

The crucial role of renal biopsy in the diagnosis of Heavy Chain Deposition Disease

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Heavy-chain deposition disease (HCDD) was first described in 1993 by Aucouturier et al. This rare condition is characterized by nonamyloid deposits of gammaglobulin heavy chains in the kidney and sometimes in other tissues. Less than 30 cases of HCDD have been reported in the literature. We report here an additional illustrative case and discuss the clinical and pathological features of HCDD.

Case record:

A 77-year old woman was referred in April 2008 because of hypertension and nephrotic syndrome with hematuria. She had a 17-year-long history of monoclonal gammopathy of unknown significance (MGUS) with an IgG kappa monoclonal component at low concentration (3 g/l). Serum creatinine (sCr) concentration was 100 $\mu\text{mol/l}$. Urinary protein excretion was 4.4 g/24 hours (albumin 62%, light chain (LC) kappa 17%). Serum albumin was 23 g/l. Serum complement was decreased (C3 0.48 g/l, C4 0.07 g/l).

Pathology:

Analysis of the kidney biopsy showed a nodular glomerulosclerosis with expansion of the mesangial matrix (**Figure 1**). Renal tubular cell basement membranes were thickened. Both thioflavin T and Congo red stains were negative. Immunofluorescence (IF) showed that the tubular, capsular, and glomerular basement membranes and the mesangial nodules stained with anti- γ -heavy-chain antibody with an expression restricted to γ_1 chain (**Figure 2**). Complement fractions were also present within the glomeruli while LC IF was negative. IF study with monoclonal antibodies that are specific of the constant domains of γHC allowed identification of a deletion of the $\text{C}_{\text{H}}1$ domain (**Figure 3**). Serum immunoblotting also showed that the monoclonal IgG kappa lacked the $\text{C}_{\text{H}}1$ domain. Bone marrow aspiration showed 11 % plasma cells, and the results of a bone marrow biopsy were consistent with the diagnosis of multiple myeloma.

Outcome:

Despite treatment with melphalan, prednisone, and thalidomide the patient required haemodialysis treatment (HD) within 1 month. Six months later, renal function recovered, allowing HD withdrawal and the patient is still HD independent with a sCr of 250 $\mu\text{mol/l}$ at 15 months follow-up.

Conclusions:

This observation underlines:

1. the essential role of renal biopsy in the diagnosis of HCDD
2. the common association between HCDD and plasma cell dyscrasia
3. the possible good renal outcome with HD withdrawal despite transitory HD.

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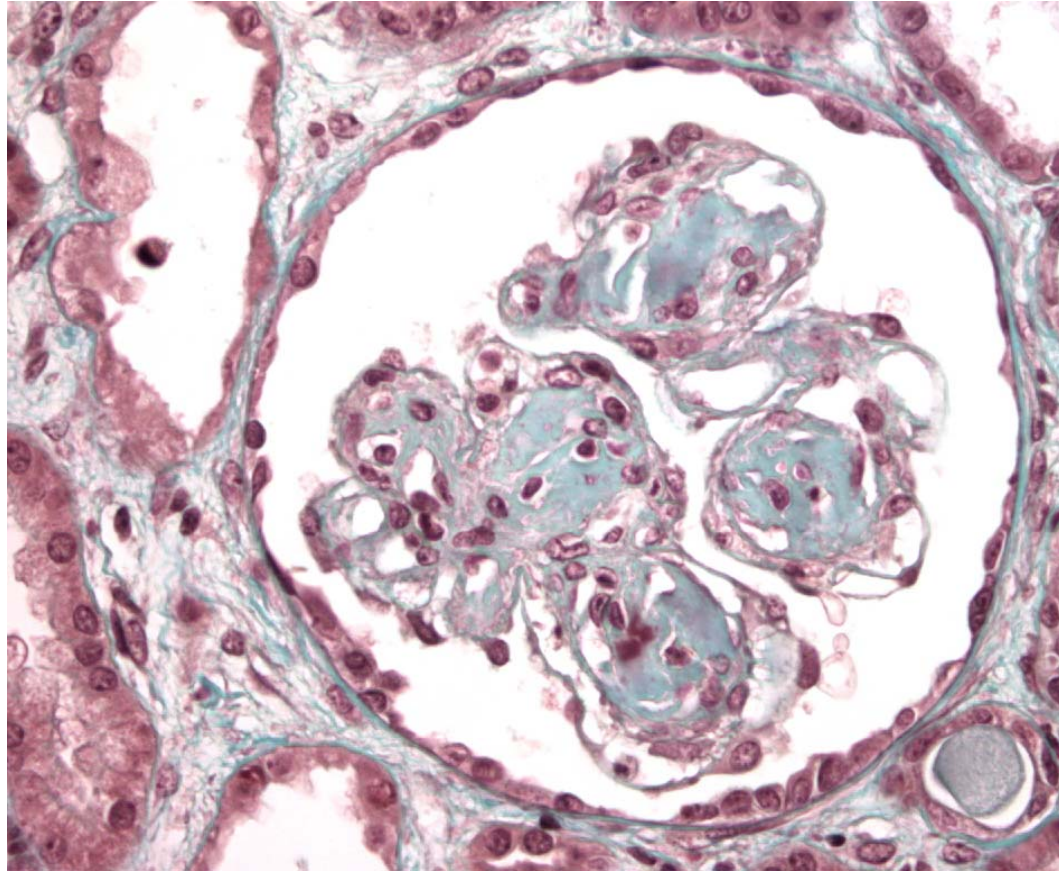


