Obinutuzumab Rescue in Rituximab Resistant Mixed Cryoglobulinemia

To The Editor: We previously reported a persistent mixed cryoglobulinemic membranoproliferative glomerulonephritis secondary to a monoclonal gammopathy of renal significance despite hepatitis C eradication.[1] While initially responsive to rituximab, the patient became refractory to it, and subsequently failed cyclophosphamide, bortezomib and bendamustine. Azathioprine proved partially efficacious as demonstrated by a relapse within a month of its cessation in order to administer bendamustine. He remained dependent on weekly plasmapheresis. To improve disease control, obinutuzumab was added to azathioprine. Four doses of 1 g were given every 3 weeks, followed by 3 additional doses every 8 weeks. This translated into

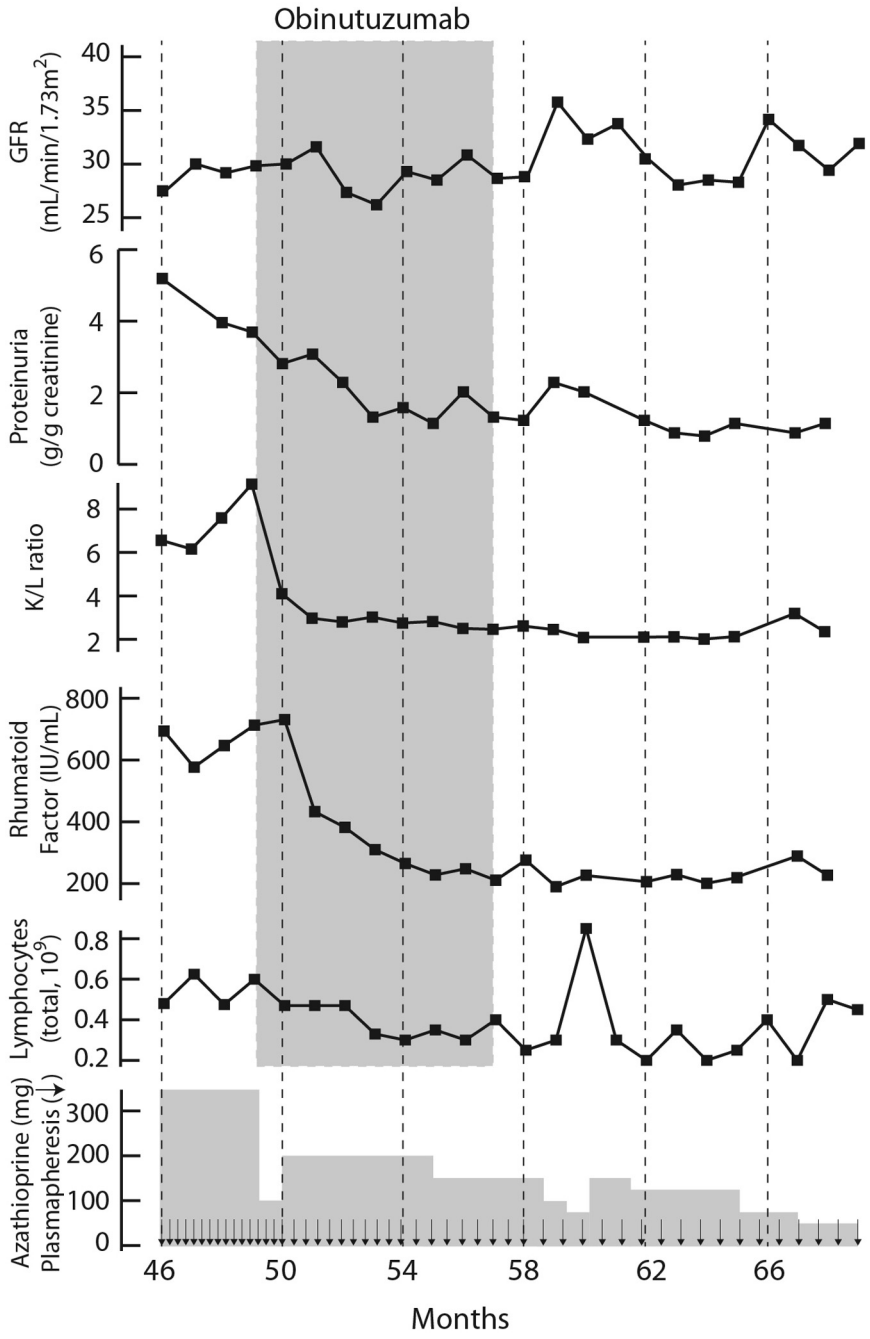

Figure 1. Clinical assessment and treatments.

lasting reductions in proteinuria, rheumatoid factor and serum free light chain ratio (Figure 1). Plasmapheresis requirements decreased, and azathioprine and prednisone doses were tapered. At 1-year post obinutuzumab therapy, CD19+/CD20+ lymphocytes remain undetectable. No opportunistic infection occurred.

Obinutuzumab is a novel humanized type II anti-CD20 monoclonal antibody with superior B-cell depleting capabilities, mediated by enhanced direct cell death via complement activation and antibody-dependent phagocytosis.[2] Although only approved for the treatment of hematological malignancies, it is being investigated in lupus nephritis and membranous nephropathy. A case of chronic lymphoid leukemia related immune-complex mediated membranoproliferative glomerulonephritis was successfully treated with it.[3] To our knowledge, this is the first report of a response to obinutuzumab in refractory monoclonal gammopathy of renal significance. It reduced the production of pathogenic monoclonal RF permitting the weaning of concomitant therapies. Rescue therapy with obinutuzumab, or other new B-cell depleting therapies, should be considered in glomerular diseases where rituximab is indicated but has failed.

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