Phosphate Nephropathy in Gitelman Syndrome

Minfang Zhang, Wenyan Zhou, Shaojun Liu, and Chuanming Hao

A man in his 20s was admitted with fatigue in the setting of proteinuria (protein excretion, 1.97 g/24 h). Additional laboratory results revealed hypokalemia (potassium, 2.2 mEq/L), hypochloremia (chloride, 97 mEq/L), hypomagnesemia (magnesium, 1.0 mg/dL; 0.41 mmol/L), and hypocalciuria (calcium excretion, 2.08 mg/d; 0.52 mmol/24 h). Serum creatinine level was 1.05 mg/dL (93 μmol/L). Serum and urinary pH were 7.45 and 7, respectively. Plasma renin activity was increased. Serum aldosterone, calcium, phosphorus, and parathyroid hormone and urinary phosphorus concentrations were within normal range. Blood pressure was 120/70 mm Hg, and physical examination findings were unremarkable.

The patient underwent kidney biopsy. Histology demonstrated finely granular and mildly basophilic particles in the interstitium and along the outside of the tubular basement membrane, peritubular capillaries (Fig 1), and Bowman capsules. von Kossa staining (Fig 2) and alizarin red staining were positive, suggesting a diagnosis of phosphate nephropathy. In addition, mild to moderate tubulointerstitial lesions accompanying a secondary segmental sclerosis glomerulus (perihilar variant) was also found. Genetic analysis revealed a missense variation of the SLC12A3 gene, confirming a diagnosis of Gitelman syndrome.

To our knowledge, this is the first reported case of Gitelman syndrome leading to kidney deposition of calcium phosphate product. The unique morphologic features of this case differ from those of acute phosphate nephropathy, which is characterized by the deposition of nonpolarizable calcium phosphate crystals within tubular lumens, destruction of tubular epithelial cells, and gradual migration of crystals into the interstitium.[1] Few studies have demonstrated abnormal kidney regulation of phosphate homeostasis in Gitelman syndrome.[2,3] The trigger for calcium phosphate deposition in this patient might be related to decreased solubility of calcium phosphate caused by long-term hypomagnesemia. Other possible mechanisms could involve the coexistent hypokalemia and tubular-interstitial lesion. This unusual pattern of nephrocalcinosis is easy to miss and vigilance is necessary to identify the characteristic features on

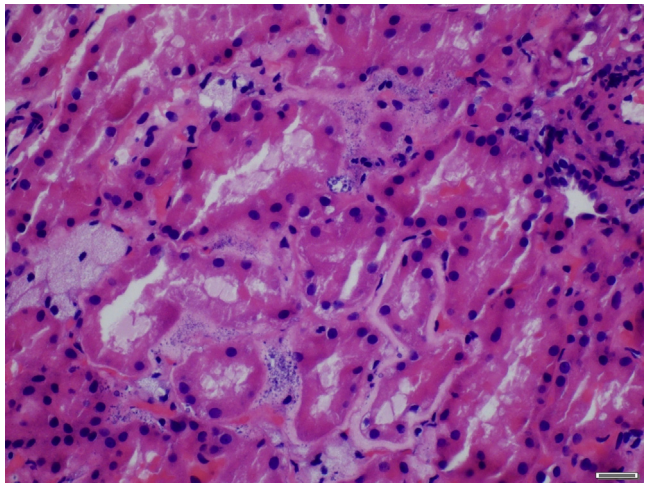

Figure 1. Morphologic characteristics of deposition were finely granular and occasionally globular. These crystals were mildly basophilic on hematoxylin-eosin staining and nonbirefringent under polarized light (original magnification, ×400; bar, 20 μm).

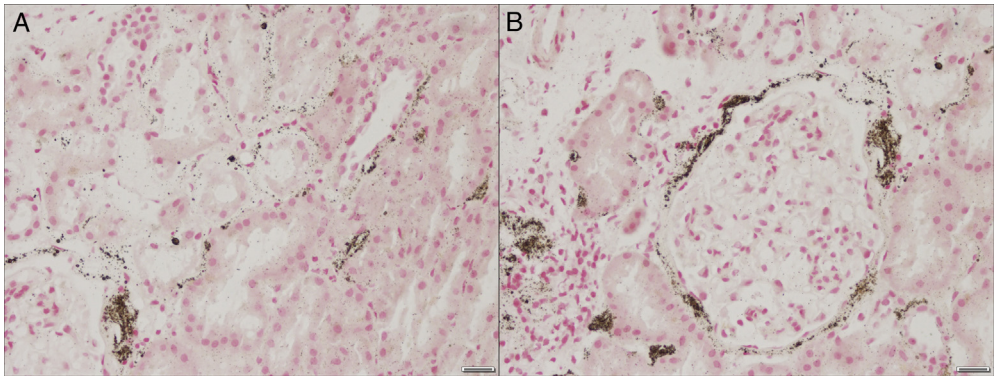

Figure 2. Finely granular particles were noted in the interstitium and along the outside of the tubular basement membrane, peritubular capillaries, and Bowman capsules. The presence of calcium phosphate crystals was confirmed by von Kossa staining (original magnification, ×400; bar, 20 μm).

hematoxylin-eosin staining. von Kossa staining can help confirm the final diagnosis.

ARTICLE INFORMATION

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REFERENCES

1. Markowitz GS, Perazella MA. Acute phosphate nephropathy. *Kidney Int*. 2009;76(10):1027-1034.
2. Katopodis K, Elisaf M, Siamopoulos KC. Hypophosphataemia in a patient with Gitelman's syndrome. *Nephrol Dial Transplant*. 1996;11(10):2090-2092.
3. Viganò C, Amoruso C, Barretta F, et al. Renal phosphate handling in Gitelman syndrome-the results of a case-control study. *Pediatr Nephrol*. 2013;28(1):65-70.