Intracapillary proliferative glomerulonephritis due to heavy chain deposition disease

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Introduction

Heavy chain deposition disease (HCDD) is a rare manifestation of plasma cell dyscrasia. Only 11 cases have been described in the literature [1]. The clinical picture is variable, but in all patients renal biopsy showed a nodular sclerosing glomerulopathy [1–5]. We report a patient with rapidly progressive glomerulonephritis in whom the renal biopsy showed mainly intracapillary proliferative glomerulonephritis due to HCDD.

Case

The patient is a 55-year-old musician with an uneventful medical history except ankylosing spondylitis diagnosed at the age of 47. Six weeks before admission he noticed foamy urine, at 2 weeks he developed generalized swelling, dyspnoea and a severe headache. Upon admission the patient was overhydrated, blood pressure was 220/130 mmHg. Blood investigations showed haemoglobin 11 g/dl, creatinine 595 μmol/l, albumin 25 g/l. Urinalysis revealed protein, 9 g/24 h; RBC, 10–20 per high power field; WBC, 0–1 per high power field. Hyalin and many granular casts were present. Serological investigations were negative for antinuclear antibodies, antineutrophil cytoplasmatic antibodies, antibodies against the glomerular basement membrane, hepatitis B and C and cryoglobulins. Complement factors C1q, C3 and C4 were all normal. Ultrasound of the kidneys showed large kidneys (12 cm on both sides) with no postrenal obstruction.

Renal biopsy (Figure 1A) showed a cortex with 20 glomeruli, one which was sclerosed. All glomeruli showed thickening of Bowman’s capsule and some widening of Bowman’s space, which in combination with chronic vascular disease was interpreted as a sign of ischaemia. Furthermore, most glomeruli showed intracapillary proliferation of endothelial and mesangial cells and an influx of mononuclear cells ranging from global to segmental. Glomerular capillaries showed some intraluminal protein accumulation, reminiscent of cryoglobulins, which was not supported by immunofluorescence or electron microscopy studies. Capillary walls revealed deposition of strongly eosinophilic deposits with occasional double contours. Extracapillary proliferation was not found. The cortical interstitium was expanded with some oedema and fibrosis, and there was focal tubular atrophy. Staining for amyloid was negative. Immunofluorescence revealed strong linear depositions of IgG along the glomerular and tubular basement membranes and in arterial and arteriolar vessel walls (Figure 1C and D). IgA, IgM, kappa and lambda were negative, also after application of two different monoclonal antibodies, one of which was positive for kappa light chain in bone marrow evaluation (see below). C3 was found in an interrupted, granular pattern along the glomerular capillary walls. Electron microscopy revealed a granular condensation of the glomerular basement membranes with widespread obliteration of podocyte foot processes and loss of endothelial fenestration with occasional double contours (Figure 1B). No signs of amyloid or cryoglobulins were found. A diagnosis of IgG HCDD was made.

Further investigations showed the presence of a paraprotein in the serum which appeared to be an IgG kappa. Quantitative assessment of IgG, IgA and IgM in blood was normal (IgG 10.7 g/l, IgA 1.2 g/l, IgM 0.4 g/l). Serum concentrations of free kappa and lambda were 2114 and 114 mg/l, respectively. Immunofixation showed two bands of IgG, one of which corresponded
with the light chain band. This suggests that the other, non-corresponding band represents the heavy chain. No cryoglobulins were detected. Immunelectrophoresis of the urine revealed a high concentration of kappa light chains (2184 mg/l), but only a few heavy chains. No lytic lesions were detected on skeletal survey. Bone marrow biopsy showed monoclonal plasmacytosis (10% infiltration) with positive staining for IgG kappa (Figure 1E and F). The treatment for multiple myeloma consisted of prednisone and melphalan initially, later followed by vincristine, adriamycin and dexamethasone. Haemodialysis was given as renal replacement therapy. This was discontinued after 3 months because of partial recovery of renal function with a creatinine clearance of 15 ml/min. However, haemodialysis treatment had to be reinstituted again 2 months later. Bone marrow biopsy was performed again in March 2002 and showed no improvement.

Discussion

To the best of our knowledge intracapillary glomerulonephritis as a result of HCDD has never been described before. All 11 patients with HCDD reported in the survey by Kambham et al. [1] suffered from nodular sclerosing glomerulonephritis. An additional presence of crescents was seen in four patients. It involved 11–75% of the glomeruli.

Six patients were treated with prednisone alone, in four patients a chemotherapeutic agent was added. Follow-up showed progressive renal failure in nearly all patients. Only one patient had a favourable outcome [5]; she was a 35-year-old woman with, compared with the other patients described, only mild laboratory disturbances (proteinuria 0.5 g/l, haematuria 10–25 RBC per high power field, serum creatinine 1 mg/dl). She was treated with prednisone alone and her
proteinuria declined. No data are available on survival rates.

The presentation of HCDD with extracapillary and intracapillary proliferation is probably due to the intraglomerular distribution and the physicochemical characteristics of the heavy chains and their capacity to bind and activate complement and bind Fc gamma receptors of recruited phagocytes [6–8], major determinants of glomerular injury. The different presentation of HCDD as compared with heavy chain disease, in which there is no deposition, might be caused by the structure of the heavy chain molecule. In HCDD the variable regions of the heavy chain molecule contain some unusual amino acid substitutions, which might cause direct precipitation of the molecule. Another cause might be the deletion of the CH1 domain which is seen in almost all cases of HCDD. However, this is thought to cause premature secretion of the molecule into the blood rather than direct precipitation [1]. Although circulating kappa light chains were detected in the patient’s serum, no glomerular deposits or signs of cast nephropathy were observed by immunofluorescence or light microscopy.

In conclusion, the histological spectrum of HCDD is highly variable. Besides nodular sclerosis, it may also have features of intracapillary proliferative glomerulonephritis.

Conflict of interest statement. None declared.

References


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