

## Case Report

# Steroid-responsive nephrotic syndrome in a patient with proliferative glomerulonephritis with monoclonal IgG deposits with pure mesangial proliferative features

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### Abstract

A 78-year-old woman developed acute-onset nephrotic syndrome. A renal biopsy showed mild mesangial proliferative glomerulonephritis. Immunofluorescence studies revealed granular IgG3- $\lambda$  deposits within the mesangial area and along the glomerular capillary walls. Electron microscopy showed mesangial and subendothelial granular electron-dense deposits. The pattern of deposition was predominantly mesangial. Serum or urine monoclonal proteins were not detected. Middle-dose steroid therapy induced a rapid remission of nephrotic syndrome. We consider that this is the first case of steroid-responsive nephrotic syndrome due to an extremely rare glomerular disease, proliferative glomerulonephritis with monoclonal IgG deposits associated with pure mesangial proliferative features.

**Keywords:** proliferative glomerulonephritis with monoclonal IgG deposits; steroid-responsive nephrotic syndrome

### Introduction

Renal diseases associated with monoclonal gammopathy are divided into two subgroups [1]. The first group is characterized by organized deposits, like fibrils or microtubules (mainly in cryoglobulinaemia). The second group represents granular electron-dense deposits, and defines entities named monoclonal immunoglobulin deposition disease (Randall type) [2] and proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID), a recently described rare renal disease [3]. PGNMID and its related disease are characterized by endocapillary proliferative, membranoproliferative, or membranous features by light microscopy, glomerular monoclonal IgG deposits restricted to a single IgG subclass and a single light-chain isotype by immunofluorescence microscopy, and immune complex-type deposits by electron microscopy [3–6].

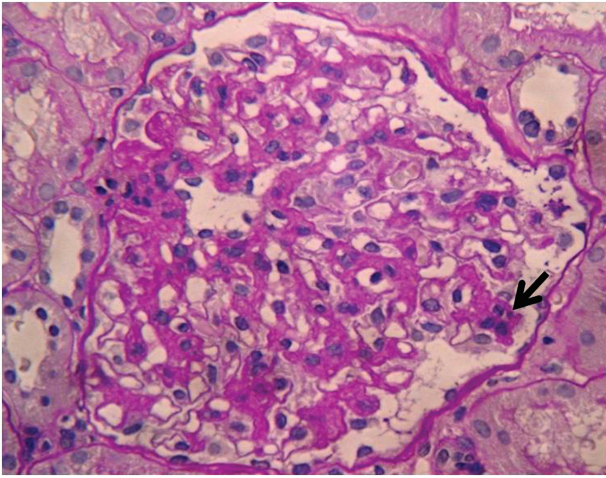
Here, we report the first case of steroid-responsive nephrotic syndrome due to PGNMID associated with pure mesangial proliferative features.

### Case report

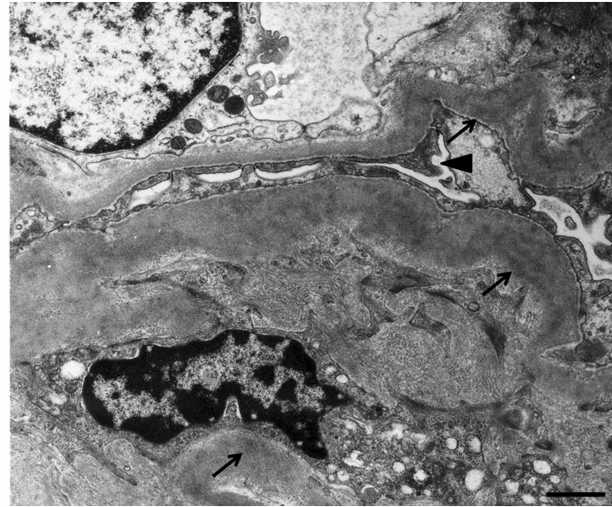
A 78-year-old Japanese woman with a 15-year history of hypertension and hyperlipidaemia and a 2-year history of bronchiectasis was admitted because of an acute onset of massive proteinuria on September 3, 2009. She had been treated with azelnidipine, pravastatin, theophylline and clarithromycin.

