

## A rare case of crescentic glomerulonephritis with monoclonal IgG deposits

Dear Editor,

A 62-year-old woman was admitted to our hospital because of edema of both lower limbs for more than 3 months and oliguria for 1 week. The patient's laboratory test results were listed in [Table 1](#). Her laboratory test results showed hemoglobin of 84 g/L, serum albumin of 25 g/L, blood urea nitrogen of 9.3 mmol/L, serum creatinine (Scr) of 687  $\mu$ mol/L. The patient had oliguria (about 0.1 L/24h). Urinalysis showed proteinuria (protein excretion, 1.64 g/24 h). Serum C3 and C4 were within the normal range. Serum immunoglobulin (Ig) G level was reduced at 5.3 g/L. Protein electrophoresis showed monoclonal spikes (IgG  $\kappa$  type) in both her serum and urine. The serum-free  $\kappa$  chain was 229.25 mg/L and the free  $\lambda$  chain was 196.00 mg/L, both were higher than normal. The serum-free  $\kappa/\lambda$  chain ratio was 1.17. A serum cryoglobulin test was negative. Hepatitis B surface antigen, anti-HIV-1/2, and automated non-treponemal reagin test were all negative. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, and anti-phospholipase A2 receptor (PLA2R) antibodies were also negative. The patient had no diagnosed history of metabolic disease, coronary heart disease, or liver disease.

An abdominal ultrasound examination showed normal renal size in both kidneys. We performed a renal biopsy for this patient after admission. Light microscopy examination showed membranoproliferative glomerulonephritis (MPGN) pattern and full of crescents ([Figure 1\(A–D\)](#)), and the percentage of renal interstitial fibrosis and tubule atrophy were about 8% under a light microscope. A renal biopsy specimen contained glomeruli ( $n = 37$ ) and about 30 glomeruli were formed with crescents, mainly large cellular crescents. With the immunofluorescence examination, IgG and Kappa were deposited along the capillary wall and mesangial area ([Figure 1\(E,G\)](#)). There were no tubular deposits. Staining for IgG subtype was positive for IgG3 only, and negative for IgG1, IgG2, and IgG4 ([Figure 1\(F\)](#)). Electron microscopy examination revealed electron-dense deposits in the mesangial and subendothelial areas ([Figure 2\(A,B\)](#)). Bone marrow biopsy showed no obvious abnormality ([Figure 3\(A,B\)](#)). No plasma cells were observed in bone marrow smear, and the percentage of plasma cells observed in flow cytometry immunofluorescence analysis of bone marrow biopsy was 0.2%. Based on these findings, we completed the diagnosis of proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID, IgG  $\kappa$  type).

Temporary hemodialysis was administered immediately after admission. After the renal biopsy, the patient received methylprednisolone therapy for 3 days (200 mg/d ivgtt) and gradually reduced the dose to 40 mg prednisone oral administration per day. In terms of immunosuppressants, we used cyclophosphamide with a cumulative dose of 2.0 g within 2 months. After the treatment of cyclophosphamide, the patient's renal function recovered, but proteinuria did not improve further. To prevent further disease progression, we used rituximab (500 mg) for multi-target and maintenance therapy. However, the monoclonal antibody therapy had to be terminated because the patient could not afford it. The specific time point is shown in [Figure 4](#). The patient's urine volume gradually recovered after 1 week of treatment, and she was able to stop dialysis after 2 weeks. One month later, the urine volume of the patient recovered to about 1 L/24h, and Scr decreased from 687  $\mu$ mol/L to 265  $\mu$ mol/L. After 3 months of treatment, her renal function returned to normal. The patient's last follow-up time was 18 August 2021, with serum albumin of 42.3 g/L, 24-h protein excretion of 0.34 g, and Scr of 118  $\mu$ mol/L. We are still closely following up on this patient.

