

Renal failure caused by undiagnosed atheroembolic disease

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Date accepted for publication 1 December 2003

Abstract

Atheroembolic disease remains a potentially under-diagnosed cause of renal failure, particularly in the elderly. As well as causing an acute deterioration in renal function following invasive procedures or the use of anticoagulants and thrombolytics, a chronic form with gradual decline in renal function has also been described, and can occur without a clear precipitating event. We describe a case of unexplained renal failure where the potential diagnosis of renal atheroembolic disease was stumbled on retrospectively, as is often the case.

Keywords

Cholesterol crystals; atheroembolic; renal; cholesterol cleft.

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Introduction

Cholesterol crystal embolisation (also known as renal atheroembolic disease) has become an important diagnosis in the older population. However, the diagnosis is elusive and often made retrospectively, such that it has been termed the Cinderella of nephrology. Although treatment is as yet limited, it remains an important condition to recognise in order to prevent patients receiving inappropriate treatment, particularly as it can mimic conditions such as vasculitis. The following case illustrates how the diagnosis is often stumbled upon retrospectively, hence the need to maintain a high index of clinical suspicion in the older population.

Case

A 67-year-old Caucasian man presented to his general practitioner with a few weeks history of lethargy, pruritis and progressive ankle oedema. Blood tests revealed advanced renal failure with a serum creatinine of 2087 $\mu\text{mol/l}$ (normal range (NR) 60–110 $\mu\text{mol/l}$).

Detailed questioning revealed symptoms of prostatic outflow obstruction. He had no significant past medical history but was noted to be a lifelong smoker.

He was referred to our unit and on admission was found to be hypertensive (160/70 mmHg). Excoriation marks were noted together with ankle oedema. He was also noted to have bilateral carotid and femoral bruits, but no renal bruits. Abdominal examination revealed the presence of a palpable bladder and catheterisation yielded a residual volume of urine of 700 ml.

Investigations revealed haemoglobin of 6.9 g/dl (NR 12–16 g/dl), white cell count $16.9 \times 10^9/\text{l}$ (NR $4\text{--}11 \times 10^9/\text{l}$) (neutrophils 14.7, eosinophils 0.8), platelet count $277 \times 10^9/\text{l}$ (NR $150\text{--}450 \times 10^9$), urea 65.5 mmol/l and creatinine 2324 $\mu\text{mol/l}$. C reactive protein was 32 mg/l, C3 0.82 g/l, C4 0.22 g/l.

Twenty-four hour urine collection of 1490 ml gave a urinary protein excretion of 10.46 g/24 h.

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An ultrasound scan showed symmetrical kidneys of 10.5 cm in length with bilateral hydronephrosis and ureters dilated down to the bladder whose wall was grossly thickened.

A diagnosis of end stage renal failure secondary to obstructive nephropathy from prostatic enlargement was made and he underwent haemodialysis. Subsequently bilateral nephrostomies were inserted and despite an output of 2 l per day and radiological resolution of his hydronephrosis, he failed to recover sufficient renal function to become dialysis independent.

At this point a CT scan of the abdomen was performed. This revealed small kidneys with reduced cortical thickness bilaterally. Bilateral nephrostomy tube drains were *in situ*. There was no retroperitoneal fibrosis or significant lymphadenopathy. No comment was made regarding the presence of any extensive atheroma within the aorta. Given these findings, and despite the heavy proteinuria, a renal biopsy was not performed as it was felt unlikely to reveal any reversible pathology, particularly as the patient was already dialysis dependent.

Later in the course of his management he underwent a cystoscopy and transurethral resection of his enlarged prostate gland. The specimen consisted of 35.0 g of prostatic chippings, all of which was submitted for histological examination. The sections uncovered an unexpected diagnosis with focal infarction and an associated foam cell and foreign body giant cell reaction to cholesterol clefts (Fig. 1), in one of the fragments of prostatic tissue, in only one of the 12 sections.

Discussion

The presence of cholesterol embolisation within the prostatic resection potentially uncovers a dual pathology for this man's renal failure and may explain why it failed to recover following relief of the obstructive component.