On admission, the blood pressure was 113/62 mmHg. A physical examination showed bilateral pretibial oedema. The total urinary protein level for 24 h was 6.7 g, and urine sediments showed no haematuria. The selectivity index of urinary protein was 0.21. The haemoglobin was 12.5 g/dL, the white cell count 6200/ $\mu$ L and platelet count 277 000/ $\mu$ L. The serum total protein was 4.9 g/dL, albumin 2.3 g/dL, blood urea nitrogen 12.2 mg/dL, creatinine 0.63 mg/dL and total cholesterol 264 mg/dL. Liver function tests were normal. Serum C-reactive protein was <0.2 mg/dL, IgG 994 mg/dL, IgA 328 mg/dL, IgM 79 mg/dL, IgE 662 IU/mL (normal <173 IU/mL), C3 185 mg/dL (normal 135–165 mg/dL) and C4 32 mg/dL (normal 13–35 mg/dL). Serum and urinary protein electrophoresis showed no monoclonal paraproteins. Anti-nuclear antibodies with a homogenous and speckled pattern were positive (160-fold). Serum cryoglobulins were negative, and circulating immune complexes were not detected by means of the C1q-binding assay. A chest X-ray showed mild bronchiectasis. Sputum cultures were negative.

A renal biopsy showed diffuse mild mesangial proliferative glomerulonephritis (Figure 1). Immunofluorescence studies showed 3+ granular staining for IgG, 2+ staining for  $\lambda$ -light chain and C3, and 1+ staining for C1q within the mesangial area and along the glomerular capillary walls,



**Fig. 1.** Light microscopy shows a mild mesangial proliferation (arrow). Periodic acid-Schiff staining ( $\times 400$ ).

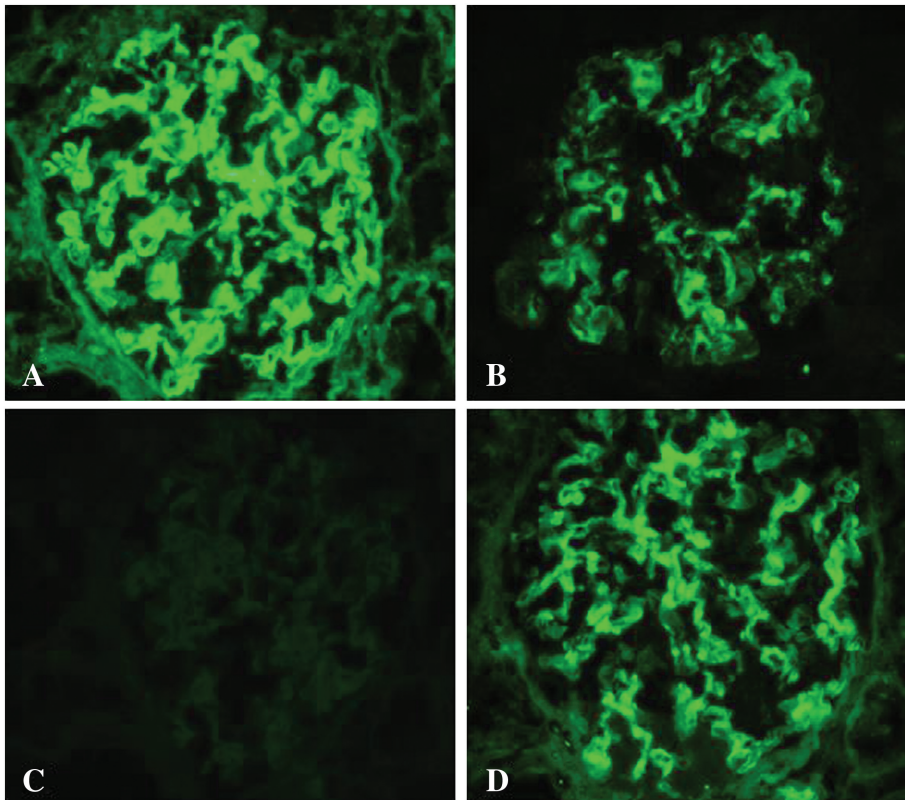


**Fig. 3.** Electron microscopy reveals granular electron-dense deposits in mesangial and subendothelial location (arrows) and podocyte foot process effacement (arrowhead). The bar represents 1  $\mu\text{m}$ .

