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Case Report

A rare case of membranous nephropathy with crescent who responded to intravenous cyclophosphamide

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ABSTRACT

Crescent formation is a rare complication of primary membranous nephropathy. It is a sign of severe glomerular injury and can lead to rapid deterioration of renal function. Primary membranous nephropathy and crescents have a lower remission rate and poor prognosis. Crescentic transformation can be associated with ANCAs or anti-GBM antibodies. Early detection and prompt management reduces the chances of progression to end stage kidney disease. Authors hereby report a case of primary membranous nephropathy with crescent who had negative ANCA and anti-GBM antibodies who responded to cyclophosphamide and achieved stabilization of GFR.

Keywords: Crescent, Cyclophosphamide, Primary membranous nephropathy, Steroid

INTRODUCTION

Membranous nephropathy (MN) is one of the causes of adult-onset nephrotic syndrome. It may be primary or secondary.[1,2] Presence of antibodies against M-type phospholipase A2 receptor (PLA2R) in plasma or kidney tissue is found in majority of primary MN cases.[3] Subepithelial immune complex deposits are characteristic of MN. Electron microscopy shows diffuse podocyte foot-process effacement. Presence of crescents, necrosis and endocapillary proliferation is rare. MN has variable prognosis. About one-third of MN patients, achieve spontaneous complete remission. Although, another one-third of patients can progress to end-stage kidney disease (ESKD).[4,5] Presence of crescent indicates a severe glomerular injury. Severity of kidney failure usually correlates with the percentage of compromised glomeruli. Presence of crescent is rarely found in cases of MN. Very few cases have been reported in the literature where there is absence of antineutrophil cytoplasmic antibody (ANCA) or anti–glomerular basement membrane (anti-GBM) positivity.[6] We hereby report a case of primary membranous nephropathy with crescent who had negative ANCA and anti-GBM antibodies. He responded to steroids and cyclophosphamide and achieved stabilization of GFR.

CASE REPORT

A 66 years old male, with no known comorbidities had complains of lower limb oedema and facial puffiness in January, 2024. It was associated with passage of froth in urine. He had a serum creatinine of 1.8 mg/dl in January, 2024. Symptoms lasted for next 4 months. In May, 2024 he presented to All India institute of medical sciences (AIIMS), Rishikesh with anasarca. 24-hour urine protein was 7.8 gm. He had creatinine of 2.15 mg/dl. He had hypoalbuminemia and dyslipidaemia. Ultrasound (USG KUB) showed normal sized kidneys with normal echogenicity. He was diagnosed to have Nephrotic syndrome with AKI. Anti pla2r titre was 632 RU/ml. He was diagnosed as a case of primary membranous nephropathy. Renal biopsy showed 18 glomeruli of which

2/18 showed global sclerosis with diffuse membranous thickening, mottling and sub epithelial spikes. Interstitial fibrosis and tubular atrophy (IFTA) was 10%. Immunofluorescence showed Ig G4- 3+ with positive pla2r staining suggestive of primary membranous nephropathy. There was no improvement of GFR after correction of hypoalbuminemia. He had a EGFR of less than 60 ml/min, hypoalbuminemia (albumin less than 2 gm/dl) and pla2r titre more than 50 RU/ml. He was categorised as high risk as per risk stratification. He was given 2 doses Rituximab 1 gm each 2 weeks apart in June, 2024. Pedal oedema and facial puffiness reduced. 24 hr urine protein came down to 2.5 gm in September, 2024. He achieved partial remission with injection Rituximab. Creatinine was static at 2 mg/dl.

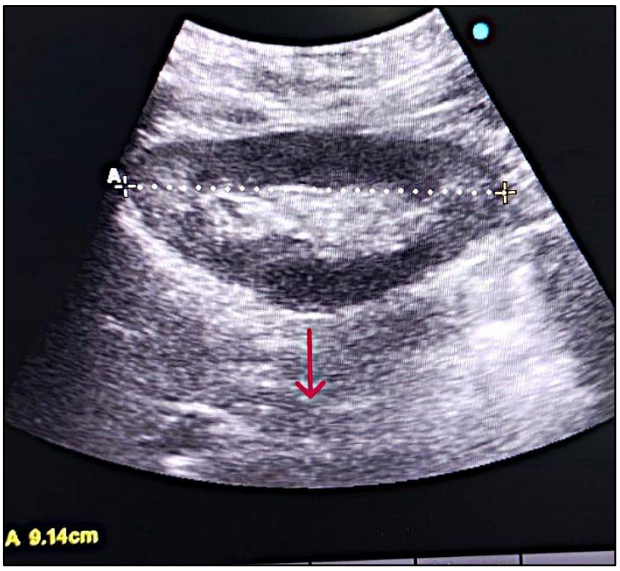

Figure 1: Right kidney of size 9.1 cm with slightly raised echogenicity.