### Discussion

PGNMID is a newly recognized disease characterized by glomerular monoclonal IgG deposition, which is first reported by Nasr et al. [1] in 2004, and its histopathological manifestations of renal biopsy show glomerular proliferative lesions. PGNMID is a rare kind of monoclonal gammopathy of renal significance with intact monoclonal IgG (single light-chain isotype and single  $\gamma$  heavy chain subtype) deposition [1]. The incidence of PGNMID diagnosis by autologous kidney biopsy is approximately 0.07%–0.17% [2,3]. MPGN (57%) and endocapillary proliferative glomerulonephritis (35%) were the most common light microscopy pathologic patterns [2]. The clinical manifestations of PGNMID are diverse. Almost all patients showed various degrees of proteinuria, hematuria and renal insufficiency. Due to its complexity, the pathogenesis of PGNMID is not fully understood and is easy to be misdiagnosed. The prognosis of PGNMID was poor, with 21.9% of patients progressing to end-stage renal disease (ESRD) and 37.5% patients with persistent renal insufficiency at a mean follow-up of 30.3 months [4]. In 2009, Nasr [2] reported several cases of PGNMID, about a quarter of these patients eventually progressed to ESRD. The common characteristics of progression to ESRD are associated

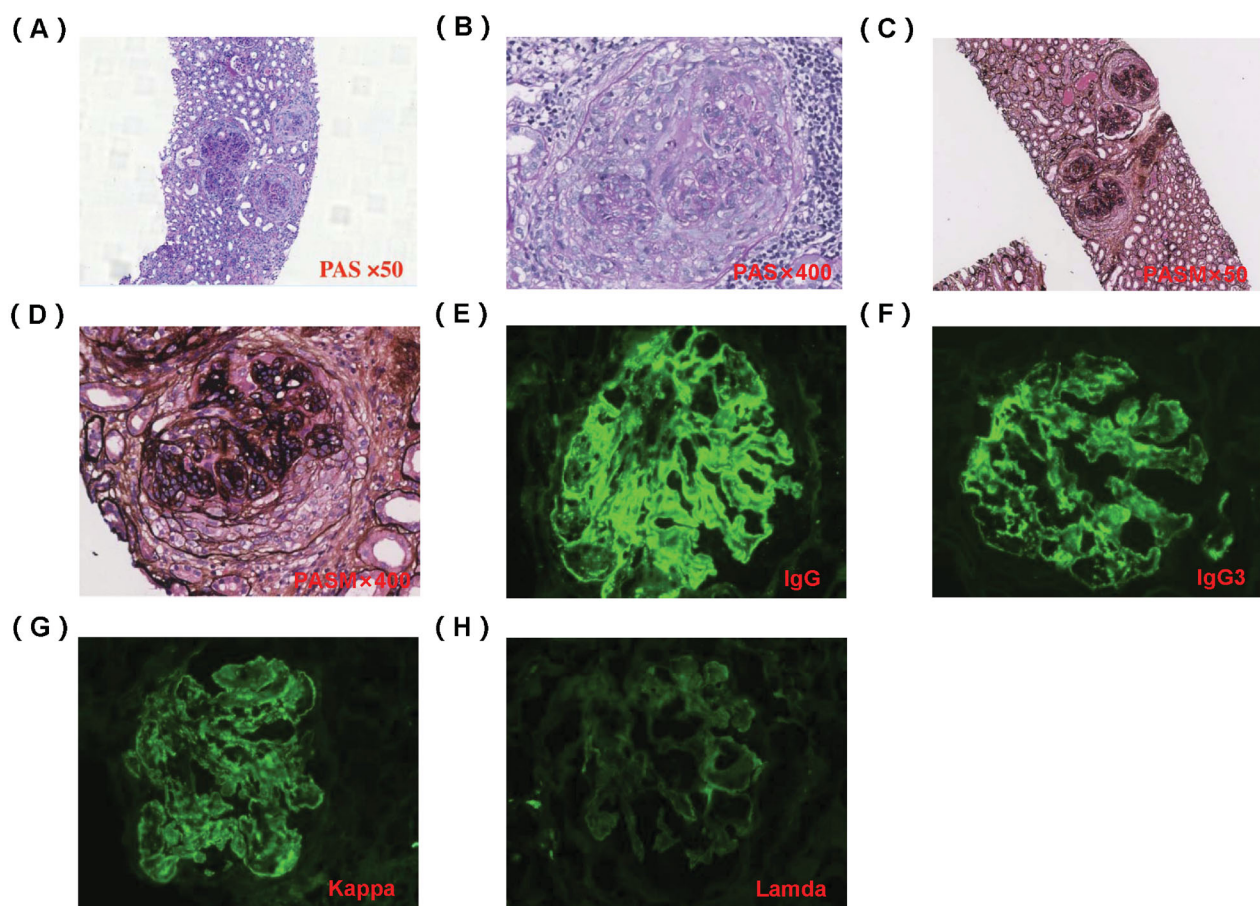
with higher creatinine at biopsy, a higher percentage of global glomerulosclerosis and crescents [2]. In this series [2], crescents were present in 32.4% of cases, but most of them only affected a mean of 20% of glomeruli, and only 5.4% of these cases were presented with crescentic glomerulonephritis (crescent body proportion over 50%).

