Monoclonal light chain crystalline podocytopathy and tubulopathy associated with monoclonal gammopathy of renal significance: a case report and literature review

Xiao-juan Yu 1,2,3,4†, Xu-jie Zhou 1,2,3,4†, Su-xia Wang 1,2,3,4,5*, Fu-de Zhou 1,2,3,4 and Ming-hui Zhao 1,2,3,4,6

Abstract

Background: Monoclonal gammopathy of renal significance (MGRS) is a recently defined group of renal diseases caused by monoclonal immunoglobulin secreted by nonmalignant proliferative B cell or plasma cell. Monoclonal immunoglobulin can form different types of structures deposited in renal tissue, including fibrils, granules, microtubules, crystals and casts, and has mostly been reported in multiple myeloma patients. Here we report a rare case with κ light chain crystals in both podocytes and tubular epithelial cells associated with MGRS, which adds more information to the spectrum of MGRS-related renal diseases.

Case presentation: A 53-year old woman presented with albumin–predominant moderate proteinuria and renal failure. She had monoclonal IgGκ in the serum and monoclonal IgGκ plus free κ in the urine. Multiple myeloma and lymphoproliferative disorders were excluded. Renal biopsy confirmed κ-restricted crystal-storing renal disease involving the podocytes and proximal tubular epithelial cells. The patient was treated with bortezomib followed by lenalidomide-based chemotherapy, and renal function was stable after 1 year of follow-up.

Conclusions: This is a rare case of combined crystalline podocytopathy and tubulopathy associated with MGRS, in which diagnosis was dependent on electron and immuno-electron microscopy.

Keywords: Monoclonal gammopathy, MGRS, Crystal deposition, Podocytopathy

Background

Monoclonal gammopathy of renal significance (MGRS) represents a group of renal diseases caused by direct deposition or indirect functional interference of monoclonal immunoglobulin (MIg), which is secreted by clonal B cells or plasma cells [1, 2]. Patients with MGRS do not meet the criteria for symptomatic multiple myeloma (MM) or lymphoma, the hematological abnormality is generally consistent with monoclonal gammapathy of undetermined significance (MGUS). However, the renal prognosis of MGRS is not benign.

The spectrum of MGRS includes a variety of renal lesions, among which renal amyloidosis, monoclonal immunoglobulin deposition disease, and cast nephropathy are the common types, whereas light chain proximal tubulopathy and crystal storing-histiocytosis, which are characterized by cytoplasmic crystallization of monoclonal light chains, are quite rare. Crystallization of MIggs can result in intravascular and/or intracellular crystal deposition, which has been reported mostly in MM [3–13] and rarely in MGRS [14, 15]. Here, we report a case of crystal-storing renal disease involving both glomerular podocytes and proximal tubular epithelial cells in association with MGRS.
Case presentation

A 53-year-old Chinese woman was admitted for a 6-month history of foamy urine. Two months before admission, her urinalysis revealed proteinuria 2+ without hematuria. Protein excretion was 2.76 to 3.15 g/24 h. Her serum albumin was 40.1 g/L (normal range: 40–55 g/L), and serum creatinine was 2.20 to 2.50 mg/dl (normal range: 0.50–1.50 mg/dl). Her serum immunoglobulin (Ig) G was 17.2 g/L (normal range: 7.23–16.85 g/L), IgA was 0.59 g/L (normal range: 0.69–3.82 g/L), and IgM was 0.83 g/L (normal range: 0.63–2.77 g/L). Monoclonal IgGk spike was identified in the serum by immunofixation electrophoresis, and monoclonal IgGk plus free κ light chain was identified in the urine. Bone marrow aspiration smear revealed 1% plasma cells. CD38, CD138 and CD56 positive cells accounted for 1.13% of bone marrow cells with κ light chain restricted expression as determined by bone marrow flow cytometry. The patient was then referred to our hospital for further evaluation.

She had a 4-year history of hypertension for which she was taking irbesartan. Family history was negative. On admission, the physical examination revealed a blood pressure of 113/65 mmHg, temperature of 36.5 °C, heart rate of 78/min, and respiratory rate of 18/min. No organomegaly was noticed. Other signs were normal.

