FAMILIAL NEPHROPATHIC AMYLOIDOSIS ASSOCIATED WITH INDOMETHACIN RESPONSIVE FEVER

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Introduction

We describe a patient with familial nephropathic amyloidosis who also has recurrent fever and polyserositis which is responsive to indomethacin. The association within families of periodic fever and nephropathic amyloid is most commonly seen in familial Mediterranean fever, but in that condition the mode of inheritance and the amyloid fibrils are different from the family described here. The family described seems to be different from other forms of familial nephropathic amyloidosis.

Case history

A 45 year old woman presented with chronic renal failure due to renal amyloid. She has a family history of autosomal dominant nephropathic amyloidosis, affecting six members of two successive generations, all descended from the patient’s apparently unaffected maternal grandmother. The family has been described in detail elsewhere [1]. Continuous ambulatory peritoneal dialysis (CAPD) was started in March 1982. During admission for training for CAPD she was noted to have recurrent episodes of fever, usually symptomless, although on one occasion there was pleuritic pain. No infection or pulmonary embolus could be demonstrated. The fevers settled after six weeks. No treatment was given. In the next nine months she had three episodes of fever and malaise each of which settled spontaneously after two weeks. There were also four episodes of apparent sterile peritonitis with abdominal pain and fever, and white cells in the peritoneal dialysate, but no organisms were grown from peritoneal fluid. In February 1983 she developed candida peritonitis for which the peritoneal catheter had to be removed and amphotericin and ketoconazole were given. There was quick recovery with no subsequent evidence of peritoneal infection.

During five subsequent months of haemodialysis she had recurrent fever (Figure 1) with intermittent pleuritic pain and flitting pleural rubs. Chest X-rays
showed small transient pleural effusions but no other lesions. Perfusion lung scan was normal. Cultures of blood, urine, and throat swabs were negative for tuberculosis, bacteria, and fungi. Viral antibody screening was negative. Rheumatoid factor and autoantibody screens were negative. Ultrasound and gallium scan of the abdomen showed no evidence of intra-abdominal abscess. Antibiotics had no effect upon the fever. She then developed pericardial pain and friction with fever, despite excellent dialysis. Pericardial ultrasound was normal. The pericardial pain was treated with indomethacin, and immediately the fever resolved for the first time for six months. After two weeks indomethacin was stopped and fever returned. On restarting indomethacin the fever subsided, but when the dose was reduced from 50mg tds to 25mg tds the fever returned, settling again with increased dosage. Indomethacin was eventually withdrawn after five months. The patient was subsequently restarted on CAPD without recurrence of fever.

The amyloid deposits in this patient showed permanganate sensitive congophilia. This is suggestive of amyloid A, as seen in reactive systemic amyloidosis and familial Mediterranean fever, but the amyloid in this family is distinct from those conditions, as there is no staining with anti-amyloid A or anti-prealbumin sera [1].

Discussion

This patient has autosomal dominant familial nephropathic amyloidosis associated with recurrent fever and polyserositis. We found no evidence of an infective cause for this, and the response to indomethacin suggests a non-infective inflammatory mechanism.

Familial nephropathic amyloidosis is rare. Ostertag [2] described a syndrome of familial nephropathic non-nephropathic amyloidosis with autosomal dominant inheritance which leads to renal failure. There was also massive hepatosplenomegaly. A second family [3] was considered to have the same syndrome although in this family there was only minimal hepatic involvement confined to vessel walls. Our patient is a member of the third family assigned to familial amyloidosis of Ostertag [2] although in this family there is also little hepatic or splenic involvement and histologically hepatic involvement is limited to small
deposits in middle sized arterioles. We propose that this syndrome is distinct from that described by Ostertag. The condition presents with severe nephropathic amyloidosis, there is polyserositis and indomethacin responsive fever, and relatively little early clinical involvement of other organs.

There are other associations of familial nephropathic amyloidosis and periodic fever. In familial Mediterranean fever nephropathic amyloidosis frequently develops, but inheritance is autosomal recessive, and the amyloid fibrils are different from those seen in this family [1]. In the Muckle-Wells syndrome [4] autosomal dominant familial nephropathic amyloidosis is associated with nerve deafness and recurrent urticaria and fever. There is no record of deafness or urticaria in our family. Of six patients recently described with a syndrome of periodic fever and hyperimmunoglobulinaemia D [5] three had a positive family history, and in one family two members in successive generations developed renal amyloidosis. The case of Fox and Morrelli [6] probably had a similar condition. As in familial Mediterranean fever, fever of this condition is responsive to colchicine. Nilsson and Fodorus also described an autosomal dominant condition in which renal amyloid occurred in association with recurrent abdominal pain and fever [7].

In familial Mediterranean fever treatment with colchicine appears to prevent recurrent fever and to slow or stop the deposition of amyloid [8,9]. It is interesting to speculate, should apparently unaffected members of this family develop recurrent fever, whether indomethacin may be of value not only in treating the fever but in preventing amyloidosis. It might also be worthwhile to study the effects of indomethacin or other prostaglandin synthetase inhibitors on fever and amyloidosis in familial Mediterranean fever or on periodic fever associated with hyperimmunoglobulinaemia D.

References

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