**Table 1.** The patient's laboratory test results on admission.

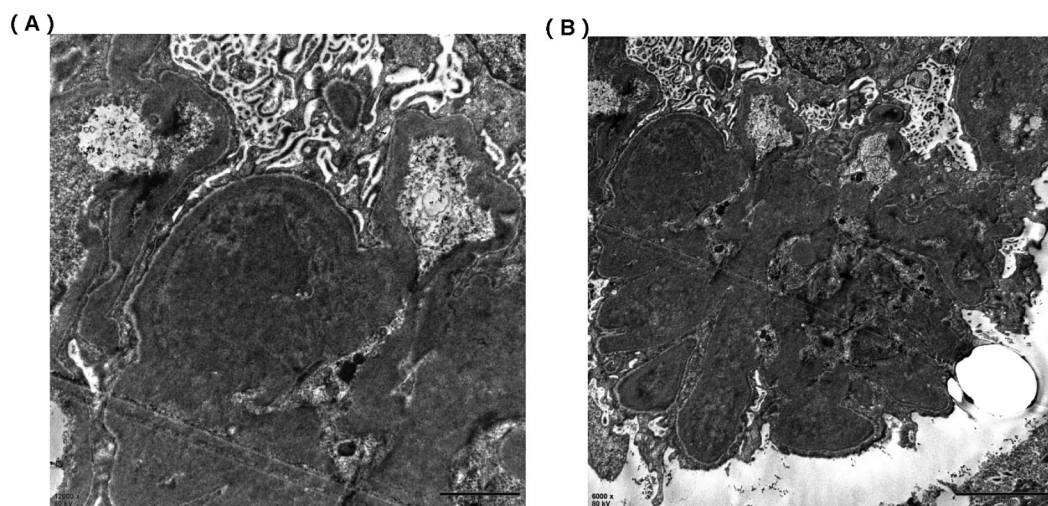
Variables	Value	Normal range
Hemoglobin (g/L)	84	115–150
Serum albumin (g/L)	25	40–55
Blood urea nitrogen (mmol/L)	9.3	3.1–8.8
Serum creatinine ( $\mu\text{mol/L}$ )	687	41–81
Serum cholesterol (mmol/L)	6.23	0.0–5.2
Urinary erythrocyte ( $/\mu\text{L}$ )	104.72	0–5
Serum C3 (g/L)	0.88	0.7–1.4
Serum C4 (g/L)	0.322	0.1–0.4
Serum IgG (g/L)	5.3	8.6–17.4
Rheumatoid factor (IU/ml)	1450	0–15.9
Serum free $\kappa$ chain (mg/L)	229.25	3.3–19.1
Serum free $\lambda$ chain (mg/L)	196	5.71–26.3
Serum-free $\kappa/\lambda$ chain ratio	1.1696	0.26–1.65

The renal pathology of the patient in our case showed about 30 glomeruli (81.8%) were accompanied with crescent bodies mainly large cell crescents, which was rarely reported and predicting the disease was highly active.

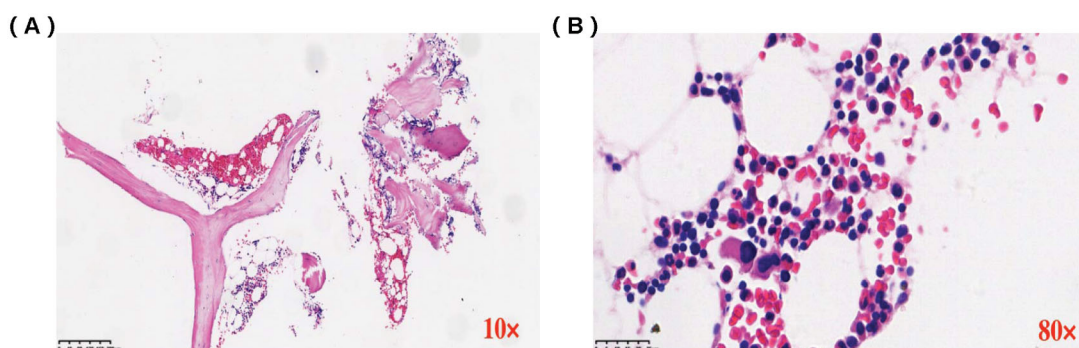
Up to now, there are no effective methods to inhibit the deposition of Monoclonal immunoglobulin (MIg) in tissues or directly remove the deposition of MIg. Treatment of PGNMID is controversial due to limited cases and uncertain pathogenesis. It has been reported that partial remission can be achieved with immunosuppressants such as prednisolone, cyclophosphamide, mycophenolate mofetil and rituximab [2]. For M-spike negative patients, conservative treatment, including RAS inhibitors, is recommended for patients without the nephrotic syndrome. Steroids and cyclophosphamide are recommended in patients with nephrotic syndrome, patients who have failed treatment with RAS inhibitors, patients with reduced GFR, or patients whose biopsy features are suggestive of progression (e.g., crescents) [5]. Rituximab alone may have a better remission rate and better tolerance than steroids and cyclophosphamide [6]. Buxeda [7] reported that using anti-



