Nephrotic syndrome with pegylated interferon alfa 2a and ribavirin for a patient with chronic hepatitis C

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Interferon therapy for hepatitis C can result in renal complications as interstitial nephritis, minimal change disease and immune complex glomerulonephritis [1]. We present the case of a 42-year-old man infected with chronic hepatitis C who developed focal and segmental glomerulosclerosis (FSGS) after treatment with pegylated interferon alfa 2a and ribavirin.

A 42-year-old man reported with incidental detection of hepatitis C virus infection (anti-HCV positive) at the time of donation. His risk factors included surgery for fracture tibia, blood transfusions and frequent use of injections possibly with reusable needles and syringes for joint pains. His physical examination was unremarkable. His baseline laboratory investigations showed hemoglobin 13 g/dL, mean corpuscular volume (MCV) 87 fl, white blood cell count 4000/cumm, platelet count 3,00,000/mm², aspartate aminotransferase (AST) 80 U/L, gamma glutamyl transpeptidase (GGT) 30 U/L, alkaline phosphate 78 U/L, albumin 3.8 g/dL, normal renal and thyroid functions, coagulogram and urinalysis. He was determined to have hepatitis C virus genotype 3 and his serum HCV RNA levels were 6,95,000 IU/mL. Ultrasound examination of abdomen showed normal liver, spleen and kidneys. Liver biopsy revealed chronic hepatitis grade 2, stage 1 and the hepatitis activity index (HAI) was 6.

He was advised pegylated interferon alfa 2a, 180 μg once a week and oral ribavirin (1000 mg/day). He had flu-like symptoms on the day of injection each time and was relieved with paracetamol. After 8 weeks of initiation of therapy, he started complaining of fatigue and bilateral ankle swelling. He returned after another 2 weeks with progressive edema that now involved whole lower limbs and periorbital puffiness. His blood pressure was normal. Rest of the general physical and systemic examination was normal. Hematological and biochemical tests were as follows: Hemoglobin 10 g/dL, total leukocyte count 3500/cumm, platelet count 25000/mm², creatinine 1.7 mg/dL, AST 85, ALT 90 U/L. Twenty-four hour urine analysis showed 4.5 g/L protein. His total serum cholesterol was 275 mg/dL and triglycerides were 240 mg/dL. In view of nephrotic range proteinuria, renal biopsy was performed and revealed FSGS, mild patchy tubular atrophy, interstitial fibrosis and mild non-specific interstitial inflammation. Immunofluorescence showed + to – staining for IgM and irregular staining for C3. Electron microscopy was not done. Both antiviral drugs were withheld. He was given ACE (I) -ramipril, diuretics- frusemide and diuretics and pedal edema regressed. His urine proteinuria declined to <1 g/day.

Antiviral therapy was reinitiated after 5 weeks. Symptoms of pedal edema and periorbital puffiness reappeared after 2 weeks of restarting therapy. Proteinuria was 4.6 g/24 h, creatinine 1.6 mg/dL, urea 35 mg/dL, albumin 3.0 g/dL and total cholesterol 215 mg/dL. Antiviral therapy was stopped and after 4 weeks of ACE (I) and diuretics he improved symptomatically and proteinuria declined to 300 mg/day.

There is ample evidence suggesting an association between chronic hepatitis C virus infection and glomerular diseases such as type 1 membranoproliferative glomerulonephritis with or without cryoglobulinemia. The combination of IFN and ribavirin is useful in patients with hepatitis C–related renal disease. However the chronology of events in our patient suggests that antiviral therapy resulted in FSGS. The remission of proteinuria on stopping interferon and the recurrence of
proteinuria on rechallenge confirms this association. Nephrotoxicity with this treatment for HCV has been infrequently reported [2].

Renal injury from interferon is typically mild and includes proteinuria (15% to 20%), mild azotemia (10%) and abnormalities in urinary findings (15%) [3, 4]. Proteinuria is usually mild, with average proteinuria <1 g/day and does not correlate with interferon dosage or renal insufficiency [4]. Proteinuria, azotemia and urinary abnormalities typically resolve on cessation of therapy. There are few case reports of development of FSGS due to interferon therapy. Other drugs and medications associated with FSGS include heroin, lithium and pamidronate [5–10].

The mechanism of interferon renal toxicity remains obscure. Immune complex glomerulonephritis due to interferon-anti interferon immune complexes is a theoretical consideration. Among the diverse speculations to explain the etiological role of interferon causing severe proteinuria, it is tempting to consider a sequence where interferon may participate in alteration of protein glomerular permeability either directly or through release of other cytokines by activating T lymphocytes [10].

It needs to be emphasized that the rare complication of FSGS can occur any time after the start of interferon therapy. Apart from cessation of the offending drug, the only other options for treating FSGS in chronic hepatitis C is to decrease proteinuria by using ACE inhibitors or angiotensin receptor blockers along with a salt—restricted low protein diet. The role of steroids and other cytotoxic agents is controversial even in idiopathic FSGS and may be risky in HCV infection [10].

In conclusion, we report a case of focal and segmental glomerulosclerosis related to pegylated interferon alfa 2a. Although, interferon has a good safety record, should be a frequent urinalysis and serum creatinine done and after starting therapy.

References