Alport Syndrome with Type I Membranoproliferative Glomerulonephritis

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Dear Sir,

In 1973 we reported the case history of a patient affected by Alport syndrome (AS) with superimposed Berger disease [1, 2].

It is well known that in AS renal biopsy shows no typical features at light microscopy, negative immunofluorescent findings, and characteristic ultrastructural lesions in about 80% of affected subjects, especially in males [3]. End-stage renal disease in males usually occurs in the 2nd or 3rd decade of life, but it is not clear how the inherited X-linked abnormality of the $\alpha 5$ chain of collagen IV of the glomerular basement membrane determines renal failure [4]. Moreover, different clinical phenotypes and progression to end-stage renal failure may be observed in male and female subjects and also within the same family; it has not yet been determined whether the different phenotypes correlate with different mutations within the gene.

AS is a relatively rare disorder and it is consequently rare to have a superimposed immune-mediated glomerular disease, but this event must nevertheless be considered.

We recently observed a 33-year-old male, coming from a family affected by AS, with a US

CL

DD

Fig. 1. Renal biopsy of a 33-year-old male patient with AS and superimposed idiopathic type I membranoproliferative glomerulonephritis. CL = Capillary lumen; US = urinary space; DD = electron-dense deposits. Electron micrograph. $\times 6400$.

DD

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serum creatinine of 2.28 mg/dl, glomerular proteinuria of 2.5 g/24 h, normal audiometric and ophthalmological findings. The histological examination of renal biopsy revealed ultrastructural glomerular lesions of AS associated with intramembranous electron-dense deposits (fig. 1), and granular deposition of C3 along the glomerular capillary walls by immunofluorescence, as in idiopathic type I membranoproliferative glomerulonephritis. The molecular analysis of the gene (COL4A5) coding for the $\alpha 5$ chain of type IV collagen in the patient's family did not reveal any lesion by Southern blotting or any point mutation detectable by SSCP technique in 8 examined exons of the gene [5].

There is no clinical or experimental evidence that the abnormalities in $\alpha 5(\text{IV})$ collagen chain of the glomerular basement membrane may favour the development of an immune-mediated glomerulonephritis. Certainly, the coexistence of an hereditary and an acquired glomerular disease is likely to result in a more rapid progression towards end-stage renal failure.

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