Teaching Point
(Section Editor: Alain Meyrier)

A 16-year-old nephrotic patient with chest pain

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Keywords: nephrotic syndrome; myocardial infarction; arterial thrombosis

Case

A 10-year-old boy who had been born in Pakistan, but had lived in England since the age of 9, initially presented to a paediatric hospital with nephrotic syndrome. He responded promptly to corticosteroids and was followed in outpatients.

For 4 years he had several relapses of his nephrotic syndrome, which were successfully treated with courses of corticosteroids. After he had been abroad without medical review for 1 year, he returned aged 15 with nephrotic range proteinuria that persisted despite taking corticosteroids and levamisole.

At the age of 16 his care was transferred to an adult nephrology unit where he was assessed in the outpatient clinic. He appeared cushingoid and the blood pressure was 120/70 mmHg. The serum creatinine was 68 mmol/l, the serum cholesterol 15.7 mmol/l, the serum albumin 28 g/l and the urinary protein excretion 5.8 g/day.

Only a few days after his first assessment at the adult nephrology unit he was admitted to hospital with gripping central chest pain. There was no history of smoking, diabetes mellitus or premature cardiac disease in his family. Physical examination was unremarkable. Figure 1 shows his electrocardiogram. The admitting doctor suspected pericarditis as a cause of his chest pain.

Later review of his laboratory results (creatine kinase 1067 IU/l, aspartate aminotransferase 105 IU/l) accompanied by continued chest pain prompted urgent coronary angiography (Figure 2). This showed partial thrombotic occlusion of the left anterior descending artery (LAD). He was treated with aspirin, thrombolysis and heparin. One day later, repeat coronary angiography showed persistent occlusion of the LAD. Thrombectomy and stent insertion were performed (Figure 3).

The patient made a good recovery and was discharged taking aspirin, clopidogrel, atorvastatin, metoprolol and warfarin.

A kidney biopsy several months later confirmed minimal change nephropathy (Figure 4). He received a 12 week course of cyclophosphamide and has remained in remission since (3 years). His serum cholesterol normalized following remission of the nephrotic syndrome. A familial cause for hypercholesterolaemia was ruled out after testing his parents and two siblings.

Discussion

Arterial thrombosis is an uncommon but serious complication of nephrotic syndrome that may lead to death, loss of limb or cerebral infarction [1]. The incidence of arterial thrombosis in nephrotic syndrome is described as 2.5% in children and 7% in adults [1]. The incidence of arterial and venous thrombosis combined is estimated at 35% [2]. The case described here is similar to cases of myocardial infarction published by others in that patients tend to be young and there may be some delay before initiation of definitive treatment [3,4].

Nephrotic syndrome is associated with altered haemostasis, which appears to predispose to thrombosis [2]. Hypercholesterolaemia and endothelial dysfunction may contribute to the risk of arterial thrombosis [5].

This case highlights the clinical problem of how to manage the thrombotic risk in long-term nephrotic patients. There are no randomized controlled trials to provide guidance for clinicians [2].

Acute arterial thrombosis has been treated with conventional therapy for arterial thrombosis (thrombolysis, stenting, anticoagulation and antiplatelet therapy) [3,4].
The optimal form of prophylaxis against thrombosis is unclear. Presuming that the risk of thrombosis is substantially reduced once nephrotic syndrome is in remission, the aim of any treatment should be early and sustained remission. While prolonged therapy with corticosteroids is effective in most patients with minimal change disease, cyclophosphamide is used to achieve sustained remission in frequently relapsing or steroid-dependent patients [6]. Serious adverse effects of cyclophosphamide (such as infertility) are a concern, but such treatment may be justified in view of an increased risk of thrombosis and the adverse effects of corticosteroid therapy [6].

Non-immunosuppressive treatment can be useful, particularly in patients with persistent nephrotic syndrome without remission. Modification of vascular risk factors (smoking, hypertension) is probably beneficial. Angiotensin-converting enzyme inhibitors are given to reduce proteinuria while their effect on the development of arterial thrombosis in nephrotic patients is unknown. Prophylactic anticoagulation with coumarine derivates is widely recommended and accepted to avoid thrombo-embolic events in patients with severe nephrotic syndrome, but prospective

Fig. 1. Electrocardiogram showing ST-segment elevation in leads V1-3 with reciprocal ST-segment depression in leads II, III and aVF.

Fig. 2. Left coronary angiogram showing a filling defect in the left main coronary artery (LAD).

Fig. 3. Left coronary appearance following LAD thrombectomy and stenting.
controlled trials are lacking [2]. Statins benefit long-term nephrotic patients beyond their lipid-lowering effect by stabilizing vascular endothelium [7]. While endothelial dysfunction was demonstrated in a group of nephrotic but not in healthy individuals [8], endothelial function improved with statin therapy and deteriorated again after its withdrawal in a group of nephrotic patients [7].

Teaching points

(i) Chest pain in patients with severe nephrotic syndrome may be due to myocardial infarction, even in those less than 20 years of age. It is essential to recognize this in order to diagnose and treat myocardial infarction rapidly.

(ii) Early and sustained remission of the nephrotic syndrome minimizes the risk of arterial or venous thrombosis.

(iii) Therapeutic anticoagulation should be considered early in nephrotic patients with severe hypoalbuminaemia.

(iv) Lipid-lowering drugs should be given to patients with persistent nephrotic syndrome without remission.

Acknowledgements

Dr M. Ferring would like to thank Mr A. Wressel, Medical Photographer, and Dr G. Langman, Consultant in Histopathology, at Birmingham Heartlands Hospital for their valuable help with the preparation of the images.

Conflict of interest statement. None declared.

References


Received for publication: 30.11.04
Accepted in revised form: 19.4.05