Cholesterol embolisation is a result of the lodging of cholesterol crystals in small vessels following rupture of atheromatous plaques within the abdominal aorta. Flory first described this clinical entity in 1945^[1]. Although a multi-system disorder, the proximity

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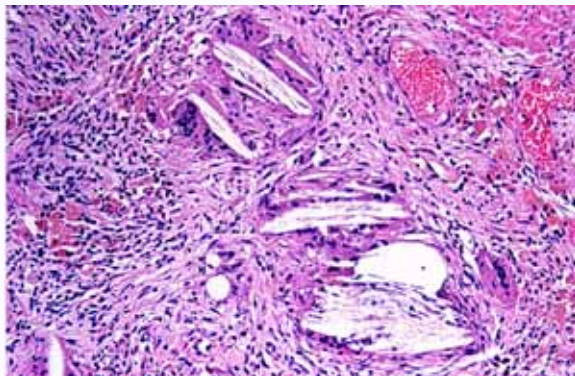


Fig. 1. Haematoxylin and eosin stained section of prostatic tissue showing the presence of cholesterol clefts.

of the renal arteries to the site of atheromatous aortic lesions means renal vessels are commonly affected. In one post-mortem study, renal involvement was seen in 50% of cases^[2]. Patients at risk are the older male Caucasian population, particularly those with diabetes mellitus, hypertension, hypercholesterolaemia, a history of smoking and/or a history of vascular disease elsewhere^[3,4]. Studies of renal biopsies suggest an incidence of 1%^[5,6], rising to 4% in elderly populations^[7]. The patchy nature of the disease means these studies may underestimate the true incidence. Although described following the use of anticoagulants, thrombolytics and invasive vascular procedures^[2,8-12], it can occur spontaneously as in the above case, making the diagnosis even more elusive. The clinical course is variable. Classically, it has been described as a sudden and dramatic decline in renal function following a precipitating event. However, a chronic, more insidious course with a gradual decline in renal function over months is also recognised^[7,13]. The latter form can mimic a number of other causes of progressive renal damage. Cutaneous manifestations such as cyanotic toes and livedo reticularis are seen in systemic disease

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in approximately 35% of cases^[14], and are hence not present in all cases. Furthermore, they can mimic skin changes seen in vasculitis and a necrotising glomerulonephritis has also been described^[15], enhancing the similarity between these two conditions. A clue to a second diagnosis in the case illustrated was the presence of nephrotic range proteinuria, which is being increasingly reported in renal atheroembolic disease^[16], and is not a feature of obstructive nephropathy. Given the level of proteinuria, a renal biopsy was considered. However, it was felt that given the patient was dialysis dependent and that the CT scan suggested small kidneys with a reduced cortical thickness, a biopsy was unlikely to uncover any reversible pathology. Other laboratory findings, which may alert the physician to atheroembolic disease, include eosinophilia, thrombocytopaenia, a raised erythrocyte sedimentation rate and hypocomplementaemia. As demonstrated by the above case, these findings are not universal and lack specificity. Hypercholesterolaemia is a known risk factor for the development of atherosclerosis, however raised cholesterol levels is not a consistent finding.

Confirmation of the diagnosis requires demonstration of the characteristic cholesterol clefts in biopsy specimens from target organs. The clefts represent spaces occupied by cholesterol crystals, which are normally dissolved during routine histological preparation. However the patchy nature of the condition means the diagnosis can be missed^[1,6].

Histological confirmation of a diagnosis of atheroembolic disease in a renal biopsy sample was not made in this case, but inferred from the findings in the prostatic biopsy. It has been suggested that the presence of a specific triad of clinical features can allow the diagnosis to be made without histological confirmation in a renal biopsy sample^[3]. This triad includes a precipitating event, subacute renal failure and peripheral crystal embolisation. Although no specific precipitating event was noted, the presence of other risk factors, namely male gender, age >60 years, Caucasian race, presence of hypertension and history of smoking, together with the prostatic biopsy findings, is felt to make the diagnosis highly likely in the case described.

Although no proven treatments are available, it is an important condition to recognise in order to prevent patients receiving unnecessary therapy. As mentioned, vasculitis is one of the main differential diagnoses, and immunosuppression is not without significant risk in

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the age group concerned. Anticoagulants should be avoided, and this has implications on dialysis modality. Haemodialysis requires the use of anticoagulation, and it has been suggested that peritoneal dialysis, by avoiding this, may improve chances of renal recovery^[17]. There are a few case reports of improvement following the use of statins^[18,19]. The role of aggressive lipid lowering therapy needs to be determined, while the role of steroids remains controversial.

Atheroembolic disease is being recognised as a cause of renal impairment with increasing frequency^[3]. It continues, however, to be a challenging diagnosis to recognise. In order to meet this challenge, physicians and pathologists alike will have to maintain a high index of suspicion in elderly patients presenting with renal impairment of unclear origin.

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