After admission, urinalysis revealed proteinuria 1.27 g/24 h. The albumin creatinine ratio (ACR) was 751.40 mg/gCr (normal range: < 30 mg/gCr). The urine sediment examination was normal. The urine pH was 5.0, and the specific gravity was 1.007. The urine N-acetyl-β-D-glucosidase (NAG) was 12 U/L (normal range: 0–21 U/L), and α1-microglobulin was 86.1 mg/L (normal range: 0–12 mg/L). Urine glucose was negative. Other laboratory data revealed serum creatinine of 2.34 mg/dl, estimated glomerular filtration rate (eGFR) of 23.00 ml/min/1.73m², serum total protein of 79.5 g/L (normal range: 65–85 g/L), and serum albumin of 42.6 g/L. The sizes of both kidneys were normal. Her serum calcium was 2.39 mmol/L (normal range: 2.11–2.52 mmol/L), phosphate was 1.22 mmol/L (normal range: 0.85–1.51 mmol/L) and the uric acid was 312 µmol/L (normal range: 90–360 µmol/L). Serum liver enzymes were normal. Her white blood cell count was 7.7 × 10⁹ cells/L (normal range: 3.5–9.5 × 10⁹ cells/L), hemoglobin was 148 g/L (normal range: 115–150 g/L) and the platelet count was 205 × 10⁹ cells/L (normal range: 125–300 × 10⁹ cells/L). The prothrombin time was 10.5 s (normal range: 9.0–11.5 s), the activated partial thromboplastin time was 28.9 s (normal range: 26.9–37.6 s) and the plasma fibrinogen level was 3.80 g/L (normal range: 2–4 g/L). She had type 1 cryoglobulinemia with IgGk. Serum free κ chain was 35.4 mg/L (normal range: 3.30–19.40 mg/L), free λ chain was 16.8 mg/L (normal range: 5.71–26.3 mg/L), and the κ/λ ratio was 2.11 (normal range: 0.26–1.65). Cranial and pelvic bone X-rays did not indicate obvious bone destruction. Echocardiography and abdominal ultrasound were normal. Hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV), anti-human immunodeficiency virus (HIV) and Treponema pallidum antibody (TP-Ab) were all negative. Plasma complement 3 (C3) was 1.240 g/L (normal range: 0.60–1.50 g/L), and complement 4 (C4) was 0.268 g/L (normal range: 0.12–0.36 g/L). Anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies and anti-phospholipase A2 receptor (PLA2R) antibodies were all negative.

MGRS was suspected, but other glomerular diseases accompanied by monoclonal gammopathy of undetermined significance (MGUS) could not be excluded and can only be confirmed by renal biopsy. The patient underwent renal biopsy. Direct immunofluorescence (IF) examination of frozen renal tissue revealed no significant immune deposits and light chains(κ, λ) in the glomeruli, tubules and interstitium. Light microscopic examination showed that 12/29 glomeruli were globally sclerosed and 5/29 glomeruli showed segmental sclerosis with cytoplasmic vacuolization of podocytes (Fig. 1a, b). Other glomeruli were nearly normal. Tubular epithelial cells exhibited focal vacuolization and eosinophilic granules in the cytoplasm and focal loss of brush border with epithelial simplification (Fig. 1c). Tubular atrophy and interstitial fibrosis were minimal. There was mild interstitial infiltration of lymphocytes, monocytes and a few eosinophils. Mild arteriosclerosis and intimal fibrosis of the artery were observed. Congo red staining for amyloid was negative. Electron microscopic examination revealed rod- or rhomboid-shaped crystals in the podocytes (Fig. 1d) and proximal tubular epithelial cells (Fig. 1e). The histiocytes did not contain any crystal inclusions. Majority of the podocyte foot processes were effaced. No electron-dense deposits were observed in the glomeruli. Immuno-electron microscopy revealed κ light chain deposition in the crystals without λ light chain (Fig. 1f).

The patient was diagnosed with crystal-storing renal disease involving the podocytes and proximal tubular epithelial cells. She was transferred to the hematological department, and received 4 cycles of CBD (Bortezomib, dexamethasone and cyclophosphamide) protocol chemotherapy. Serum immunofixation electrophoresis still showed IgGk and urine with IgGk plus free κ light chain. The patient was considered to be resistant to CBD treatment and switched to Rd. (Lenalidomide and dexamethasone). The patient showed good compliance, and the treatment was well tolerated without clinically significant side effects. The patient was followed up for 12 months until now, and the serum
creatinine was approximately 2.26 mg/dl with a proteinuria of 0.3–0.5 g/24 h.