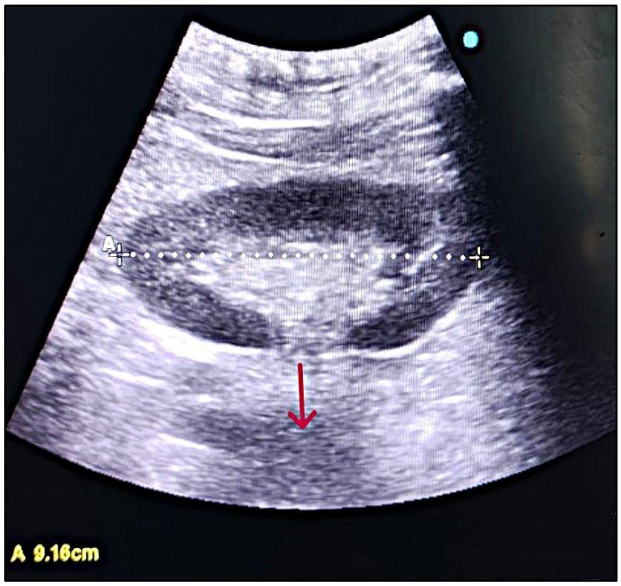

Figure 2: Left kidney of size 9.1 cm with slightly raised echogenicity.

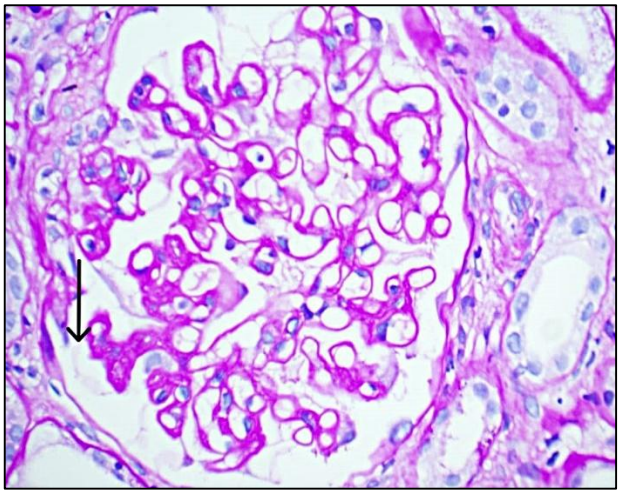

Figure 3: Light microscopy renal biopsy PAS stain 40X magnification showing a segmental cellular crescent with diffuse thickening of capillaries, intramembranous mottling.

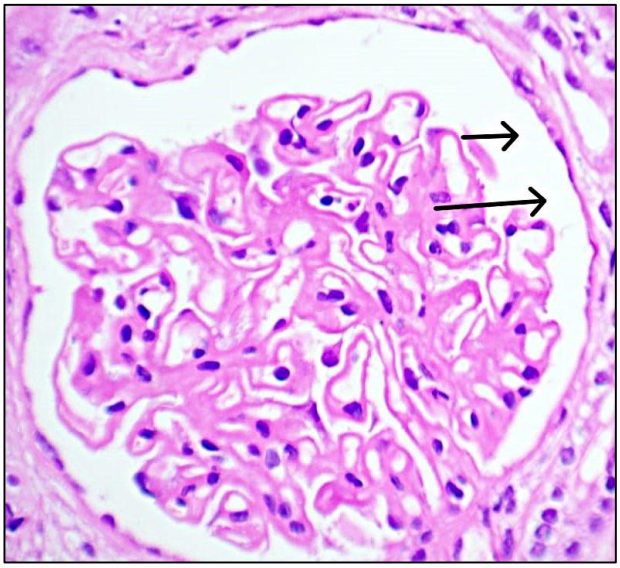

Figure 4: Light microscopy renal biopsy H and E stain 40X magnification showing thickening of capillary membranes.

