Remission of Nephrotic Syndrome Related to AA Amyloidosis after Hepatic Adenomectomy

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Dear Sir,

Systemic AA amyloidosis is a rare complication of hepatic tumour which can be either malignant or benign [1]. In such cases, renal amyloidosis usually results in the nephrotic syndrome. Only very few case reports have been published on its regression after removal of the tumours [1, 2]. In addition, it has been established that long-term oestrogen therapy can induce hepatic tumours. However, in such cases, the link between amyloidosis and oestrogen therapy has never been quoted. We report a case of nephrotic syndrome due to AA amyloidosis associated with a hepatocellular adenoma induced by oestrogen, which was cured by removal of the tumour.

A 28-year-old female who had taken the combined oral contraceptive pill since 11 years was admitted on August 1987 for abdominal pain. There was no history of hepatic disease or drug addiction. A large hepatic tumour was discovered. Clinical biochemistry indicated mild hepatic cytolysis and three-fold increase in alkaline phosphatase levels. In addition, ++ proteinuria was detected. Microscopic examination of the urine sediment was normal. At laparotomy a large tumour weighing 1,200 g and infiltrating segments VI and VII of the liver were discovered. Macroscopic examination of the other intra-abdominal organs was normal. Histology demonstrated a benign adenoma. AA amyloid deposits were discovered in the walls of the vessels surrounding the hepatic adenoma (fig. 1). Ten days postoperatively, whilst the patient had left the surgical ward, oedema developed. Over the following month, total

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Fig. 1. Hepatic specimen: Congo red staining showing the presence of amyloid deposits in hepatic vessels surrounded by inflammatory cells, at the edge of the adenoma (magnification $\times 150$).

Fig. 2. Renal biopsy: Immunoperoxidase technique showing labelling of amorphous amyloid deposits in the intercapillary space of glomeruli using antisera directed against A amyloid protein (magnification $\times 150$). Negative staining was obtained using anti-kappa, anti-lambda light chains and anti κ/λ microglobulin antisera.

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Table 1. Characteristics of the nephrotic syndrome following removal of the hepatic adenoma
body mass increased by 13 kg with development of the nephrotic syndrome. Total urinary protein was 5-10 g/24 h, serum albumin was 15 g/l and serum cholesterol 7.69 mmol/l. Serum C-reactive protein concentration was 25 mg/l. A renal biopsy was performed which revealed diffuse AA amyloid deposits within glomeruli and vessel walls (fig. 2). The patient was put on a low-salt high-protein diet and received albumin infusions and diuretics. A year after, there was complete resolution of the nephrotic syndrome with no evidence of recurrence at 3 years. The patient declined iterative renal biopsy.

This case report demonstrates the disappearance of a nephrotic syndrome due to AA amyloidosis after removal of a non-malignant tumour of the liver (table 1) resulting from long-term combined oral contraceptive pill administration. The relationship between oestrogen therapy taken for more than 5 years and the development of hepatic adenoma is well established, whereas a longer exposure to the drug is required to induce hepatocellular carcinoma [3]. At the time of hepatic surgery only mild proteinuria was present. It seems that the stress of surgery precipitated the development of the nephrotic syndrome, although the two events may have been coincidental. The hepatic adenoma is likely to be the cause of amyloidosis. Serum AA amyloid levels were not measured, nevertheless the levels of acute phase reactant proteins such as C-reactive protein, fibrinogen and haptoglobin were increased at the time the tumour was discovered. They returned to normal levels in the months following surgery. Serum amyloid A levels have been shown to parallel those of C-reactive protein [4].

The mechanisms by which hepatic tumours cause amyloidosis is not fully understood. Whether the tumoral cells release excess of A amyloid proteins and growth factors that stimulate normal hepatic cell secretion is not known. Proteolysis of AA amyloid protein may be reduced by an inhibitory factor present in the serum, such as the factor described in patients with familial Mediterranean fever and other AA amyloidosis related to chronic inflammation [5].

To conclude, serum amyloid A protein may be a putative link between hepatocellular adenoma and renal amyloidosis. When present, a nephrotic syndrome can disappear after the removal of the tumour. The risk of developing amyloidosis is a factor that has to be taken into account when considering hepatectomy for liver adenoma.

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