Discussion and conclusions

Our patient presented with moderate proteinuria and chronic renal failure. Fanconi’s syndrome was insignificant. She had monoclonal IgGκ plus free κ gammapathy that did not meet the criteria of multiple myeloma or lymphoma. Renal biopsy confirmed monoclonal κ-restricted crystal-storing renal disease affecting the podocytes and renal tubular epithelial cells, which confirmed the diagnosis of MGRS.

MGRS-associated renal lesions comprise a wide variety of kidney disorders caused by monoclonal immunoglobulins and their fragments, including light chains or heavy chains. The MIgs can cause renal diseases by direct deposition in the renal tissue in most cases of MGRS or by interfering with complement or coagulation system in rare settings, such as C3 glomerulopathy or atypical hemolytic syndromes due to MIgs [1, 16]. Different MGRS manifestations depend on the specific biochemical characteristics of the pathogenic MIg and light/heavy chains involved. Precipitated MIg may occur in the extracellular or intracellular location of renal cells. The former is represented by crystallglobulin-induced nephropathy and cryoglobulinemic glomerulonephritis (GN), which are characterized by intravascular crystals in the thrombi and crystals in the glomerular deposits (mainly subendothelial), respectively. The latter include light chain proximal tubulopathy (tubular cytoplasmic crystals) and crystal-storing histiocytosis (crystals in the cytoplasm of histiocytes or macrophages) [1]. In addition, intracellular crystals have been reported in glomerular endothelial cells, mesangial cells, podocytes, and parietal epithelial cells [3, 4, 14]. However, combined crystalline podocytopathy and tubulopathy have seldom been described.

Our patient had type I cryoglobulinemia, but the renal biopsy exclude cryoglobulinemia-related renal injury. Instead, the renal biopsy revealed crystalline podocytopathy, tubulopathy, and secondary focal segmental glomerulosclerosis (FSGS). Thirteen similar previously reported cases are summarized in Table 1 [3–15]. Most patients (6/13) had a glomerular FSGS pattern or, rarely, collapsing FSGS (especially MM patients treated with pamidronate). The FSGS pattern in these patients is mostly likely secondary FSGS due to crystal deposition-induced podocyte injury, and most of the patients (11/13 patients) had mild to moderate proteinuria, which is similar to our case. However, our patient had a 4-year history of hypertension. The current renal biopsy revealed 12/29 globally sclerosed glomeruli with ischemic change and mild arteriolar and arterial sclerosis, which suggested that hypertension may also have contributed to the renal injury in this patient. In previous reports, ten patients had renal insufficiency and Fanconi syndrome was present in only 2 patients. Majority of the patients (11/13) had myeloma, and all patients including this case were monoclonal IgGκ. Mostly importantly, in

![Patient renal biopsy findings.](image-url)
Table 1: Previous reports of crystalline podocytopathy and tubulopathy

