

# CJASN

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*Ishan Paranjpe, Kumardeep Chaudhary, Manish Paranjpe, Ross O'Hagan, Sayan Manna, Suraj Jaladanki, Arjun Kapoor, Carol Horowitz, Nicholas DeFelice, Richard Cooper, Benjamin Glicksberg, Erwin P. Bottinger, Allan C. Just, and Girish N. Nadkarni*

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#### On the Cover

##### Case Description:

An 84-year-old man with a history of stage 3 CKD and recent diagnosis of Waldenström's macroglobulinemia presented with confusion, acute kidney failure, and purpuric papules on the lower extremities, 3 weeks after starting treatment with rituximab. Laboratory evaluation revealed elevated cryoglobulin levels (33%), normal serum viscosity (1.4 centipoise), monoclonal serum IgM  $\kappa$  at 374 mg/dl, negative rheumatoid factor, low serum C3 and C4 (45 and 9 mg/dl, respectively), high serum free  $\kappa$  light chains (212.7 mg/dl) and a  $\kappa/\lambda$  ratio of 3.78. Cryoglobulin immunofixation showed a monoclonal IgM  $\kappa$  (type I) cryoglobulin. Urinalysis showed proteinuria (100 mg/dl), hematuria (10–19 RBCs/HPF), and fine granular casts. A skin biopsy was indicated for assessment of lower extremity rash, and a kidney biopsy was performed due to acute kidney failure.

##### Image Description:

Left image: Purpuric papules and plaques with focal erosion and crusting are noted on the bilateral lower extremities.

Center image: Skin biopsy with numerous intracapillary hyaline thrombi, consistent with cryoglobulin (H&E stain, 200 $\times$ ).

Right image: Kidney biopsy showing most of the glomerular capillaries were occluded by hyaline thrombi positive for IgM  $\kappa$  on immunofluorescence that had no definitive substructure on electron microscopy (not shown) (H&E stain, 400 $\times$ ).

##### Teaching Points:

The findings were consistent with type I cryoglobulinemia. Approximately 10% of patients with Waldenström's macroglobulinemia develop type I cryoglobulinemia, which may be precipitated by rituximab treatment due to a sudden rise in IgM levels. In our patient, this has led to renal and cutaneous hyaline thrombi formation, despite normal serum viscosity. *In vitro* studies have shown that rituximab as well as intravenous immunoglobulin can stimulate IL-6 production by monocytes, and IL-6 stimulates IgM secretion by lymphoplasmacytic lymphoma cells (the neoplastic population that secretes IgM in Waldenström's macroglobulinemia). This is usually a transient phenomenon with later recovery of kidney function and should not be construed as an indication of treatment failure. This patient received intravenous cyclophosphamide, plasmapheresis, and hemodialysis. His mental status and kidney function improved, and dialysis was discontinued 4 weeks after presentation. He is currently on ibrutinib, and at most recent follow-up, serum creatinine was 1.23 mg/dl, IgM decreased to 339 mg/dl, cryoglobulin level was 3%, and urine protein was 30 mg/dl.

(Images and text were provided by Clarissa A. Cassol, MD, and Catherine Chung, MD, Department of Pathology, Ohio State University, Columbus, Ohio; and Amy G. Johnson, MD, and Sethu Madhavan, Department of Internal Medicine, Ohio State University, Columbus, Ohio)