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BRIEF REPORT

Coexisting glomerular IgA deposition and IgG-kappa multiple myeloma

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Abstract

Multiple myeloma (MM) is a common malignancy that often results in many kinds of kidney injuries for the abnormal monoclonal immunoglobulin. Here, we present an IgG-kappa type MM case accompanied by renal IgA deposition combined with IgG-kappa. The patient was treated with prednisone plus mycophenolate mofetil, and got a satisfactory remission. Although it cannot be determined whether the IgA deposition was secondary to MM, this was the first report of coexisting mesangial proliferative nephritis with IgA deposition and IgG-kappa type MM.

Keywords

Immunoglobulin A, mesangial proliferative nephritis, multiple myeloma, proteinuria

History

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Introduction

Multiple myeloma (MM) is a malignant disease characterized by massive hyperplasia of monoclonal plasma cells that can infiltrate into bone marrow, soft tissues and other organs. Renal impairment is a manifestation and complication of MM with an incidence as high as 50%, contributing to the poor outcomes even after chemotherapy or high-dose stem cells transplantation.[1,2]

Myeloma nephropathy (MN) is also referred to as myeloma cast nephropathy (MCN), which is the most frequent renal complication of MM.[3,4] Usually glomerular lesions of MM result from monoclonal immunoglobulin light chains. Classical paraprotein-associated lesions include AL type amyloidosis, monoclonal immunoglobulin deposition disease (MIDD), type I cryoglobulinemic glomerulonephritis, and light chain proximal tubulopathy. It was reported that IgA myeloma can lead to Henoch-Schönlein purpura and IgA nephropathy, although the glomerular IgA deposition in MM is extremely rare.[5] Here, we present a case of coexisting mesangial proliferative nephritis with IgA deposition and type IgG-κ MM.

Clinical information

A 69-year old man presented with hematuria, proteinuria, elevated serum creatinine and monoclonal IgG-κ. Renal biopsy showed negative immunofluorescence of IgG, IgM and IgA as well as negative Congo red staining. Additionally, there were 15 glomeruli, including 3 sclerosed and 12 without obvious lesions. Some atrophic tubules with many protein casts were observed. Moreover, there were extensive infiltrations of inflammatory cells in the interstitial region, including many lymphocytes and some plasma cells. Under electron microscopy, glomerular lesions and electron dense were not found. The bone marrow biopsy showed significantly active proliferation and that plasmocytes accounted for 26% of the total cells, satisfying the criteria of MM (Figure 1A). The patient was diagnosed as MM accompanied with interstitial nephritis. The renal function was improved after 4 cycles of Bortezomib treatment.

Two years later the recurrent proteinuria and edema occurred to the patient and reached a diagnosis of nephrotic syndrome. No rashes, hemorrhagic spots, xanthochromia or superficial lymph node enlargement were observed. Urinalysis showed WBC 27/μl, RBC 600/μl, urine protein 8.2 g/24 h, urine IgG1.2 g/L, urine κ light chain 417 mg/L and urine λ light chain 275 mg/L. Blood test results were as followed: serum albumin 23 g/L, ALT 6 U/L, total bilirubin 10.1 μmol/L, total cholesterol 6.80 mmol/L, serum creatinine 151 μmol/L, K^+ 3.2 mmol/L, Cl^- 109 mmol/L, Ca^{++} 1.86 mmol/L, IgG 19.0 g/L, IgA 2.7 g/L, IgM 0.5 g/L, κ chain 2.35 g/L, λ chain 1.49 g/L, positive anti-HBs, negative anti-HCV, negative ANA and ANCA. An X-ray scan showed osteoporosis in cranial bones, multiple low-density shadows in lower jawbones and bilateral thigh bones. The repeated bone marrow biopsy did not find plasmocytes in clusters (Figure 1B).

The repeated renal biopsy showed that there were 16 glomeruli observed, including 3 sclerosed and 13 mesangial proliferative glomeruli with moderately increased matrix. Cellular crescents were found in three glomeruli, and