| Sex/age | Duration of onset | Clinical renal manifestation | Plasma cell dyscrasia | Glomerular pathology | Crystal distribution | IHC | Treatment | Prognosis |
|---------|------------------|-----------------------------|-----------------------|----------------------|---------------------|-----|-----------|-----------|
| M/29 [12] | 12 months | Recurrent proteinuria after two kidney allografts, PCR 6 g/dL, Scr 2.3 mg/dL | MGUS→IgG-κ MM | Recurrent FSGS | Podocytes, proximal TEC | IF/IHC: Positive for κ in TEC, λ negative | Bortezomib, lenalidomide, dexamethasone | Lacking |
| F/66 [11] | During evaluation for back pain | SCr 1.7 mg/dL, Fanconi syndrome, albumin 29 g/L, PCR 3.11 μg/mgCr | IgG-κ MM | Non-specific | Podocytes, MC, GEC, TEC, tubular lumen, histiocytes | IF: Positive for κ, negative for λ | Bortezomib, melphalan, prednisolone | Overall improvement in her myeloma related laboratory results |
| F/52 [10] | Routine health examination | Proteinuria 2.62 g/dL, Scr 1.3 mg/dL | IgG-κ MM | FSGS | Podocytes, proximal TEC | IHC: Positive for κ, negative for λ in TEC, λ negative | Lacking | Lacking |
| M/45 [9] | Routine annual physical examination | Proteinuria 7.925 g/dL, glycemia 1.85 mg/dL | IgG-κ MM | Collapsing FSGS | Podocytes, MC, TEC | IF/IHC: Negative for κ and λ in crystal areas | Therapy, details lacking | 2 m later, Scr 1.5 mg/dL, proteinuria 3.627 g/dL |
| M/53 [15] | 78 months of MGUS | SCr 1.3 mg/dL, proteinuria 1.18 g/dL, albumin 38 g/L | IgG-κ MM | Foamy substance in podocytes | Podocytes and TEC | IF: Positive for κ, TEC positive; λ negative | 4 cycles of DF and lenalidomide | Scr returned to 1.0 mg/dL |
| F/54 [13] | 24 months of MM, 19 months of proteinuria | Proteinuria 3.9 g/dL (2 yrs), albumin 14 g/dL (2 yrs, pamidronate), albumin 29 g/L | IgG-κ MM | Collapsing FSGS and LCN | Proximal TECs, podocytes, tubular casts | IF: Negative for κ and λ, IHC: Positive for κ, negative for λ | DF, CYC, thalidomide, bortezomib, HCT | Scr 1.8 mg/dL |
| M/56 [8] | < 1 month | Proteinuria 9.2 g/dL (3 m), albumin 5 g/L | IgG-κ MM | NA, ATN | Podocytes, TEC, interstitial macrophages, tubular lumen, BM, urine | IF: Negative for both κ and λ | Vincristine, doxorubicin, DF, HCT | Scr 6.3 mg/dL |
| F/46 [7] | Unknown | Renal dysfunction | IgG-κ MM | NA | Podocytes, TECs, Interstitial histiocytes | IF: Positive for IgG-κ | Chemotherapy followed by HCT | SCr↓, crystalline-containing podocyte ↓ |
| M/51 [6] | 6 months | Bence-Jones proteinuria 1.54 g/L, albumin 41.8 g/L | IgG-κ MM | Nonspecific | Podocytes, GEC, MC, TEC, Interstitial histiocytes, MCs, hepatocytes and macrophages in liver | NA | Chemotherapy deferred due to lung carcinoma surgery | Died shortly after lung surgery due to multi-organ failure |
| M/52 [5] | 60 months | Proteinuria 1.8 g/dL (5 yrs), albumin 34 g/L | IgG-κ MM | 3/S G sclerosed | Podocytes, PEC, TEC, Interstitial histiocytes | IF: Negative for κ and λ, IHC: Positive for κ, negative for λ | NA | NA |
| F/40 [14] | 14 months | Proteinuria 14.3 g/dL, albumin 30 g/L, Scr 1.8 mg/dL | IgG-κ MM | MGUS | Podocytes, PEC, distal TECs, tubular lumina, BM | IHC: Positive for κ, negative for λ | NA | NA |
| M/75 [4] | 60 months of MM | Proteinuria and chronic renal failure | IgG-κ MM | NA | Podocytes, PEC, TEC, interstitial histiocytes, cornea, myeloma cell, choroid plexus | IHC: Positive for κ and λ | NA | NA |
| M/57 [3] | 6 months | Proteinuria 2 g/dL | IgG-κ MM | FSGS | Podocytes, MC, GEC, PEC, proximal TEC, histiocytes and fibroblasts in the interstitium, synovium and BM | IF: Negative | Cytosan, carbamustine and prednisone, discontinued due to complications | 15 years later Scr 3.9 mg/dL, died due to cardiac arrest |

Abbreviation: FSGS focal segmental glomerulosclerosis, MM multiple myeloma, MGUS monoclonal gammopathy of undetermined significance, Scr serum creatinine, GEC glomerular endothelial cell, TEC tubular epithelial cell, MC mesangial cell, PEC parietal epithelial cell, BM bone marrow, NA not available, HCT autologous hematopoietic cell transplantation, ATN acute tubular necrosis, DF dexamethasone, IHC immunohistochemistry, PCR protein/creatinine ratio, LCN light chain cast nephropathy.
crystal-storing renal injury, the IF staining of the light chain on frozen tissue was negative, which may be due to the light chain epitope hiding in the crystal pattern. However, immunostaining for light chains on paraffin tissue after antigenic retrieval and immuno-electron microscopy study can show monoclonal light chain deposition in the crystals, which is very important for the diagnosis.

