Treatment With Rituximab in a Patient With Membranoprolipherative Glomerulonephritis Associated to Hepatitis C Virus Infection

To the Editor: Membranoprolipherative glomerulonephritis (MPGN) is the most frequent renal complication of hepatitis C virus (HCV) infection.[1,2] Its treatment is based on controlling the HCV infection through the use of interferon and ribavirine.[1] Situations in which, due to the severity of the renal affection, there is lack of efficacy or secondary effects of antiviral treatments, make it necessary to use glucocorticosteroids, plasmapheresis, and immunosupressants.[3,4] Rituximab is a chimeric monoclonal antibody directed against CD20 antigen on B lymphocytes which has been used on occasion for the treatment of HCV associated cryoglobulinemia (CM) MPGN, as an alternative to classic immunosupressant treatment.[5-7] We present a case in which the result of treatment with rituximab in a woman with HCV associated MPGN, intolerant to ribavirine and with a poor response to interferon treatment is analyzed. A 44 year-old woman with HCV infection presented polyarthritis and purpura in September 2005. Laboratory testing showed: creatinine, 0.9 mg/dL; creatinine clearance (CrCl), 90 mL/min/1.73 m^2; rheumatoid factor (RF), 114 IU/mL; C3c, 75 mg/dL (normal, 90-180 mg/dL); liver enzymes in normal ranges; antinuclear antibodies, ANCA, cryoglobulins, anticardiolipin antibodies, and lupus anticoagulant, negative; viral load, 700 000 IURNA-HCV/mL; genotype 1b, 24 h microhematuria and proteinuria, 700 mg. In october 2005 treatment with peg-interferon was started (Pegasys® 180µg/weeks) and ribavirine 1000 mg/day, with a complete remission of symptoms. Proteinuria reached 360 mg/24 h. After 4 months of treatment, treatment was stopped due to skin lesions. In september 2006 she presented edema of the lower extremities. Laboratory analysis showed: creatinine, 1.7 mg/dl; proteinuria, 7.67 g/24 h; CrCl, 49 ml/min/1.73 m^2; microhematuria and viral load >700 000 IURNA-HCV/mL. Renal biopsy was compatible with MPGN. After proving that the skin reaction was due to ribavirine, treatment with peg-interferon was restarted. Creatinine reached 1.4 mg/dL, CrCl 77 mL/min/1.73 m^2, the viral load became undetectable but intense microhematuria persisted and proteinuria stabilized at 3-4 g/24 h. Edema and elevated blood pressure persisted in spite of treatment with spironolactone, furosemide, amlodipine, doxazosine, and telmisartan. Therefore, in february 2007 we suspended interferon and in april we decided to initiate prednisone (1 mg/kg/day) and 6 sessions of plasmapheresis, without observing improvement. In may, serum creatinine was 1.7 mg/dL and CrCl, 34 mL/min/1.73 m^2. Three boluses of 500 mg of methylprednisolone and two 1g-doses of rituximab, with an interval of 15 days between doses, were administered. Since october, blood pressure has been under satisfactory control and edema has dissapeared. In november 2007 two more doses of rituximab were administered. The last laboratory analysis (february 2008) showed serum creatinine of 1.5 mg/dL; CrCl, 45 mL/min/1.73 m^2; and proteinuria, 0.31 g/24 h. Microhematuria persisted. The viral load was >700 000 IURNA-HCV/mL, with normal liver enzymes. The dose of prednisone had been reduced to 12.5 mg/day. Liver ultrasound was normal. In HCV-associated MPGN, cryoglobulins are detected in 50%-70% of cases.[1] Occasionally, the small and variable concentration of cryoglobulins and the need to extract and maintain the sample at a temperature of 37°C make their detection difficult.[8] In our patient, elevated RF and the reduction on complement levels indicated the affection, although determinations were repeatedly negative. Treatment of HCV-associated MPGN is not well established.[1,3,4] Therefore, we believe that this experience adds to that published by other authors that consider rituximab as an alternative to cyclophosphamide in patients with MPGN due to HCV.[4,6,7] We have employed a dose approved for rheumatoid arthritis. Regarding the safety of its use, the increase in the viral load that we detected did not seem to influence liver function, as has been communicated by other authros.[5,9]

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