Kidney Res Clin Pract 33 (2014) 112–115

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Case Report

A case of Fanconi syndrome accompanied by crystal depositions in tubular cells in a patient with multiple myeloma

Do Hee Kim [1], A Young Lim [1], Hye Bin Gwag [1], Ji Hyeon Lee [1], Ki Sun Jung [1], Keol Lee [1], Wooseong Huh [2], Dae Joong Kim [2], Yoon-Goo Kim [2], Ha Young Oh [2], Kihyun Kim [3], Gee-Young Kwon [4], Jung Eun Lee [2,*]

[1] Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[2] Division of Nephrology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[c] Division of Hematology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[4] Department of Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Article history:
Received 23 January 2014
Received in revised form
25 March 2014
Accepted 18 April 2014
Available online 3 June 2014

Keywords:
Fanconi syndrome
immunoglobulin kappa-chains
multiple myeloma
proteinuria

Abstract

Fanconi syndrome (FS) is a rare condition that is characterized by defects in the proximal tubular function. A 48-year-old woman was admitted for evaluation of proteinuria. The patient showed normal anion gap acidosis, normoglycemic glycosuria, hypophosphatemia, and hypouricemia. Thus, her condition was compatible with FS. The M peak was found behind the beta globulin region in urine protein electrophoresis. Upon bone marrow examination, we found that 24% of cells were CD138+ plasma cells with kappa restriction. From a kidney biopsy, we found crystalline inclusions within proximal tubular epithelial cells. Thereafter, she was diagnosed with FS accompanied by multiple myeloma. The patient received chemotherapy and autologous stem cell transplantation, and obtained very good partial hematologic response. However, proximal tubular dysfunction was persistent until 1 year after autologous stem cell transplantation. In short, we report a case of FS accompanied by multiple myeloma, demonstrating crystalline inclusion in proximal tubular cells on kidney biopsy.

Introduction

Fanconi syndrome (FS) is a rare disease characterized by defects in proximal tubular function, including impairment of reabsorption of solutes such as glucose, uric acid, phosphate, amino acid, and bicarbonate [1]. Patients with FS may present normoglycemic glycosuria, low molecular weight proteinuria, hypophosphatemia, and normal anion gap metabolic acidosis.

It has been described that Multiple myeloma may induce tubular dysfunction and FS [2]. Multiple myeloma is a neoplastic bone marrow disease characterized by clonal proliferation of plasma cells and overproduction of monoclonal protein [3]. Free light chain overproduction is associated with toxic effects to proximal tubular cells in the kidneys, which may induce FS [4].

In this case, the patient who had presented proteinuria initially was diagnosed with FS and multiple myeloma, after reviewing her results from blood laboratory work, urine analysis, and bone marrow examination. In addition, kidney pathology confirmed the presence of rod-shaped casts in proximal tubules.

Case report

A 48-year-old woman visited the nephrology clinic for proteinuria, which was detected at a local hospital. She had been producing foamy urine and experiencing nocturia for

* Corresponding author. Division of Nephrology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul, 135–710, Korea.
E-mail address: jungeun34.lee@samsung.com (JE Lee).

2211-9132/$ - see front matter © 2014. The Korean Society of Nephrology. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
http://dx.doi.org/10.1016/j.krcp.2014.04.002

2 months, and she was suffering from bilateral flank pain for 6 months. She did not appear to have edema or to gain weight. She had no specific underlying disease or related family history. However, she had been taking a course of Chinese medicine for the past 6 months.

At presentation, her vital signs were stable (blood pressure: 128/80 mmHg, heart rate: 62 beats/minute, respiration rate: 18 breaths/minute, body temperature: 36.4°C), and her general physical examination was unremarkable.

Results from the blood testing, which included complete blood count, coagulation test, total bilirubin, aspartate transaminase, alanine transaminase, cholesterol, glucose, erythrocyte sedimentation rate, C-reactive protein, and thyroid function test were in the normal range. The patient's protein level was 6.6 g/dL and her albumin level was 4.9 g/dL, so her globulin was low (1.6 g/dL). Her creatinine was 1.02 mg/dL, with a mildly decreased estimated glomerular filtration rate of 58 mL/minute/1.73 m^2. Hypouricemia (0.9 mg/dL) and hypophosphatemia (2.3 mg/dL) were observed. Serum sodium/potassium/chloride (139/3.5/109 mmol/L) and calcium (8.8 mg/dL) were in normal ranges. Arterial blood gas analysis showed normal anion gap metabolic acidosis (pH 7.324, pCO_2 31.2 mmHg, pO_2 108.9 mmHg, HCO_3 15.9 mmol/L).