The exact mechanisms by which monoclonal immunoglobulins form crystals and their different locations in various cells have not been elucidated clearly. Monoclonal immunoglobulins or free light chains are resistant to lysosome enzyme proteolysis due to unique mutations in the variable (V) domains of the monoclonal κ light chain that result in substitution of polar residues by hydrophobic residues [17–19]. The undigested light chains formed highly organized crystals within the endolysosomal compartment under certain conditions. There were very rare reports of crystal formation by the λ light chain in the tubular cells and histiocytes [20, 21]. The renal prognosis of crystalline podocytopathy and tubulopathy is variable; most cases progress very slowly, and death is due to extrarenal complications. The treatment of crystal renal disease is debatable. Multiple myeloma patients should be treated with chemotherapy to improve survival, but whether the chemotherapy would prevent renal progression is unclear. However, some previous reports have shown decreased proteinuria and serum creatinine as well as hematological remission after chemotherapy [9, 11, 15], suggesting a benefit of chemotherapy for these patients. This case was treated with standard bortezomib followed by lenalidomide-based chemotherapy, and her renal function was stable with a standardized bortezomib followed by lenalidomide-based therapy for these patients. This case was treated with chemotherapy to improve survival, but whether the chemotherapy would prevent renal progression is unclear. However, some previous reports have shown decreased proteinuria and serum creatinine as well as hematological remission after chemotherapy [9, 11, 15], suggesting a benefit of chemotherapy for these patients. This case was treated with standard bortezomib followed by lenalidomide-based chemotherapy, and her renal function was stable with a significant decrease in proteinuria after 1 year of follow-up.

This is a rare case of combined crystalline podocytopathy and tubulopathy associated with MGDS. The historical features manifested as FSGS with podocyte crystal formation of κ-light chain restriction as well as tubular injury. The diagnosis was made based on a detailed pathological examination, especially electron microscopy and immuno-electron microscopy. The exact process by which monoclonal immunoglobulins form crystals requires further investigation.

Abbreviations
ACR: Albumin creatinine ratio; ATN: Acute tubular necrosis; BM: Bone marrow; C3: Complement 3; C4: Complement 4; CBD: Bortezomb, dexamethasone and cyclophosphamide; DF: Dexamethasone; eGFR: Estimated glomerular filtration rate; EM: Electron microscopy; FSGS: Focal segmental glomerulosclerosis; GEC: Glomerular endothelial cell; GN: Glomerulonephritis; HBSAg: Hepatitis B surface antigen; HCT: Autologous hematopoietic cell transplantation; HCV: Hepatitis C virus; IF: Immunofluorescence; IgA: Immunoglobulin A; IgG: Immunoglobulin G; IgM: Immunoglobulin M; IHC: Immunohistochemistry; LCN: Light chain cast nephropathy; MC: Mesangial cell; MGDS: Monoclonal gammopathy of renal significance; MGUS: Monoclonal gammopathy of undetermined significance; Mlg: Monoclonal immunoglobulin; MM: Multiple myeloma; NA: Not available; NAG: N-acetyl-β-D-glucosidase; PCR: Protein/creatinine ratio; PEC: Parietal epithelial cell; RD: Lenalidomide and dexamethasone; Scr: Serum creatinine; TEC: Tubular epithelial cell; TP-Ab: Treponema pallidum antibody

Acknowledgements
Not applicable.

Funding
This study was supported by grants from National Natural Science Foundation of China (No. 81470996 and No. 81500653). The grants supported the design of the study and collection, analysis and interpretation of the data and writing of the manuscript.

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Authors’ contributions
YXJ, ZXJ and ZMH analyzed and interpreted the patient clinical data. ZXJ performed the literature review. YXJ was a major contributor in writing the manuscript. WSX performed the histological examination of the kidney biopsy and was a major contributor in writing the manuscript. ZFD followed up the patient and collected the clinical data. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent for publication was obtained from the patient and a copy of the written consent is available upon request.