**Figure 1.** Pathology of renal biopsy. (A) Light microscopy (LM) shows cellular crescent, PAS staining  $\times 50$ . (B) Large cellular crescent formation, PAS staining  $\times 400$ . (C) LM showed an MPGN pattern and full of crescents, PASM staining  $\times 50$ . (D) Cellular crescent formation and compressed capillary loops, PASM staining  $\times 400$ . (E) Immunofluorescence shows granular IgG deposition along the capillary wall and in the mesangial area ( $\times 200$ ). (F) Immunofluorescence shows IgG subtype is IgG3. (G) Immunofluorescence shows granular  $\kappa$  light chain deposition along the capillary wall and in the mesangial area ( $\times 200$ ). (H) Immunofluorescence shows negativity for lambda light chain ( $\times 200$ ).



**Figure 2.** Electron microscope of renal biopsy specimens. (A) Electron microscope shows the electric-dense deposits in the mesangial area ( $\times 12,000$ ). (B) Electron microscope shows the electric-dense deposits in subendothelial areas of glomeruli ( $\times 6000$ ).



**Figure 3.** Bone marrow biopsy analysis. (A) Lymphocytes and plasma cells are scattered ( $\times 10$ ). (B) There was no increase or aggregation of primitive/naive cells, lymphocytes, and plasma cells ( $\times 80$ ).

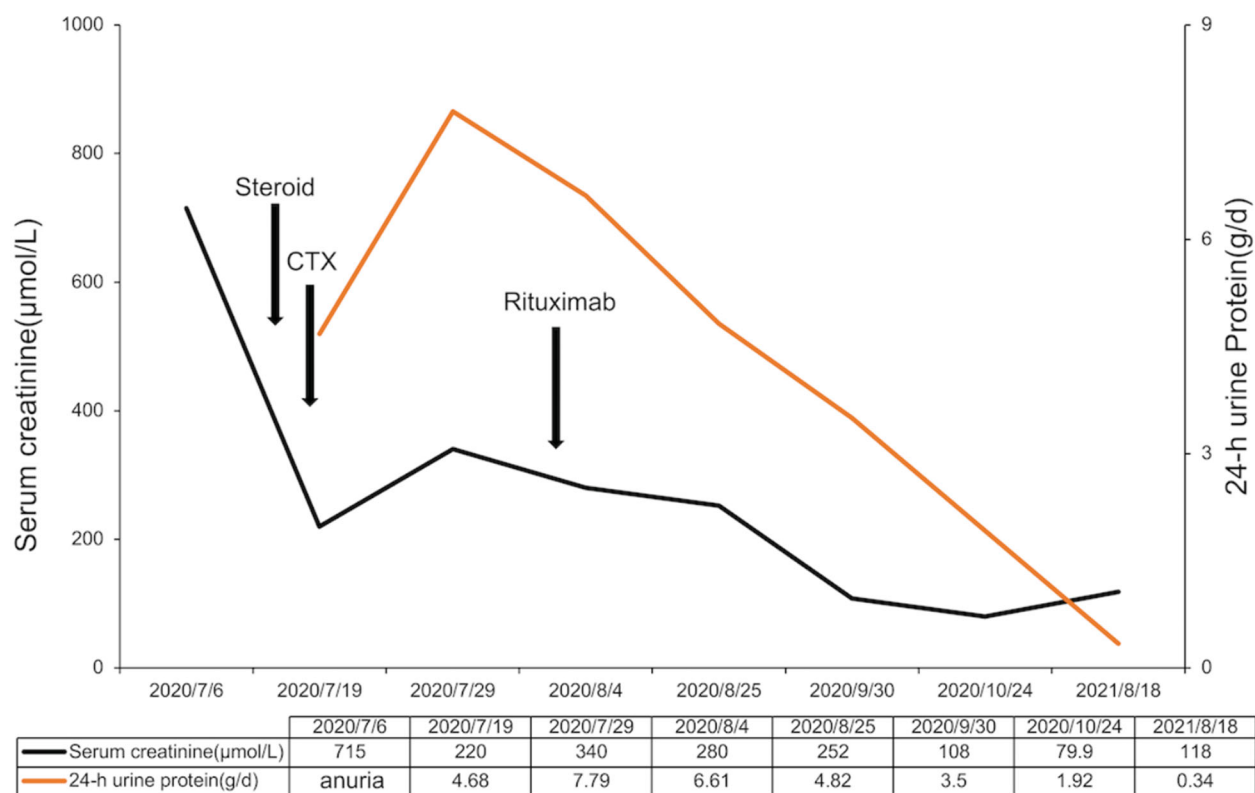
CD20 monoclonal antibodies to treat recurrent PGNMIDs with kidney allografts is effective. Nine relapsed patients only received anti-CD20 antibody (rituximab) treatment, and both their glomerular filtration rate and proteinuria were improved. The patient in our case was a 62-year-old Chinese woman who presented with acute renal failure and nephrotic syndrome, and about 30 glomeruli (81.8%) were accompanied with crescent bodies mainly large cell crescents. Japanese scholars reported a very similar case [8] that the pathology of the patient showed that almost all glomeruli showing cellular and circumferential global crescents. They treated the patient with methylprednisolone 500 mg for 3 days and subsequent oral administration of 40 mg/day of prednisolone, but no improvement of renal function was observed after 2 weeks. Intravenous cyclophosphamide and 6 days of plasmapheresis treatment were additionally performed, but severe proteinuria persisted and his serum creatinine level remained a high level, and the patient had to continue to maintain

