Membranous nephropathy superimposed on Churg-Strauss syndrome

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ABSTRACT

The association of membranous nephropathy with Churg-Strauss syndrome is not widely reported. We present a patient with myeloperioxidase–perinuclear antineutrophilic cytoplasmic antibody (MPO-pANCA)-positive necrotizing and crescentic glomerulonephritis who later developed membranous nephropathy.

Key words: Churg-Strauss syndrome, membranous nephropathy, MPO, pANCA

Introduction

The association of membranous nephropathy with Churg-Strauss syndrome is not widely reported. We report a patient who was first diagnosed as having Churg-Strauss syndrome and after 6 years, upon evaluation for a new onset nephrotic syndrome, the patient was found to have membranous nephropathy.

Case Report

A 37-year-old man was treated for Churg-Strauss syndrome 6 years back. It was diagnosed when he had history of problems such as breathlessness, wheezing, sticky sputum, weight loss, and myalgias. He also had history of cough and expectoration. He had these symptoms for 10 years before that presentation. He had joint pains, particularly metacarpophalangeal, interphalangeal, and wrist joints. He complained of subcutaneous nodules over upper and lower limbs. He also had rhinorrhea and later he was found to have nasal polyp. He had no symptoms such as abdominal pain, diarrhea, gastrointestinal bleeding, weakness of limbs and symptoms related to stroke, ophthalmologic involvement, and cardiac failure. His previous investigations are reported in Table 1.

At present, he complained of facial puffiness which gradually progressed to entire body. There was no antecedent history of fever or skin disease. There was history of increased frothiness of urine. There was no history of oliguria and hematuria. He also complained of breathlessness, wheezing, cough, and expectoration, particularly in the morning. His blood pressure was 160/90 mm of Hg. The present investigations are reported in Table 1.

On light microscopy, kidney biopsy revealed the following: 15 glomeruli, 3 sclerosed, and 5 showed focal necrosis and cellular crescents. Glomeruli showed diffuse thickening of glomerular basement membrane [Figure 1]. Spikes were present. Tubules, vessels, and interstitium were unremarkable. Immunofluorescence assay revealed: IgG 3+, IgM 1+, κ 1+, and λ 1 + in glomeruli. Electron microscopy was not performed. HbsAg Hepatitis B surface antigen and anti-HCV anti- hepatitis C virus antibodies were negative. Human immunodeficiency virus was non-reactive. Cytoplasmic antineutrophilic cytoplasmic antibody cANCA, anti nuclear antibody ANA, and anti double stranded DNA antibody anti-dsDNA were negative. Complements were within normal limits.

At first presentation, he was treated with methylprednisolone 15 mg/kg/d intravenous for 3 days followed by oral prednisolone 0.5 mg/kg/d for 3 months

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Table 1: Investigations

Investigation	At first presentation	After 6 years
Hemoglobin (g/dl)	9.0	14.0
Total leukocyte count (×10^9/l)	14.0	9.5
Absolute eosinophil count (×10^9/l)	1.9	1.7
Platelet count (×10^9/μl)	5.5	2.3
Serum creatinine (mg/dl)	1.4	1.9→2.3
Blood urea (mg/dl)	20	52→80
Total serum proteins (g/dl)	6.5	4.4
Serum albumin (g/dl)	4.2	2.1
Serum cholesterol (mg/dl)	195	355
24-h urine protein (g)	0.09	8.7
RBCs in urine (/hpf)	15-20	Plenty; RBC casts present
pANCA on immunofluorescence	Positive	Positive
MPO on ELISA	Positive	Positive
Kidney biopsy	Not done	Done

RBC: Red blood cells, ELISA: Enzyme-linked immunosorbent assay

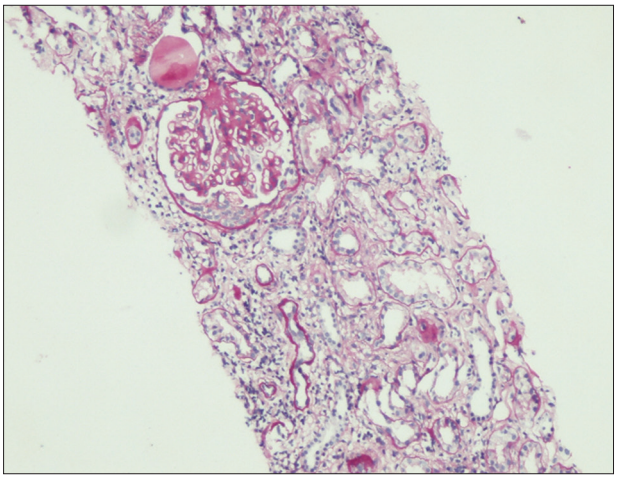

Figure 1: Glomerulus showing thickening of glomerular basement membrane with a cellular crescent (PAS Periodic acid stain, ×100)

and was tapered to 10 mg/day by 6 months. He was continued on that dose, till the present complaints.

At present, he received intravenous methylprednisolone 15 mg/kg/d intravenous for 3 days followed by intravenous cyclophosphamide 500 mg and oral prednisolone 0.5 mg/kg/d. He also received monthly doses of intravenous cyclophosphamide 500 mg for 6 months. At the end of 6 months, azathioprine (2 mg/kg/d) was started and angiotensin-converting inhibitors and angiotensin receptor blockers were continued. After 18 months of follow-up, the proteinuria was 0.2 g/day, RBCs in urine were absent, and serum creatinine was 1.2 mg/dl.

Discussion

At first presentation, the patient had respiratory symptoms, joint pains, subcutaneous nodules, nasal polyp, raised absolute eosinophil count, and MPO–pANCA positive. All pointed to the diagnosis of Churg-Strauss syndrome. At second presentation, nephrotic syndrome and the subsequent kidney biopsy suggested the diagnosis of membranous nephropathy. The RBC casts in urine, renal impairment, raised absolute eosinophil count, cellular crescent on kidney biopsy, and PANCA-MPO positive suggested the diagnosis of Churg-Strauss syndrome. In English literature, not many reports of membranous nephropathy associated with Churg-Strauss syndrome were available, and there was none from India. In the present patient at second presentation, it was concurrent occurrence of necrotizing crescentic glomerulonephritis superimposed on membranous nephropathy. In the largest series[1] of 14 patients with both pANCA and cANCA associated necrotizing and crescentic glomerulonephritis and membranous nephropathy, MPO-pANCA positivity was present in four patients and pANCA was positive in three more patients. End stage renal disease (ESRD) was the outcome in three of the seven patients. Hanamura *et al*,[2] reported six patients of MPO positivity on ELISA (ANCA not reported) in patients of membranous nephropathy. Out of them, four patients deteriorated to ESRD. Yu *et al*,[3] reported both pANCA and cANCA positivity along with only MPO positivity in four patients of membranous nephropathy. Three of these patients reached ESRD. In addition, there were six reports[4-9] of eight patients with MPO-pANCA positivity. Only one of these six patients reached ESRD. A recent report[10] presented the coexistence of MPO-pANCA-associated glomerulonephritis and anti-phospholipase A_2 receptor antibody positive membranous nephropathy.

It has been postulated[2] that in some patients of ANCA-associated glomerulonephritis, MPO may serve as an antigen and form immune complexes to develop membranous nephropathy-like lesions.

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