Urine dipstick testing showed the following characteristics: specific gravity (1.036), pH (6.5), blood (+), albumin (++), and glucose (++). A urine electrolyte test showed 51 mmol/L of sodium and 23.5 mmol/L of potassium. Fraction excretion of phosphorus was 44.17%, despite hypophosphatemia. Fraction excretion of uric acid was also increased to 104.16% despite hypouricemia. A spot urine test showed a urine protein/creatinine ratio of 10.61 mg/mgCr and a urine albumin creatinine ratio of 401.69 μg/mgCr. Based on the above information, we concluded that the patient had generalized proximal tubular dysfunction and overflow proteinuria.

An anti-kappa abnormal band was observed in serum and urine immunofixation. The patient had an elevated serum kappa/lambda ratio of 5,113.1. Through urine protein electrophoresis, the M peak was observed behind the beta globulin region (2,911.6 mg/day).

Bone marrow examination showed normocellular marrow with 24% CD138+ plasma cell staining with kappa restriction. The patient was diagnosed with multiple myeloma (kappa type) and FS.

A renal biopsy was performed for accurate diagnosis of FS and to exclude renal amyloidosis or monoclonal immunoglobulin (Ig) deposition disease. The biopsy revealed 26 glomeruli, three of which showed global sclerosis. The other glomeruli were unremarkable with no evidence of proteinous deposits. Mesangial matrix was not increased. Capillary loops were thin and delicate. Tubules revealed focal acute damage without interstitial fibrosis (Fig. 1A). Immunofluorescence staining for IgA, IgG, IgM, C3, kappa, and lambda was negative.

Under electron microscopy, the glomerular basement membrane was slightly irregular in contour with mild effacement of epithelial foot processes. Numerous rod- or rhomboid-shaped crystalline inclusions were present in the cytoplasm of proximal tubular epithelial cells (Fig. 1B). Most of the crystalline inclusions were electron dense and floating in the cytoplasm (Fig. 1C). However, they were not found in the glomerular cells

Table 1. Renal and hematologic laboratory results at baseline and during treatment*

	Admission (October 2012)	Prior to transplantation (February 2013)	After 1 year from transplantation (March 2014)†
Serum phosphate (mg/dL)	2.3	1.5	3.0
Serum uric acid (mg/dL)	0.9	0.8	1.3
Serum HCO_3 (mmol/L)	15.9	15.3	22.5 (tCO2)
Serum potassium (mmol/L)	3.1	3.3	4.0
Glycosuria	++ (S.G. 1.036)	++++ (S.G. 1.020)	++ (S.G. 1.015)
Albumin/creatinine ratio (μg/mgCr)	401.69	–	439.89
Protein/creatinine ratio (mg/mgCr)	10.61	–	1.69
Serum immunofixation	Anti-kappa	Anti-kappa	Absent
Serum κ/λ ratio	5,113.1	591.55	7.20
Urine M protein (mg/day)	2,911.6	649.1	98.2

* Treatment (thalidomide/cyclophosphamide/dexamethasone): from October 2012 to January 2013; autologous peripheral blood stem cell transplantation: March 2013.
† One year after transplantation, she was taking 2,040 mg of phosphate, 0.75 μg of calcitriol, 3,600 mg of potassium chloride, 100 mg of spironolactone, and 3,000 mg of sodium bicarbonate daily.
S.G., specific gravity.

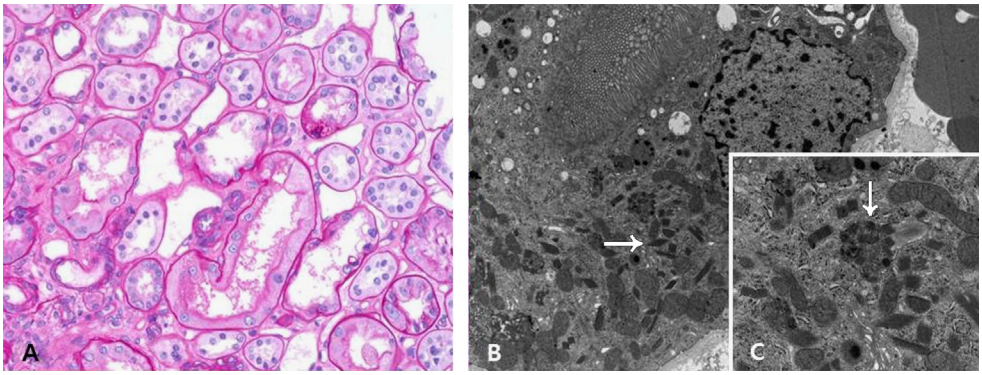

Figure 1. Histopathologic features. (A) Minimal mononuclear cell infiltration with focal atrophy is seen in tubule after staining with hematoxylin and eosin (light microscope, ×400). (B) Cytoplasm of proximal tubular epithelial cell contains multiple intracellular rectangular shape crystalline inclusions (arrow) (electron microscope, ×17,000). (C) Numerous rod-shaped and rhomboid-shaped crystalline inclusions are lying free within cytoplasm (arrow) (electron microscope, ×55,000).