Case Report

Simultaneous occurrence of fibrillary glomerulopathy and AL amyloid

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Introduction

We report on a case of fibrillary glomerulonephritis associated with AL amyloidosis in a patient suffering from Waldenström’s macroglobulinaemia (WM). This association is tantalizing in view of the possibility that fibrillary and amyloid deposits could be two expressions of the same disease, although coincidence can certainly not be excluded.

Case

A 59-year-old man underwent renal evaluation in July 1996. His medical history had been unremarkable until December 1995 when hypertension was diagnosed. Soon afterwards, proteinuria and renal insufficiency were evidenced.

On physical examination the patient complained of asthenia and shortness of breath. His overall state was good; supine blood pressure was 175/95 mmHg, and no adenopathy or hepatosplenomegaly were present.

Laboratory investigations yielded the following results: serum creatinine 198 μmol/l, BUN 14 mmol/l, total protein 63 g/l, albumin 37 g/l, calcium 2.12 mmol/l, and normal electrophoresis. C3 was 0.3 g/l (N 0.8–1.6), C4 0.09 g/l (N 0.2–0.4), IgM 9 g/l (N 0.5–1.5), IgG 4 g/l (N 6–12 g/l), and IgA 0.6 g/l (N 1.0–3.4). Haemoglobin was 9.0 g/dl, haematocrit 0.28, white blood cells 5600/mm³ with normal differential count, platelets 192 000/mm³, and erythrocyte sedimentation rate 28 mm/1st h. Serum immunofixation disclosed a monoclonal IgM bearing lambda light chains. Rheumatoid factor, hepatitis B and C serologies, cryoglobulins, antinuclear antibody, and the other autoantibodies were negative.

Proteinuria was 3 g/day with 100% of albumin; urinary sediment revealed microscopic haematuria and leukocyturia. Immunofixation showed no free light chains in urine. Renal sonography showed that both kidneys were normal. Bone-marrow biopsy revealed a very mild lymphocytic proliferation without IgM lambda monoclonality. Total body tomodensitometry revealed no lymphadenopathy or hepatosplenomegaly.

The renal biopsy specimen was divided into three parts for light microscopy (LM), direct immunofluorescence (IF), and electron microscopy (EM). For LM, tissue was fixed in 2.5% glutaraldehyde and sections were stained with Masson’s trichrome. Glomeruli were enlarged by fibrocellular proliferation and some capillaries were hyalin, few in number, and stained by Congo-red (Figure 1). In the lumen of the glomerular capillaries, a few thrombi were observed. Tubules were normal. In the interstitium a very mild lymphocytic proliferation was present with few normal plasma cells.

Immunofluorescence

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Fig. 1. Glomerulus with massive extracellular fibrinoid deposits in the mesangium and the subendothelial space (large arrowheads). Hyalin deposits were also present (small arrowheads). Masson's trichrome, original magnification ×400.

Fig. 2. Positive Congo-red deposits in the mesangium of two glomeruli (large arrowheads) and in the wall of an artery (small arrowheads). Original magnification ×250.

and anti-lambda anti-sera as well as with the anti-C3 and anti-C1q anti-sera. No staining was seen with the other anti-sera.

Electron microscopy
Ultrastructural examination showed diffuse infiltration of the mesangial matrix and the subendothelial space by criss-crossing non-randomly oriented bundles of fibrils, 15–20 nm thick, without clear-cut tubular substructure. This infiltration corresponded to the non-amyloid deposits. Beside them were typical amyloid fibrils, made of 8–10 nm non-branching microfibrils (Figure 3).

Treatment was started with chlorambucil 0.2 mg/kg/day and prednisone 0.5 mg/kg/day. After 6 months, hypertension persisted but IgM decreased to 3 g/l, creatinine was 162 μmol/l, and proteinuria 1 g/day.
plus fibrillar deposits in three cases [5–7]. This strongly suggests that these three diseases induced by the tissue-processing of the monoclonal Ig could be different expressions of the same disease.

The difference between the three types of glomerular deposits probably resulted from differences in the fragments of the light chains that precipitated or from differences in the Ig physical or chemical properties. In fact the IgM we evidenced had a specific property since complement was consumed by precipitation into the glomeruli. Complement consumption is very rare in MW [8]. This underscores that monoclonal Igs may have different physical or chemical properties, which would explain why they behave differently when processed in tissues. In addition, the association of fibrillar and amyloid deposits demonstrated that an Ig can have properties that allow it to precipitate under different patterns.

In conclusion this case report demonstrates that in patients suffering from lymphoproliferative malignancies with monoclonal Ig, the glomerular deposits can either be a single pattern or a mixture of different patterns. This underlines the need for accurate diagnosis by means of renal biopsy since prognosis and treatment differ in the three types of renal involvement.

**Discussion**

This observation is unique for two reasons. First, renal involvement is rare in WM. When present, it is caused by infiltration of the interstitium with lymphoid cells, by AL amyloidosis, or by IgM deposits in the glomerular capillaries (reviewed in [1]). Renal involvement in our patient was quite unusual because the IgM deposits were massive and localized not only in the glomerular capillaries but also and mainly in the mesangium and in the subendothelial space.

Second, this patient is the first in whom simultaneous fibrillar and AL amyloid glomerular deposits have been observed. When a monoclonal immunoglobulin (Ig) is secreted in lymphoproliferative disorders, usually only one of the three patterns of glomerular deposits is evidenced. The pattern may be the Congo-red-positive fibrillary pattern corresponding to AL amyloid, the Congo-red-negative granular pattern corresponding to light-chain deposition disease (LCDD), or the Congo-red-negative fibrillary pattern (also called amyloid-like deposits [2]) corresponding to fibrillary or immunotactoid glomerulonephritis.

Our case brings evidence that a monoclonal Ig can precipitate under two different patterns. So far, five cases of such an association have been described: LCDD plus AL amyloid in two cases [3,4], and LCDD plus fibrillar deposits in three cases [5–7]. This strongly suggests that these three diseases induced by the tissue-processing of the monoclonal Ig could be different expressions of the same disease.

**References**


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