Clinical Case Report

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A case report of POEMS syndrome with renal involvement as immunotactoid glomerulopathy

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Abstract

Rationale: POEMS syndrome is a rare multi-system disorder, which sometimes involves the kidney. Immunotactoid glomerulopathy (ITG) is an uncommon glomerular disease resulted from deposits of immunoglobulins and its derivatives. ITG caused by POEMS syndrome is rarely reported.

Patient concerns: A 63-year-old man was presented with acute kidney injury. In addition, it's found that he had abnormal serum free κ /λ ratio, polyneuropathy, Castleman's disease, organomegaly, endocrinopathy and skin changes.

Diagnoses: POEMS syndrome was diagnosed, Renal biopsy revealed an ITG.

Interventions: Dexamethasone and thalidomide were given, as well as hemodialysis and other supportive treatments.

Outcomes: The patient's extrarenal manifestations improved gradually and his renal function also showed slight improvement.

Lessons: ITG caused by POEMS syndrome is rare, however, it makes sense that the monoclonal proteins produced by the plasma cells could cause ITG. Chemotherapy similar to that employed in multiple myeloma may be beneficial for these patients.

Abbreviations: HCT = hematopoietic cell transplantation, IFE = immunofixation electrophoresis, IMWG = International Myeloma Working Group, ITG = immunotactoid glomerulopathy, SCr = serum creatinine, VEGF = vascular endothelial growth factor.

Keywords: immunotactoid glomerulopathy, POEMS syndrome, renal involvement

1. Introduction

POEMS syndrome is a multi-system disease caused by monoclonal plasma cell disorder. The main manifestations include polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes. Although not included in the acronym or the diagnostic criteria, renal involvement is commonly seen in POEMS syndrome. The typical kidney pathologic changes include membranoproliferative glomerulonephritis-like lesions, microangiopathic lesions, and mesangiolytic lesions.[1,2] In this article, we report a case of POEMS syndrome with renal involvement presented as immunotactoid glomerulopathy (ITG), which is an uncommon glomerular disease resulted from deposits of immunoglobulins and its derivatives. The ethical approval for this case report is considered unnecessary by the ethics committee of our hospital.

2. Case report

A 63-year-old Chinese man was presented with nausea, vomit, and low-grade fever (temperature < 100 °F) for 3 weeks. He received antibiotics for suspected infection for 1 week without clinical improvement. Two weeks prior to admission, patient was seen at the other hospital. Laboratory test results showed hemoglobin of 93 g/L and serum creatinine (SCr) of 13.3 mg/dL. Urine analysis showed 2+ urine protein and 3+ red blood cell; 24-hour urine protein was 2.87 g/d (urine output was 850 mL). He was then referred to our hospital. He had a previous history of tuberculous pleurisy 40 years ago and hypertension for 3 years.

On admission, the temperature was 97.9 °F, and blood pressure was 150/85 mmHg. There were bilateral inguinal lymph nodes enlargement, splenomegaly, bilateral lower extremity edema, and local skin hyperpigmentation (Fig. 1). Neurologic examination was significant for hyperalgesia, therohyperesthesia, meroparesthesia, and hypopallesthesia below both knees. Patellar tendon reflex was diminished bilaterally.

Laboratory studies revealed a further decrease of hemoglobin to 56 g/L. Serum IgA was elevated (5.39 g/L), IgG and complements C3, C4 were within normal range. ANA, ENA, anti-dsDNA antibody, ANCA, anti-GBM antibody, and serum cryoglobulin were all negative. Serum and urine immunofixation electrophoresis (IFE) found no monoclonal protein, but serum free light chains were elevated. κ Light chain was 902.5 mg/L (normal range 3.3–19.4 mg/L), λ light chain was 422.5 mg/L (normal range 5.7–26.3 mg/L), and κ /λ ratio was 2.136 (normal range 0.26–1.65). Luteinizing hormone (LH) and prolactin levels were 9.54 U/L↑ and 107.14 ng/mL↑, respectively. Serum IL-6 was 140.4 pg/mL↑ and serum VEGF level was normal. CT scan of the chest, abdomen and pelvis showed no osteosclerosis. Nerve conduction studies revealed prolonged distal motor latencies, slowed nerve conduction velocities, and decreased compound muscle action potential amplitudes. Bone marrow biopsy revealed 4% plasma cells with normal immune phenotype. The inguinal lymph node biopsy showed interfollicular plasmacytosis, consistent with Castleman's disease (Fig. 2).