but no significant staining for  $\kappa$ -light chain (Figure 2A, C and D). Immunofluorescence staining for  $\gamma$ -heavy chain subclasses showed 2+ granular staining for IgG3 (Figure 2B) with negative staining for IgG1, IgG2 or IgG4. Electron microscopy revealed granular electron-dense deposits in the mesangial area and subendothelial space (predominantly mesangial) and podocyte foot process effacement (Figure 3). From these findings, she

was diagnosed with PGNMID associated with pure mesangial proliferative features.

She was treated with 30 mg/day of prednisolone from September 18. On September 30, 24-h urinary protein excretion reduced to 0.02 g, and the serum albumin level increased to 2.8 g/dL. At a follow-up in the out-patient clinic on December 7, she was well and treated with 10 mg/day



**Fig. 2.** Immunofluorescence microscopy for IgG-heavy chain (A),  $\gamma 3$ -heavy chain (B),  $\kappa$ -light chain (C) and  $\lambda$ -light chain (D) displays a strong staining for IgG-heavy chain,  $\gamma 3$ -heavy chain and  $\lambda$ -light chain within the mesangial area and along the glomerular capillary walls with a granular texture, but no significant staining for  $\kappa$ -light chain ( $\times 400$ ).

of prednisolone. At that time, the urine gave a negative test for protein, and the serum albumin was 4.2 g/dL.

## Discussion

In 2004, Nasr *et al.* [3] described 10 patients with a novel form of glomerular injury related to monoclonal IgG deposition, which they termed PGNMID. Diagnostic criteria include (i) the presence of glomerular monoclonal IgG deposits restricted to a single IgG subclass and a single light-chain isotype, associated with endocapillary proliferative, membranoproliferative, or membranous features; (ii) the presence of granular deposits by electron microscopy; and (iii) the absence of clinical and laboratory evidence of cryoglobulin. Recently, Nasr *et al.* [6] enlarged their experience with PGNMID to 37 cases. In their series of patients, the fourth and rarest pattern, observed in one case only, was pure mesangial proliferative glomerulonephritis.

On the basis of clinicopathological findings, our patient was diagnosed with PGNMID associated with pure mesangial proliferative features. Steroid therapy induced a rapid remission of nephrotic syndrome. Our patient had not taken any known drug causing nephrotic syndrome, and had no history of neoplasia or autoimmune disorder associated with nephrotic syndrome. An increased serum level of IgE and hypercomplementaemia were observed in our patient with bronchiectasis, but there were no symptoms of allergy or infection at the onset of nephrotic syndrome.

The pathogenesis of PGNMID remains elusive. The absence of underlying autoimmune, infectious or other systemic disease in the vast majority of patients and the light-chain and heavy-chain subclass restriction argue against antigen-antibody immune complex deposition [6]. In reported patients with PGNMID, common clinical findings are nephrotic syndrome and renal insufficiency [3,5,6]. Prognosis appears to be poor despite immunomodulatory

therapy, especially in patients with membranoproliferative features [5]. On the contrary, patients with PGNMID-related disease associated with membranous features appear to respond well to steroid therapy [4]. In Nasr's series of PGNMID [6], one patient had pure mesangial proliferative glomerulonephritis, but clinical findings including the level of proteinuria were not described in detail. It is uncertain whether patients with this rare form of PGNMID are prone to develop steroid-responsive nephrotic syndrome. The accumulation of cases is needed for further determination of its clinical features and outcome. As stated by Nasr *et al.* [6], renal biopsy with careful attention to light chain and IgG isotype staining is essential for diagnosis of PGNMID, because the majority of patients do not have a monoclonal spike in both serum and urine on standard electrophoresis as in our patient.

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