Clinical Case Reports

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CLINICAL IMAGE

Rituximab therapy for hepatitis C virus-associated cryoglobulinemic membranoproliferative glomerulonephritis

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Key Clinical Message

Membranoproliferative glomerulonephritis associated with mixed cryoglobulinemia is the most common form of kidney disease observed in relation to hepatitis C virus (HCV) infection. Rituximab, a monoclonal antibody against CD20, is an effective treatment for severe and/or refractory HCV-related vasculitis and may evade the need for dialysis as in our patient.

Keywords

Cryoglobulinemia, hepatitis C, membranoproliferative glomerulonephritis, rituximab

A 55-year-old woman with a history of liver cirrhosis from hepatitis C virus (HCV) infection was admitted for abdominal pain and ascites. She was never treated for HCV before. Serum creatinine at presentation was 1.6 mg/dL (baseline: ~0.8 mg/dL) and worsened requiring initiation of hemodialysis despite paracentesis and intravenous albumin therapy. Urinalysis was significant for hematuria and proteinuria (protein-creatinine ratio ~2 g/g). Serum complement C4 was <8 mg/dL (ref: 13–50). A renal biopsy demonstrated cryoglobulinemic membranoproliferative glomerulonephritis (Fig. 1). She was treated with four weekly doses of intravenous rituximab 375 mg/m² and prednisone. Soon after that, her renal function recovered and was discharged off dialysis, with a plan to start antiviral therapy as outpatient. Serum creatinine was 1.03 mg/dL at 2-week follow-up, with minimal proteinuria (~400 mg/g).

Cryoglobulinemia is a pathologic condition in which the blood contains immunoglobulins that exhibit the property of reversible precipitation from serum cooled to 4°C. HCV is known to be associated with mixed Cryoglobulinemia, which usually involves monoclonal IgM (or IgG or IgA) and polyclonal Ig (mainly IgG). Rituximab is an effective treatment for severe and/or refractory HCV-related vasculitis and it should be used in conjunction with antiviral therapy, as the relapses are typically associated with the absence of virologic control [1]. For instance, in a study [2] comprising of 32 HCV-positive patients with vasculitis treated with PEGylated interferon alfa-2b plus rituximab ($n = 20$) versus rituximab monotherapy ($n = 12$), a complete clinical response was achieved in 80% versus 58% of the patients, respectively. After a mean follow-up period of 23 months, 22% of patients experienced a clinical relapse, all of which were associated with absent virologic control. Moreover, 78% of the relapses were associated with B-cell recovery. In an interesting case series of five patients, Cornella et al. [3] have found that patients with cirrhosis tend to have a decreased ability to clear immune complexes despite completion of triple therapy with newer oral antiviral agents (boceprevir, telaprevir or sofosbuvir). Therefore, they suggested that a longer treatment duration than the standard 24 weeks with triple therapy could aid in the clearance of

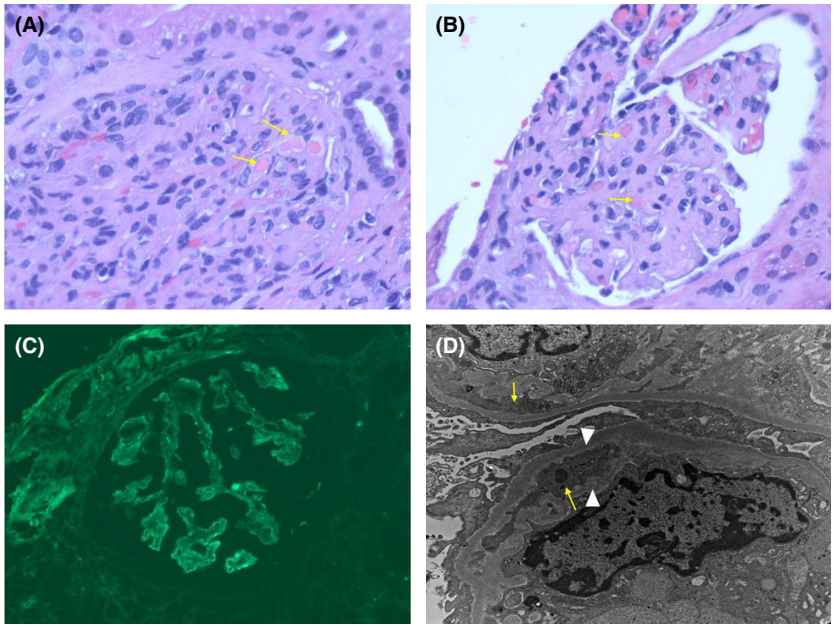

Figure 1. (A and B) Renal biopsy demonstrating cryoglobulin precipitates [arrows] in the glomerular capillaries on light microscopy; (C) Immunofluorescence demonstrating glomerular monoclonal IgM deposition; (D) Electron microscopy showing sub-endothelial deposits [arrows] with "double contouring" of the glomerular basement membrane [triangular arrows].

immune complexes and cryoglobulins in these patients. In conclusion, treatment of cryoglobulinemic vasculitis should be tailored to individual patients' needs and take into consideration the severity of the disease.

Informed Consent

Informed consent has been obtained for the publication of this clinical image.

Conflict of Interest

The authors have declared that no conflict of interest exists.

Authorship

All the authors made substantial contribution to the preparation of this manuscript and approved the final version for submission. AK: drafted the manuscript; XZ: provided pathology images and pertinent input.

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