Renal biopsy was performed. Under light microscope, 6 glomeruli were harvested, one of which was globally sclerosed. The others showed mild mesangial proliferation with one cellular crescent formation. Vacuolar and granular degeneration were

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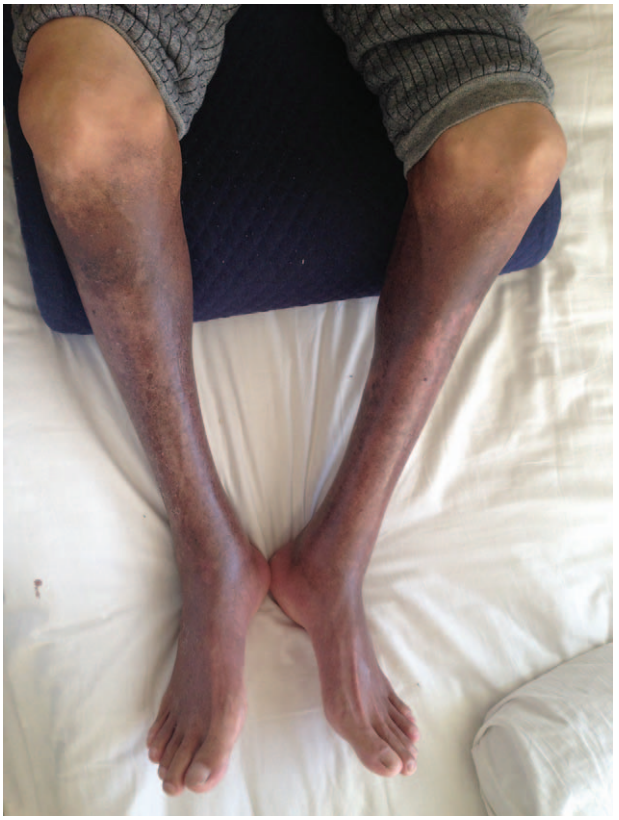

Figure 1. Photographs of patient showing hyperpigmented skin of lower limbs.

seen in renal tubular epithelial cells, with focal renal tubular brush border shedding, tubular atrophy and lumen dilation. Thick proteinaceous casts were easily seen (Fig. 3). Interstitial infiltration of lymphocytes, monocytes and plasma cells along with interstitial fibrosis were found (Figs. 4 and 5). Immunofluorescence study revealed that the casts contain κ light chain, with negative staining for immunoglobulin, complement, λ light chain and Congo red. Electron microscopy revealed abundant deposition of tubulofibrillar structures in the glomerular basement membrane and mesangial area. They were amorphous non-branching fibrils, approximately 30 to 50 nm in diameter. (Fig. 6 A and B) The overall pathologic diagnosis was ITG accompanied with subacute tubular interstitial nephropathy.

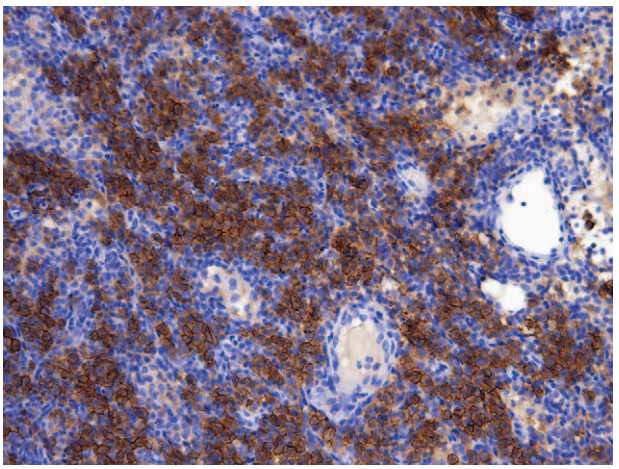

Figure 2. Inguinal lymph node biopsy revealed interfollicular plasmacytosis demonstrated by CD138 staining (immunohistochemical stain, ×200).

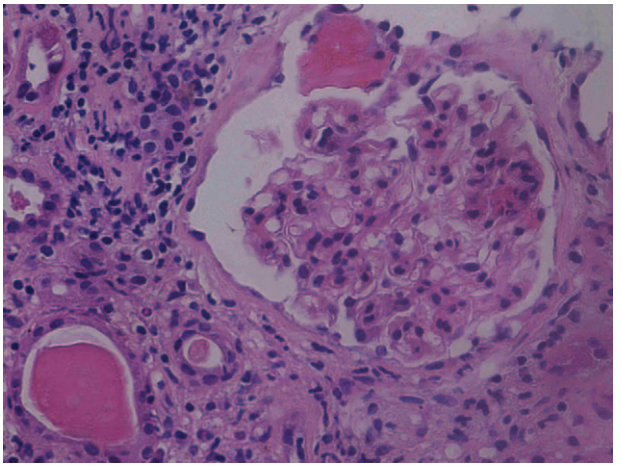

Figure 3. Renal biopsy under light microscope: diffuse infiltration of plasma cells, lymphocytes and monocytes in the interstitium (hematoxylin-eosin stain, ×400).