Figure 1 : nodular glomerulosclerosis with mesangial deposition

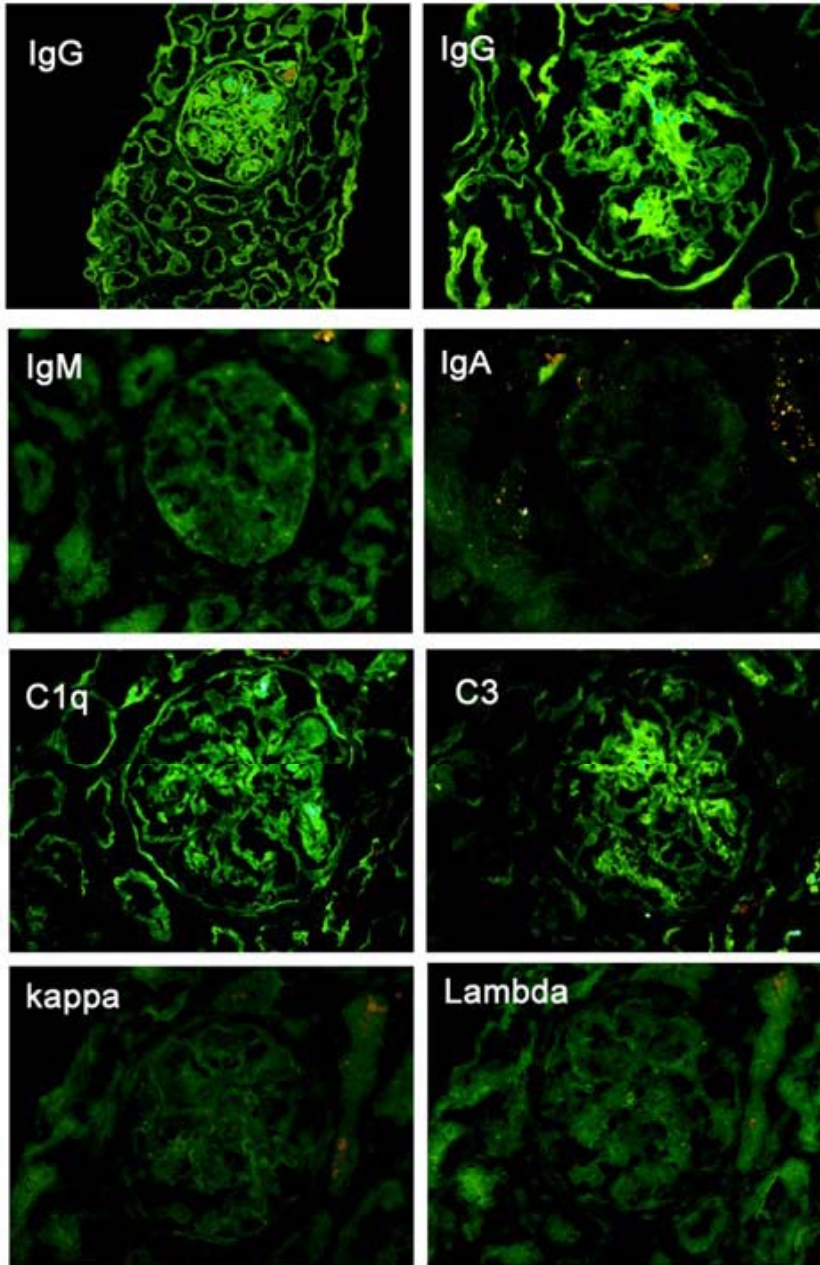


Figure 2 : Immunofluorescence study

Labeling of the glomeruli and of the renal tubular cell basement membrane restricted to the γ -heavy chain and to C1q and C3 complement fractions.

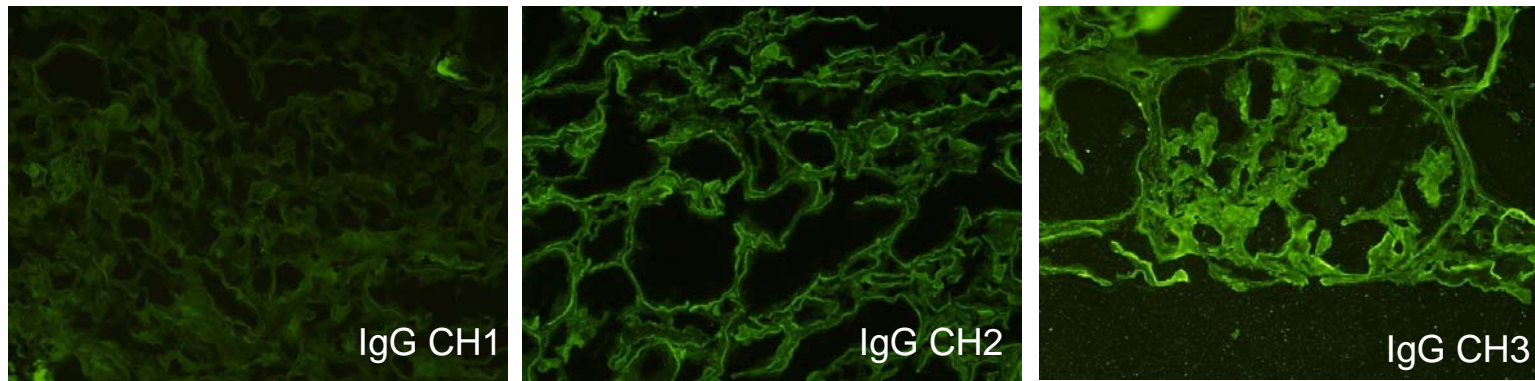


Figure 3: deletion of the CH1 domain