Hereditary renal amyloidosis
associated with a novel mutation
in the apolipoprotein AII gene

Sir,

Hereditary amyloidosis is a rare disorder associated with mutations encoding seven proteins: transthyretin, apolipoproteins AI and AII, gelsolin, cystatin C, lysozyme and fibrinogen A. We report a case of renal amyloidosis affecting six members of a family, associated with a novel non-stop mutation in the apolipoprotein AII gene.

A 42-year-old Caucasian male with nephrotic syndrome and renal failure underwent renal biopsy, revealing renal amyloidosis; the AA type was excluded by immunohistochemistry. Diagnostic procedures (echocardiogram, electromyogram, and liver examination) ruled out extra-renal involvement. As five members of his family (four sisters and a nephew) also displayed nephropathy, we characterized his amyloid fibril type by DNA analysis. We found a novel mutation in the apolipoprotein AII gene, a single-base substitution 359T→A, resulting in the replacement of the stop codon by arginine at position 78. Renal apolipoprotein AII amyloidosis has been previously described in two kindreds, associated with Stop78Gly and Stop78Ser variants.1

The patient’s progression to end-stage renal disease forced us to consider the issue of double kidney-liver transplantation. The therapeutic approach to these disorders potentially includes double transplantation, since the liver is the source of the mutant protein.2 The most extensive experience with liver transplantation for hereditary amyloidosis is in the transthyretin-related familial amyloidotic polyneuropathy mutant form, where the procedure virtually eliminates variant transthyretin from the plasma, and reduces amyloid deposits.3 However, the patient’s otherwise normal liver function (except for apolipoprotein AII synthesis) and the slow progression of nephropathy inclined us to avoid the inherent risks of liver transplantation; our patient is currently on a waiting list for renal transplantation only. This decision has been supported by recent reports, where patients who received a renal transplant alone have no evidence of amyloidosis relapse at long-term follow-up.4,5

DNA analysis is mandatory in patients with systemic hereditary amyloidosis, since new mutations are constantly being discovered, as here. Management of this condition by double liver-renal transplantation may not be appropriate, because of the absence of relapse in renal allografts, and the significant risks related to liver transplantation.

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