Membranous nephropathy and carbamazepine

Sir,

Membranous nephropathy is the most frequent cause of nephrotic syndrome in adults.[1] The cause cannot be ascertained in about 62-86% cases.[2] Drugs account for 6-9% of secondary membranous nephropathy.[3] The classic offenders are gold, penicillamine, non-steroidal anti-inflammatory drugs and captopril, though there are case reports for many others. We report a patient of secondary membranous nephropathy due to use of carbamazepine.

A 35-year-old man suffered episodes of complex partial seizures about 2 years back. He was initiated on tablet carbamazepine, a controlled release preparation, 200 mg twice a day. He had been using it without interruption. About 6 months before presentation, he noticed swelling of feet and face and increased frothiness of urine. There was no compliant of oliguria, hematuria or graveluria. His pulse was 80 bpm and blood pressure was 110/70 mmHg. Systemic examination was unremarkable. His investigations were reported in Table 1.

Table 1: Investigations

Test	Result
Hemoglobin	14.2 g/dl
Urine-albumin	4+
RBC and WBC	Nil
24 h urine protein	6800 mg
Random blood glucose	95 mg/dl
Serum creatinine	1.2 mg/dl
Total serum proteins	3.7 g/dl
Serum albumin	1.4 g/dl
Serum cholesterol	450 mg/dl
Serum triglycerides	375 mg/dl
HbsAg	Negative
Anti-HCV Ab	Negative
HIV	Non-reactive
Chest radiograph	Normal study
Upper gastrointestinal endoscopy	Normal study
Ultrasound abdomen	Kidneys: Right: 9.5 cm×4.1 cm, left: 9.8 cm×4.2 cm

RBC: Red blood cell, WBC: White blood cell, Anti-HCV Ab: Anti-hepatitis-C virus antibodies, HIV: Human immunodeficiency virus, HbsAg: Hepatitis B surface antigen

A renal biopsy showed 17 glomeruli. All glomeruli were normal in size and non-proliferative. Capillary loops were stiff, round and patent with a thick basement membrane. Silver methenamine stain showed spikes. Tubules and vascular system was unremarkable. Immunofluorescence showed diffuse granular deposits with IgG (4+) and C3 (2+) along the capillary loops. The features were suggestive of membranous nephropathy.

Carbamazepine was gradually tapered and replaced by sodium valproate. The proteinuria came down to 1.0 g at the end of 6 months. There was an improvement in serum albumin and the serum creatinine was always <1.2 mg/dl. The remission of proteinuria had a temporal relation with withdrawal of the drug. However, spontaneous remission of the membranous nephropathy

could also be another possibility. After 2 years of follow-up, he remains symptom free and proteinuria is <1 g/day.

The adverse effects of carbamazepine affecting kidneys include acute tubular necrosis resulting from the toxic effect of carbamazepine,[4] acute tubulointerstitial nephritis[4] and granulomatous interstitial nephritis.[5] In addition, there is one report of carbamazepine induced membranous nephropathy,[4] in which the patient received both phenobarbitone and carbamazepine. After 3 years of use of carbamazepine, he was found to have proteinuria of 7.1 g/day. The renal biopsy revealed membranous nephropathy. The replacement of carbamazepine with sodium valproate ameliorated the proteinuria.

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