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Focal segmental glomerulosclerosis and granulomatous interstitial nephritis caused by bisphosphonate

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Case Study: Bisphosphonate is used for the treatment of osteoporosis or various hypercalcemia-associated diseases. Clinically, bisphosphonate-induced nephropathy can be manifested in the form of podocytopathy or acute interstitial nephritis, although it is rare. Herein, we report a case in which focal segmental glomerulosclerosis (FSGS) and granulomatous interstitial nephritis develop simultaneously.
A 73-year-old female was referred due to persistent proteinuria and edema. She have administered pamidronate monthly in the recent 3 months. Her laboratory data were followings: serum creatinine, 1.24 mg/dL; serum albumin, 3.9 g/dL; C3, 107 mg/dL; C4, 26 mg/dL; urine protein-creatinine ratio (UPCR), 3.11 g/g. We performed renal biopsy. Pathologic findings showed increased size of glomeruli and hypercellularity in mesangium. Segmental sclerosis of focal glomeruli was also seen. Small portions of renal medulla close to renal pelvis showed focal granulomatous inflammation with a few Langhans' giant cells. Urine PCR for tuberculosis were negative. Serum angiotensin I-converting enzyme showed negative finding. After 1 year of conservative treatment, UPCR was reduced to 1.6 g/g and her renal function was relatively preserved.
Bisphosphonate can impair cytoskeletons and cellular signals of podocytes and renal tubular epithelial cells. Thus, bisphosphonate clinically can lead toxic acute tubular necrosis and FSGS. Bisphosphonate leads to form intra-tubular crystals and the crystals result in tubulointerstitial nephritis. The cystal-induced nephritis may be expressed more prominently in the distal tubules because of concentrating of urine and crystals in distal portion. Thus, the granulomatous interstitial nephritis in medullary portion may be thought to have been associated with bisphosphonate. Moreover, there were no clinical evidences of tuberculosis and sarcoidosis.
When renal dysfunction without nephrotic proteinuria appear during the management, steroid-therapy may be needed due to the granulomatous lesion. Therefore, clinicians should consider a different approach from other FSGS treatment in patients with simultaneous lesion of granulomatous inflammation and FSGS caused by bisphosphonate.

Figure 1. Renal biopsy findings (Light microscpoic findings)