

Afreen Jasim https://orcid.org/0009-0000-0121-5175
Maria E. Vergara-Lluri https://orcid.org/0000-0002-4576-849X

REFERENCES

1. Voma CB, Levinson SS. Analysis, detection and quantitation of mixed cryoglobulins in HCV infection: brief review and case examples. Clin Chem Lab Med. 2016;54:1853–59.
2. Czuchlewski DR. Miscellaneous identifications. In: Glassy EF, Blomberg D, Galagan KA, editors. Color atlas of hematology: an illustrated field guide based on proficiency testing. 2nd ed. Northfield (IL): College of American Pathologists; 2018. p. 342–45.
3. Broner J, Arnaud E, Bisiou S, Artiaga A, Fantone M, Gonzalez S, et al. A rare case of small-vessel necrotizing vasculitis of the bone marrow revealing granulomatosis with polyangiitis. Rheumatology. 2021;60(8):3956–57.
4. de la Cámara Fernández I, Lozano Morillo F, Morillas López L, Martínez López M. A case report of granulomatosis with polyangiitis with granulomas in bone marrow. Reumatol Clin. 2019;15:e60–e61.

How to cite this article: Jasim A, Vergara-Lluri ME. Cryoglobulinemic vasculitis with blood schistocytosis and bone marrow vasculitis. eJHaem. 2023;4:1168–1169. https://doi.org/10.1002/jha2.810