Competing interests
The authors declare that they have no competing interests.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1Renal Division, Department of Medicine, Peking University First Hospital, Beijing 100034, People’s Republic of China. 2Institute of Nephrology, Peking University, Beijing 100034, People’s Republic of China. 3Key Laboratory of Renal Disease, Ministry of Health of China, Beijing 100034, People’s Republic of China. 4Key Laboratory of CKD Prevention and Treatment, Ministry of Education of China, Beijing 100034, People’s Republic of China. 5Laboratory of Electron Microscopy, Pathological Centre, Peking University First Hospital, Beijing 100034, People’s Republic of China. 6Peking-Tsinghua Center for Life Sciences, Beijing 100087, People’s Republic of China.

Received: 13 April 2018 Accepted: 19 October 2018
Published online: 12 November 2018

References
1. Bridoux F, et al. Diagnosis of monoclonal gammopathy of renal significance. Kidney Int. 2015;87(4):698–711.
2. Leung N, et al. Monoclonal gammopathy of renal significance: when MGUS is no longer undetermined or insignificant. Blood. 2012;120(22):4292–5.
3. Cantens PH, Woo D. Crystalline glomerular inclusions in multiple myeloma. Am J Kidney Dis. 1989;14(1):56–60.
4. Yamamoto T, et al. Crystal-storing histiocytosis and crystalline tissue deposition in multiple myeloma. Arch Pathol Lab Med. 1991;115(4):351–4.
5. Kowalewska J, Tomford RC, Alpers CE. Crystals in podocytes: an unusual manifestation of systemic disease. Am J Kidney Dis. 2003;42(3):605–11.
6. Papla B, et al. Generalized crystal-storing histiocytosis as a presentation of multiple myeloma: a case with a possible pro-aggregation defect in the immunoglobulin heavy chain. Virchows Arch. 2004;445(1):83–9.
7. Tomioka M, et al. Widespread crystalline inclusions affecting podocytes, tubular cells and interstitial histiocytes in the myeloma kidney. Clin Nephrol. 2004;62(3):229–33.
8. Keller LS, et al. Crystalloid deposits in the kidney. Nephrology (Carlton). 2005;10(1):81–3.
9. Akilesh S, Alem A, Nicosia RF. Combined crystalline podocytopathy and tubulopathy associated with multiple myeloma. Hum Pathol. 2014;45(4):875–9.
10. Jeon YL, et al. Crystalloid podocytopathy with focal segmental glomerulosclerosis in PCM: a case report. Diagn Pathol. 2015;10:213.
11. Lee EJ, et al. Crystalloid podocytopathy and tubulopathy without overt glomerular proteinuria in a patient with multiple myeloma. Kidney Res Clin Pract. 2016;35(4):259–62.
12. Khalighi MA, et al. Light chain Podocytopathy mimicking recurrent focal segmental glomerulosclerosis. Am J Transplant. 2017;17(3):824–9.
13. Nair SH, et al. Multiple myeloma, nephrotic syndrome and crystalloid inclusions in podocytes. Kidney Int. 2006;69(3):616–20.
14. Matsuyama N, et al. Crystalloid inclusions in the glomerular podocytes in a patient with benign monoclonal gammopathy and focal segmental glomerulosclerosis. Am J Kidney Dis. 1994;23(6):859–65.
15. Elliott MR, et al. Plasma cell dyscrasia causing light chain tubulopathy without Fanconi syndrome. Am J Kidney Dis. 2010;55(6):136–41.
16. Jokiranta TS, et al. Nephritogenic lambda light chain dimer: a unique human miniautoantibody against complement factor H. J Immunol. 1999;163(8):4590–6.
17. Leboulleux M, et al. Protease resistance and binding of Ig light chains in myeloma-associated tubulopathies. Kidney Int. 1995;48(1):72–9.
18. Deret S, et al. Kappa light chain-associated Fanconi’s syndrome: molecular analysis of monoclonal immunoglobulin light chains from patients with and without intracellular crystals. Protein Eng. 1999;12(4):363–9.
19. Messiaen T, et al. Adult Fanconi syndrome secondary to light chain gammopathy. Clinicopathologic heterogeneity and unusual features in 11 patients. Medicine (Baltimore). 2000;79(3):135–54.
20. Thorner PS, Bedard YC, Fernandes BJ. Lambda-light-chain nephropathy with Fanconi’s syndrome. Arch Pathol Lab Med. 1983;107(12):654–7.
21. Seth S, et al. Crystal-storing histiocytosis involving the kidney in a low-grade B-cell lymphoproliferative disorder. Am J Kidney Dis. 2002;39(1):183–8.