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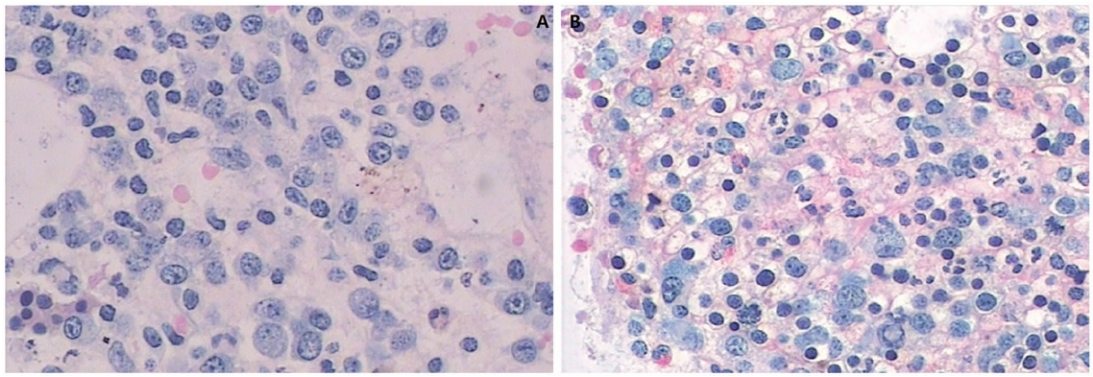

Figure 1. Pathological changes of marrow biopsy. (A) The initial marrow biopsy (2010), (B) the repeated marrow biopsy (2012). The initial marrow biopsy showed active myelosis and 26% plasmocytes. The myeloma cells were distributed in clusters (Figure 1A). Second time marrow biopsy showed plasmacytes spreading around, but no plasmacytes in clusters (Figure 1B).

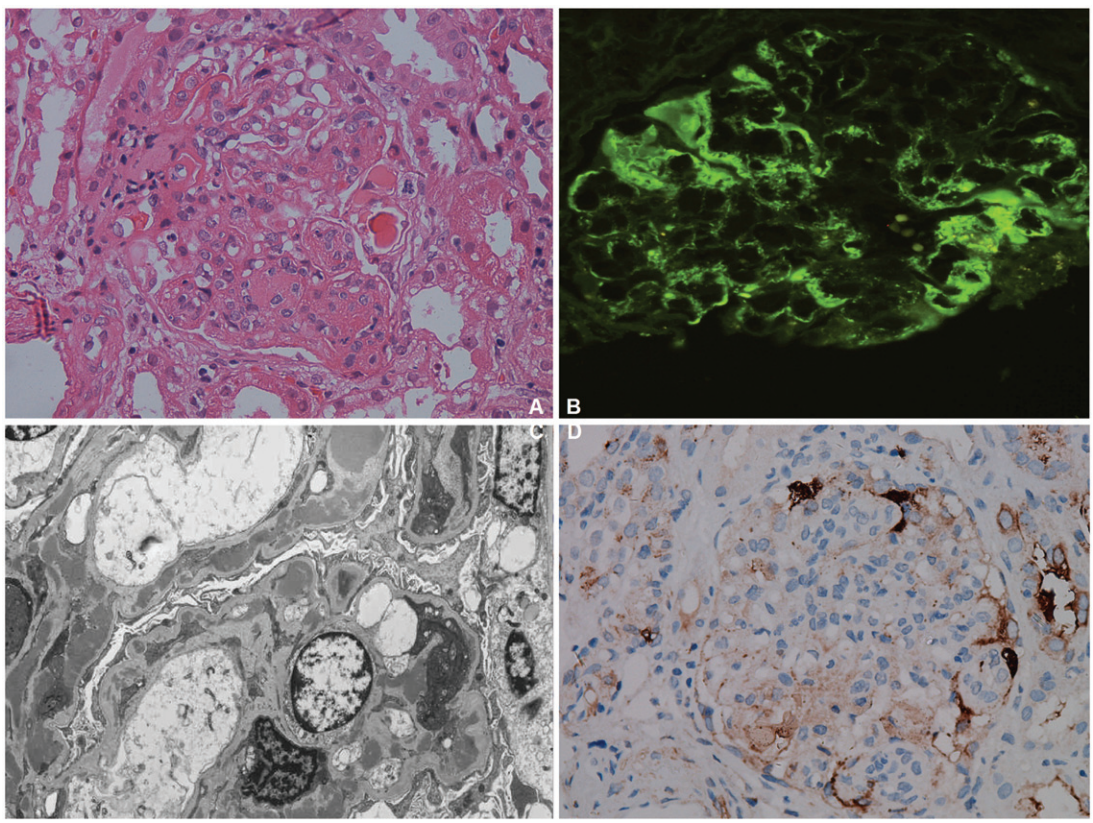

Figure 2. Pathological changes of renal biopsy. (A) Pathological changes of glomerular under bright microscopy (HE, 400×). (B) Immunofluorescent staining of IgA (400×). (C) Pathological changes under electron microscopy (10000×). (D) Kappa chain detected by immunohistochemistry (400×). Mesangial cell hyperplasia, increased matrix, mesangial eosinophilic substance deposition and ''false thrombus'' in some capillary cavity were observed (Figure 2A). IgA was observed in mesangial area and some capillary loop (Figure 2B). There were large amount of electron dense deposits in expanded mesangial area and under endothelial space. The podocyte foot processes diffusely effaced (Figure 2C). Positive immunoglobulin kappa chain was found in some mesangial area and capillary loop, whose distribution in accord with the eosinophilic substances of H.E. staining, and positive kappa chain was also observed in some renal tubules (Figure 2D).

