The Interesting Case

Renal failure in a patient with two renal diseases: renal amyloidosis and rapidly progressive glomerulonephritis

F. J. Andreu¹, J. Almirall², I. Jurado¹, M. Larrosa³, M. Carreras⁴ and M. Rey¹

¹Pathology, ²Nephrology, and ³Medicine Services, Consorci Hospitalari del Parc Taulí, Sabadell, and ⁴Pathology Service, Hospital Princeps d’Espanya, Bellvitge, Barcelona, Spain

Key words: renal amyloidosis, rapidly progressive glomerulonephritis, crescentic glomerulonephritis.

Introduction

Rapidly progressive glomerulonephritis (RPGN) is characterized by a rapid deterioration of renal function and by an extensive cellular proliferation of parietal epithelium of Bowman’s capsule. Without treatment, 80–90% of the patients develop terminal renal failure in less than 6 months.

We report on a 65-year-old woman with rheumatoid arthritis (RA) and rapidly progressive renal failure. A renal biopsy showed amyloid deposition and crescentic glomerulonephritis.

Case report

A 65-year-old female had been suffering from seronegative rheumatoid arthritis with severe symptoms of articular inflammation since the age of 40. Medical history included an acute episode of myocardial infarction at the age of 60. She had been treated with non-steroidal anti-inflammatory drugs (NSAIDs), chloroquine, and glucocorticoids at low-doses. Routine controls of laboratory data were always normal. Four months before presentation the patient had been treated surgically for an umbilical hernia. Laboratory data at that time showed serum creatinine of 1.9 mg/dl, 24-h urinary protein of 3.5 g and urinary sediment with 10–15 haematoes per field. A biopsy of subcutaneous fat showed no deposits consistent with amyloid and treatment with NSAIDs was discontinued. A few weeks after discharge, her renal function deteriorated, reaching a serum creatinine level of 3.4 mg/dl, BUN of 75 mg/dl, 24-h proteinuria of 8 g, creatinine clearance of 10 ml/min, and the urinary sediment contained more than 50 haematoes per field. Immunoglobulins and complement were normal and antineutrophil cytoplasmic antibodies (ANCA) and antiglomerular basement membrane antibodies (anti-MBG) were negative. The patient was admitted to the hospital for further evaluation and a percutaneous renal biopsy was performed.

Histological findings

By light-microscopy the renal biopsy included four glomeruli, none of them was sclerosed. An extensive amyloid deposition, demonstrated by Congo-red stain, was observed in the mesangium as a diffuse, global, nodular pattern and in the walls of interstitial vessels. Congo-red staining was negative when the sections were pretreated with potassium permanganate. In addition there was an extensive and circumferential cellular proliferation in Bowman’s space (crescents), with rupture of the capsule and infiltration by mononuclear cells (Figure 1). The coexistence of cellular crescents and amyloid deposition was noted in all four glomeruli. There was severe interstitial inflammatory infiltration of mixed type, with focal destruction of the tubular epithelium and a moderate interstitial fibrosis. Immunofluorescence studies revealed homogeneous, non-granular, non-linear staining, most prominently in the mesangium, for IgG, IgM, and C3, which was considered as non-specific. On electron-microscopic examination, numerous amyloid fibrils and occupation of the urinary space by epithelial cells were found. No electron-dense deposits were detected (Figure 2).

Treatment with intravenous pulse methylprednisolone (3 bolus, 500 mg/day) was started, followed by oral low-dose glucocorticoids plus cyclophosphamide (100 mg/day). The renal function improved transiently during the first 2 months of treatment; the serum creatinine was 2.1 mg/dl, a BUN of 56 mg/dl and creatinine clearance of 25 ml/min, with 24-h proteinuria of 2.2 g and normal urinary sediment. The renal function progressively worsened and the patient died suddenly at home, 5 months later. A post-mortem was not performed.
Rapidly progressive glomerulonephritis (RPGN) is clinically characterized by a nephritic sediment (dysmorphic haematuria and cylindruria) and a rapid deterioration of renal function (by more than 50% in 6 weeks), and histologically by a cellular proliferation of the parietal epithelium of Bowman’s capsule (circumferential deposition and more than 50% of glomeruli affected). It has been reported in primary glomerular disease as well as in various systemic diseases. At present, crescentic nephritis or RPGN are categorized according to a variety of clinical, morpho-
logical, immunohistological, and serological criteria. None of the classification systems is entirely satisfactory; crescent formation is the result of a disease rather than a disease in itself. The different diseases that are associated with crescent formation share enough similarities to justify a common approach to management, and especially with regard to the urgent need for treatment [1].

The coexistence of cellular crescents and amyloid deposition seems to be quite rare. Such an association has not been reported in large series of renal amyloidosis, or in those of rapidly progressive glomerulonephritis [2]. Panner in 1980 [3], reported the first two cases of possible renal amyloidosis (not fully documented) which were presented as rapidly progressive glomerulonephritis. One of the two patients was suffering from rheumatoid arthritis. By 1995, five more cases were clearly documented, all but one was associated with long-standing rheumatoid arthritis. One case was also associated with antiglomerular basement membrane disease. In all cases, amyloid was characterized as a secondary type [4–8].

It is worthy of note that this rare report of an association between amyloidosis and RPGN could possibly be explained by the fact that patients with diagnosis of amyloidosis with rapid deterioration of renal function are not submitted for a renal biopsy. It is assumed that this rapid deterioration is the natural course of disease or is caused by concurrent haemodynamic factors, renal vein thrombosis, or rapid progression of amyloid deposits at interstitial vessels [9]. Nevertheless in large series of amyloidosis or GNRP patients, including cases from post-mortems, such an association has not been reported [10,11].

The fact that the majority of cases of such an association have been seen in patients with long-standing rheumatoid arthritis, suggests some kind of pathogenic relationship. While amyloidosis has been reported in 30% of patients with RA and clinical renal disease, a systemic rheumatoid vasculitis (necrotizing vasculitis), commonly associated with rapidly progressive glomerulonephritis with extracapillary proliferation, has been observed in no more than two of 110 RA patients with clinically evident renal disease [12]. The latter rare complication is exclusively observed in patients with severe inflammatory disease. Glomerular amyloid deposition could be associated with extracapillary proliferation due to therapy with non-steroidal anti-inflammatory drugs, gold salts or n-penicillamine [13,14]. However, such a relationship has not been convincingly demonstrated in our case or in the literature.

Watanabe et al. [4] reported on the possible relationship between extracapillary reaction and amyloid glomerular basal membrane lesion, which allows fibrin deposition into the urinary space with the consequent proliferation of crescents. In our case, lack of detection of electron-dense deposits at electronic examination and the negative ANCA values support such a non-immunological mechanism of crescentic proliferation.

Conclusion

We report a rare case of renal amyloidosis associated with crescentic glomerulonephritis. A renal biopsy is needed for the accurate diagnosis of crescentic glomerulonephritis as the cause of rapidly progressive renal insufficiency in this setting. Some functional improvement can be expected from an aggressive therapy with immunosuppressive agents, steroids, and cytotoxic drugs. However, in patients with renal amyloidosis, the theoretical benefits of these treatments should be carefully evaluated before their prescription.

References


Received for publication: 27.3.96
Accepted in revised form: 15.5.96