Membranous nephropathy associated with the use of levodopa-carbidopa combination

Sir,

Membranous nephropathy (MN) is the cause of nephrotic syndrome in approximately 25% of adults.[1] In over 75% of patients of MN, no aetiological agent can be determined. Drugs account for 6–9% of secondary MN.[2] Drug associated MN can develop at any age and typically develops soon after exposure to the offending agent.[3] The classic offenders are gold, penicillamine, nonsteroidal anti-inflammatory drugs and captopril, though there are reports for many other drugs. We could not find, after a thorough literary search a single report of levodopa-carbidopa combination associated with MN.

We present a 45-year-old male patient who has been on regular follow up for Parkinson's disease (PD) for the past 6 months. He was being treated with levodopa-carbidopa combination, 110 mg twice a day. He presented with history of gradually worsening swelling of feet and face of 2 months duration. There was a history of oliguria and increased frothiness of urine. His blood pressure at presentation was 120/80 mmHg. Investigations were given in the Table 1.

Renal biopsy showed 11 glomeruli. All glomeruli were normal in size. The capillary loops were stiff, round and patent with thick basement membrane. Silver methanamine stain showed spikes. Tubules and vascular system were unremarkable. Immunofluorescence showed diffuse

Table 1: Investigations

Test	Result
Hemoglobin	14.7 g/dl
Urine-albumin	4^{+}
RBC and WBC	Nil
24 h urine protein	3600 mg
Random blood glucose	103 mg/dl
Serum creatinine	0.82 mg/dl
Total serum proteins	6.0 g/dl
Serum albumin	3.0 g/dl
Serum cholesterol	224 mg/dl
Serum triglycerides	365 mg/dl
HbsAg	Negative
Anti HCV Ab	Negative
HIV	Nonreactive
Chest radiograph	Normal study
Ultrasound abdomen	Kidneys: right: 9.9 cm×3.8 cm, left: 9.6 cm×3.4 cm

RBC: Red blood cell, WBC: White blood cell, HbsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus

granular deposits with immunoglobulin G (IgG) 3^+, IgA trace, IgM trace and C3 2^+ along the capillary loops. The features were suggestive of MN. Serum anti-phospholipase-A (2)-receptor (PLA2R) antibodies, done by enzyme-linked immunosorbent assay, were negative. Suspecting that the levodopa-carbidopa combination would be a cause of MN, it was stopped. Ropinirole 0.5 mg, half tablet bid was started. During next 4 weeks, the swelling of feet and face have disappeared, the proteinuria declined to 414 mg/day, serum total proteins and serum albumin improved to 6.7 g/dl and 3.9 g/dl respectively.

Serum anti phospholipase-A2-receptor antibodies are present in 70% of patients with idiopathic MN with active disease.[4] The anti-PLA2R antibodies were found to be present in reports of patients with secondary MN. These patients were one out of 20 patients of systemic lupus erythematosus, one out of 16 patients of hepatitis B associated MN, three out of 10 patients of malignancy associated MN and one report of sarcoidosis associated MN. The accuracy of anti-PLA2R antibodies to identify idiopathic MN and to exclude secondary causes of MN awaits well-designed prospective studies, which are currently underway.[5]

In our patient, the temporal relation of use of the levodopa-carbidopa with the onset of symptoms, the reduction of the proteinuria consequent to its stoppage and absence of anti PLA2R antibodies all pointed to a possible association of levodopa-carbidopa combination with the MN. Spontaneous remission of the MN could also be another possibility.

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Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.145130