Severe systemic sclerosis developing in a patient of membranous nephropathy

Sn, SSC is a multisystem connective tissue disorder of unknown aetiology characterized by fibrosis, degenerative changes and vasculopathy involving skin and multiple organs such as lungs, heart, kidney and gastrointestinal system. Renal involvement in SSC ranges from less severe renal abnormalities, including hypertension, proteinuria and a rise in serum creatinine (in 45–60% of patients), to overt life-threatening scleroderma renal crisis (SRC) [1]. MPO-positive pauci-immune crescentic nephritis has been reported, both with and without D-penicillamine therapy, and these may have a nephritie-range proteinuria [2, 3]. However, nephrotic syndrome has rarely been reported. We present a patient with membranous nephropathy who developed features of SSC 5 years after the onset of nephrotic syndrome.

A 12-year-old female patient first presented to us 5 years ago, with nephrotic syndrome. Her blood pressure was 132/90 mmHg, proteinuria was 3.05 g/day, with the urinalysis showing no red blood cells or casts and creatinine was 0.8 mg/dl. Anti-nuclear factor and anti-dsDNA were negative and C3 was within normal limits. A renal biopsy was performed, which showed nine glomeruli, relatively hypocellular, showing patchy area of basement membrane thickening. Interstitium showed mild lymphomononuclear cell collection with focal myxoid degeneration. Tubules and blood vessels were normal. IF was positive for immunoglobulins A, M, G, and C3 in a granular deposition along basement membranes. The pathological diagnosis was membranous nephropathy.

She was initially treated with angiotensin-converting enzyme inhibitors (ACEi), then with 6 months of therapy with oral CYC and prednisolone on alternate months. This treatment resulted in a partial remission (proteinuria of 0.95–1 g/day); she then continued on ACEi. Four years later, she had a relapse of proteinuria, and this reached 11.3 g/day. Another renal biopsy was done, and this showed features of membranous nephropathy also. She was then put on tacrolimus at 2 mg twice daily. Her proteinuria declined again to <1 g/day and she became free of oedema. Six months later (and 6 months before her current admission), she presented with abrupt onset of RP, accompanied by progressive tightening of skin around fingers, mouth and eyes and wasting in both arm muscles. She had epigastric pain, reflux, with occasional vomiting and pigmentation over exposed areas. Severe pain occurred in the fingers of the right hand, and dry gangrene developed in the fingers over the next 2 months and also occurred over fingertips on the left hand and one toe. Blood pressure increased to 180/110 mmHg. The radial and brachial pulses on the left side were not palpable. Her creatinine rose to 1.68 mg/dl and Hb dropped to 7.2 g/dl with a normal total leucocyte count, ESR rose to 130 mm. Urine sediment showed a bland sediment and a proteinuria of 1.85 g/day. Coagulation screen was normal.

A skin biopsy was performed, which suggested scleroderma, with epidermis showing hyperkeratosis, increased pigmentation of basal cell layer, increased dermal collagen and atrophic appendages. The cANCA and pANCA were negative, as were anti-Scl-70 titres. CT angiogram revealed an occlusion at the level of the right subclavian artery (Fig. 1). High resolution CT thorax revealed interstitial thickening in the lower lobes, suggestive of interstitial lung disease. With enalapril and other supportive care, her blood pressure stabilized at 130/92 mmHg and her symptoms improved. Proteinuria remained at 1.12 g/day; serum creatinine declined to a baseline of 1.23 mg/dl.

Nephrotic syndrome in scleroderma has been described before in the setting of SRC [4], with minimal changes [5], with secondary amyloidosis [6] and with rapidly progressive renal failure and proliferative changes with crescents and associated factor X deficiency [7]. Membranous nephropathy has previously been reported with only two patients of scleroderma. Membranous nephropathy and scleroderma were described in a patient with renal cell carcinoma [8] and in a 60-year-old woman, with a simultaneous onset of both conditions, which improved with CYC [9].
Our patient presented with scleroderma 5 years after the onset of membranous nephropathy. It may represent a coincidental occurrence; however, in view of the previous reports, an association (albeit rare) between the diseases cannot be ruled out. Narrowing of medium-sized vessels has been noted in scleroderma; however, obstruction of a major arterial trunk may be due to thrombosis [10], which may occur in the setting of nephrotic syndrome. The onset of membranous nephropathy was at the age of 12 years; thus she is one of the youngest (among the patients in literature) to present with this combination of diseases.

Rheumatology key message

- Severe SSc, with vascular occlusion, may develop in longstanding membranous nephropathy.

Disclosure statement: The authors have declared no conflicts of interest.

Dipankar Sarkar1, Geetabali Sircar2, Rajesh Waikhom1, Arpita Raychowdhury1, Rajendra Pandey2 and Alakendu Ghosh2

1Department of Nephrology and 2Department of Rheumatology, Institute of Postgraduate Medical Education and Research, Kolkata, West Bengal, India.

Accepted 25 March 2011

Correspondence to: Dipankar Sarkar, Department of Nephrology, Institute of Postgraduate Medical Education and Research, Kolkata, West Bengal, 700060, India. E-mail: deepsircar@gmail.com

References