fibrinoid necrosis of the capillary loop was found in one glomerulus. In addition, much eosinophilic substance was found in mesangial matrix, which extended to the basement membrane of the capillary loop. Moreover, some ''false thrombi'' were found in the capillary cavity. Some lymphocytic infiltration and fibrous tissue proliferation can be seen in the interstitial regions (Figure 2A). Positive IgA (+++) and C3 immunofluorescence were found in mesangial area and some capillary loops (Figure 2B). Furthermore, the Congo red staining result was negative. Mesangial cell hyperplasia, large amounts of electron dense deposits in expanded mesangium, and podocyte foot processes diffusely effacing can be observed under electron microscopy (Figure 2C). The immunohistochemistry results showed positive immunoglobulin κ chain in some mesangial area and capillary loop, of which distribution was consistent with the eosinophilic substances with H.E. staining (Figure 2D). Positive κ chains were also found in some renal tubules.

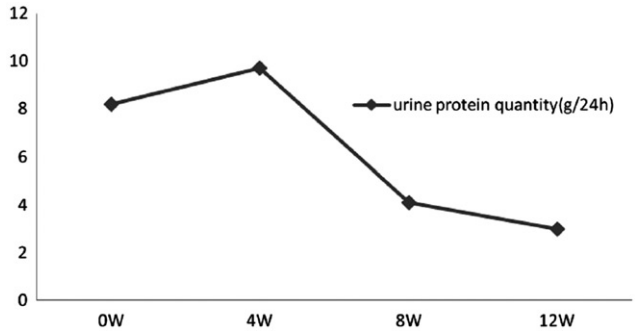

Figure 3. Proteinuria changes in follow-up. The levels of urine protein gradually decreased with the treatment.

The patient was diagnosed with MM accompanied by mesangial proliferative nephritis with IgA deposition and nephrotic syndrome. Considering the weak physical condition of the patient and the low toxicity of mycophenolate mofetil, he was treated with 30 mg prednisone and 1.0 g mycophenolate mofetil per day. Other treatments included anti-coagulation, diuretics, angiotensin II receptor blocker and other supportive therapies. During the follow-up of the patient, the urine protein qualification decreased gradually to 3.0 g/24 h after 3 month treatment (Figure 3). The serum creatinine remained within the range of 150–200 μmol/L.

Discussion and conclusion

In this case, the initial renal biopsy supported the diagnosis of MN, but IgA deposits in mesangial region and positive IgG-κ chain in glomeruli were found in the repeated renal biopsy. Furthermore, prednisone and mycophenolate mofetil were effective to this patient. The final diagnosis was MM accompanied by mesangial proliferative nephritis with IgA deposition and nephrotic syndrome. It looked like IgAN but not a typical primary IgAN.

The spectrum of renal lesions in MM is heterogeneous. A research on 190 cases of MM renal biopsies revealed that 73% patients had paraprotein-associated lesions.[3] The glomerular lesions of MN mainly include AL type amyloidosis and light chain deposit disease. Besides, there may be other secondary glomerulonephritis to MM and MIDD.[6–10] It has been reported that IgA MM presented with clinical features of Henoch-Schönlein purpura nephritis, O-glycosylation abnormality of IgA1, and positive IgA type ANCA.[5] Another report demonstrated the occurrence of Henoch-Schönlein purpura and nodular polyarteritis in IgA type MM.[11,12]

As the patient received sustained glucocorticoid therapy after the initial biopsy, the probability of developing a new type of autoimmune disease is relatively low. Thus, there might be some association between the mesangial proliferative nephritis with IgA deposition and the primary MM. On the other hand, it is very difficult to find direct evidence that the IgA deposition be secondary to MM in this case. As MM and IgAN are both common diseases in China, their coexisting in this case may possibly be just pure coincidence.

In summary, there are many pathological types of renal injuries in MM. This is the first report of coexisting mesangial proliferative nephritis with IgA deposition and IgGκ MM. It is worthy of clinical attention and further study on complicated renal diseases secondary to MM.

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Declaration of interest

The authors have no conflicts of interest to disclose.

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