In November, 2024, he had lower limb oedema and facial puffiness with decrease in urine output. Table 1 shows the investigations at presentation. He was oliguric. Haemodialysis was initiated in view of fluid overload and metabolic acidosis. There was no evidence of infection or renal vein thrombosis. He was given diuretics and albumin for anasarca. There was rapid decline in renal function. Anti pla2r titre was 48.2 RU/ml. Anti-GBM and ANCA titres were negative. USG KUB showed normal sized kidneys with slightly raised echogenicity. Figure 1 and 2 shows right and left kidney images respectively. Renal biopsy showed 17 glomeruli of which 4/17 showed global sclerosis, 1 segmental cellular crescent. IFTA was 10-15%. Immunofluorescence showed Ig G4- 3+ with other features suggestive of primary membranous nephropathy.

Figure 3 and 4 shows renal biopsy light microscopy PAS and H and E stain images respectively. He was planned for management as a case of rapidly progressive crescentic glomerulonephritis. He was given pulse steroids in the form of injection Methylprednisolone 500 mg for 3 consecutive days followed by oral steroids in the form of Prednisolone (1 mg/kg/day) as per PEXIVAS regime. Injection cyclophosphamide 500 mg total 6 doses were given as per CYCLOPS regime as per clinical profile. He was on intermittent haemodialysis weekly thrice basis via jugular tunnelled catheter. Eventually, his urine output improved. Haemodialysis was stopped after 3 months of start of CYCLOPS regime in March, 2025. 24-hour urine protein was 700 mg. Serum creatinine came down to 2.3 mg/dl with stabilization GFR.

Table 1: Investigations at presentation in November, 2024.

Parameters (units)	Patient values	Reference range
Haemoglobin (gm/dl)	9.5	12-15
TLC (×10^3/ul)	5.7	4-11
Platelet count (×10^3/ul)	229	150-400
Urea (mg/dl)	167	17-43
Creatinine (mg/dl)	6.6	0.55-1.02
Serum albumin (gm/dl)	2.1	3.5-5.2
Serum cholesterol (mg/dl)	302	123-200
Serum triglyceride (mg/dl)	269	50-150
24-hour urine protein (gm/day)	8.7	0.04-0.15

DISCUSSION

The case discussed above was a case of membranous nephropathy with single segmental cellular crescent that presented with rapid deterioration of renal function. Li et al, concluded that there was a lower remission rate in the patients with crescents and primary membranous nephropathy. Crescent formation and proteinuria are independent risk factors for poor renal outcomes (P<0.001 and P<0.05) respectively.[7] In this case, patient responded to intravenous cyclophosphamide doses and steroids. Patient became dialysis independent 3 months after the start of therapy. Nikolopoulou et al, concluded that patients with membranous nephropathy and crescents present with haematuria, proteinuria and acute kidney injury.[8,9] They should be managed like a case of rapidly progressive glomerulonephritis. Prognosis is found to be variable. In around 40% of patients, there is progression to end-stage kidney disease.[8] In this case, patient had stabilization of GFR with the medical therapy. Membranous nephropathy with crescents associated with anti-GBM antibodies or ANCAs is very rare.[8] In this case both anti-GBM and ANCA titres were found to be negative. Nayak et al, reported a case of membranous nephropathy who developed new onset oedematous illness. Patient had rapid deterioration of renal function. Patient had positive anti-GBM antibodies. There was presence of 100 percent circumferential crescents with linear Ig g deposition in renal biopsy. Although, plasmapheresis, steroids and oral cyclophosphamide were given, there was no response to the therapy. Patient was later on maintenance haemodialysis.[10] In the contrary, this case responded to intravenous cyclophosphamide and pulse steroids followed by oral steroids. A repeat renal biopsy should be considered in case of acute deterioration in renal function in patients with membranous nephropathy to rule out possible crescentic transformation.

CONCLUSION

Our case represents a distinct and rare entity of membranous nephropathy with crescent. We should always keep possibility of crescentic transformation when there is rapid decline in renal function in a case of primary membranous nephropathy even though anti-GBM and ANCA titres are negative. Early detection and prompt management reduces the chances of progression to end stage kidney disease.

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