POEMS syndrome was diagnosed based on International Myeloma Working Group (IMWG) criteria. For treatment, oral thalidomide (100 mg/day) and oral dexamethasone (20 mg/day) were given on day 1 to 4, 8 to 11, 15 to 18 of every 28-day cycle, for a total of 5 cycles. Hemodialysis and other supportive treatments including iron supplements, erythropoietin, and antihypertensive medications were also administered. Ten months later, his symptoms such as fever, nausea, and paresthesia were relieved; he also had a weight gain of 5 kg and slight shrinkage of the lymph nodes confirmed by CT scan. However, there was no obvious improvement of the hyperpigmentation. As to his renal function, his urine output increased to more than 1000 mL/day, 24-hour urine protein decreased to 1.54 g/d, SCr before dialysis decreased to 5.47 mg/dL even though hemodialysis was reduced to twice a week.

3. Discussion

We report a case of POEMS syndrome with renal involvement as ITG, the patient's extrarenal manifestations improved after chemotherapy, his renal function also showed slight improvement.

POEMS syndrome is a rare disorder. Although the cause is unknown, chronic overproduction of pro-inflammatory and cytokines seems to be its major feature.[3] The incidence is unknown due to the complexity of the clinical manifestations. According to the IMWG criteria, the diagnosis of POEMS syndrome must include 2 mandatory criteria (polyneuropathy and monoclonal plasma cell proliferative disorder), plus at least 1 major criterion (osteosclerotic or mixed sclerotic/lytic lesion, Castleman's disease, elevated vascular endothelial growth factor (VEGF) levels), and at least 1 minor criterion (organomegaly, extravascular volume overload, endocrinopathy, skin changes, papilledema, thrombocytosis, or polycythemia).[4] In this case, POEMS syndrome was diagnosed based on polyneuropathy, monoclonal plasma cell disorder with abnormal κ /λ ratio, Castleman's disease, endocrinopathy, organomegaly, and skin changes.

This case is unique for 2 reasons. First, the renal injury presented as ITG. Renal involvement is common in POEMS

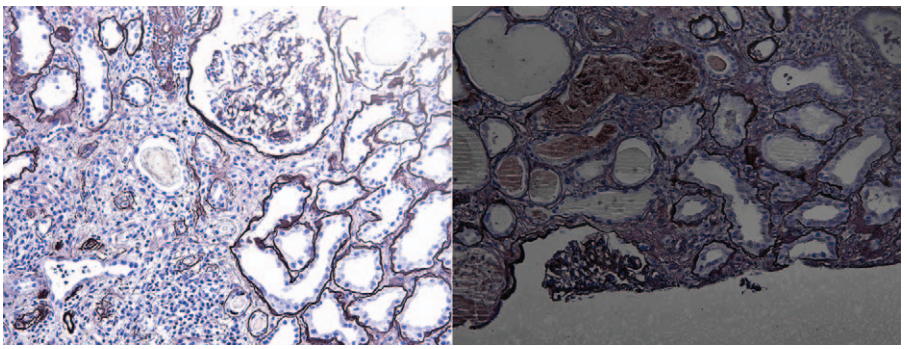

Figure 4. Renal biopsy under light microscope: thick proteinaceous casts in dilated distal nephron segments (periodic acid-Schiff stain, ×200).

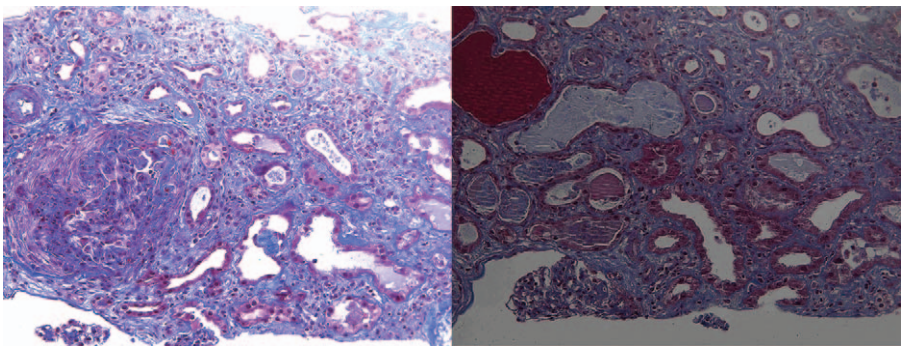

Figure 5. Renal biopsy under light microscope: interstitial fibrosis was present (Masson stain, ×200).