hemodialysis [8]. In our case, We chose steroids and cyclophosphamide to induce remission since her crescentic glomerulonephritis (Figure 4). Rituximab was also used in combination with multi-target therapy and maintenance therapy during treatment. A three-month short-term observation suggested that the patient had achieved partial remission. The patient's last follow-up time was 18 August 2021, with serum albumin of 42.3 g/L, 24-h protein excretion of 0.34 g, and Scr of 118  $\mu\text{mol/L}$ . The patient is still followed closely in the clinic, including M-spike monitoring.

## Conclusion

We report a PGNMID patient presented with acute renal failure and nephrotic syndrome, and her renal biopsy suggested crescentic glomerulonephritis. The patient achieved partial remission rapidly after the treatment of





**Figure 4.** The patient's treatment follow-up chart. The chart includes the time and dose of the patient's steroid use and the timing of the use of immunosuppressants and the alterations of clinic parameters including urine protein and serum creatinine during the treatment.

steroid and cyclophosphamide, suggesting that early administration of immunosuppressive therapy may contribute to reverse progression.

## Acknowledgments

The authors thank the members and staff of the Department of Nephrology of the Shanghai East Hospital who contributed to this case. The authors thank the patient for consenting us to publish her case data to write this case.

## Informed consent

Written informed consent was obtained from the patient for publication of this case (including publication of images).

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## Funding

This study was supported by the National Nature Science Foundation of China grants [82070791, 81670690, 81470991 and 81200492 to N.L., 82070700, 81830021 and 81670623 to S.Z., 82000645 to L.S.], the Outstanding Leaders Training


Program of Pudong Health Bureau of Shanghai (PWR12021-02 to N.L.), the Shanghai Scientific Committee of China [20ZR1445800 and 13PJ1406900 to N.L.], the Key Discipline Construction Project of Pudong Health Bureau of Shanghai [PWZxk2017-05 to N.L.], and the Branch Grant of National Key R&D Program of China [2018YFA0108802 to S.Z.].

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Xiaoyan Ma, Xun Zhou, Yi Wang, Min Tao, Lili Sheng and  
Na Liu  
*Department of Nephrology, Shanghai East Hospital, Tongji  
University School of Medicine, Shanghai, China*  
 [naliubrown@163.com](mailto:naliubrown@163.com)

Shougang Zhuang  
*Department of Nephrology, Shanghai East Hospital, Tongji  
University School of Medicine, Shanghai, China*  
*Department of Medicine, Rhode Island Hospital and Alpert  
Medical School, Brown University, Providence, RI, USA*

Received 26 July 2021; revised 2 September 2021;  
accepted 11 October 2021

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