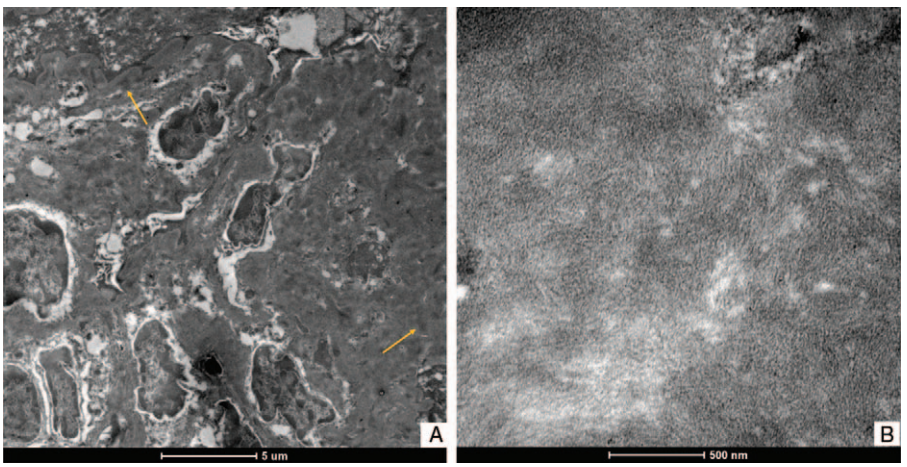

Figure 6. Renal biopsy findings under electron microscope: (A) Electron dense deposits (arrow) could be seen in the basement membrane and mesangial area (electron micrograph, ×6000). (B) The dense deposits were well-arranged amorphous fibrils, about 30 to 50 nm in diameter (electron micrograph, ×20500).

syndrome. According to a report from China, the incidence of renal involvement in POEMS syndrome was 22.4%.[5] A review summarized 52 cases of reported POEMS syndrome with renal involvement, and found that the major pathologic changes were glomerular lesions, manifested as glomerular enlargement, cellular proliferation, mesangiolysis, and marked swelling of the endothelial and mesangial cells.[6] Light chain deposition in kidneys has been reported in POEMS syndrome as well.[7] However, renal involvement as ITG in POEMS syndrome has only been reported in one case.[8] It was a 32-year-old female patient with nephrotic syndrome and IgG κ monoclonal gammopathy, renal biopsy revealed ITG. ITG is an uncommon glomerular disease resulted from deposits derived from immunoglobulins, characterized by the formation of microtubules on electron microscopy. The microtubules are 30 to 50 nm in diameter, usually formed by excessive polyclonal or monoclonal immunoglobulins and their degradation products.[9–11] As POEMS syndrome is generally considered to be a monoclonal plasma cell disorder, it's plausible to expect that the monoclonal proteins produced by the plasma cells may cause ITG.

Secondly, the type of light chain found in this patient was κ. As we know, although κ light chain could be seen, the proliferating monoclonal plasma cells in POEMS syndrome are almost always λ-restricted.[12] The underlying mechanism is not clear. It is also not clear if there is any clinical manifestation difference between κ and λ light chain in POEMS syndrome due to limited number of reported cases.

As to the treatment of POEMS syndrome, there is no standard therapy thus far.[13,14] In general, patients with limited isolated bone lesions may be treated with radiation therapy. Chemotherapy and hematopoietic cell transplantation may be beneficial for widespread osteosclerotic lesions or severe symptoms. Dexamethasone and thalidomide were chosen for this patient based on his systemic symptoms, renal involvement, lack of isolated bone lesions, and economic conditions. He responded to the therapy with improved peripheral neuropathy, lymph node enlargement, and nutritional status. His renal function also seemed to get better with increased urine output, decreased SCr and lower dialysis frequency. However further follow-ups are necessary to evaluate his renal function since he remained in chronic hemodialysis.

In summary, we report a case of POEMS syndrome with renal involvement manifested as ITG. Systemic therapy similar to that employed in multiple myeloma may be beneficial for these patients.

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