Renal failure due to cholesterol embolisation

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Summary

Five cases of cholesterol crystal embolisation resulting in impaired renal function are reported and their investigation and management discussed.

Keywords: renal failure, cholesterol, embolisation

Introduction

The syndrome of cholesterol crystal embolisation was first described in 1862 with further descriptions in the 1940s.^{2,3} It is thought to be a relatively rare condition, although subclinical cases may be undiagnosed. Two studies have demonstrated a high incidence of cholesterol embolisation following angiography and aortic surgery.^{4,5}

In this report five cases of cholesterol crystal embolisation resulting in impaired renal function are presented, highlighting this condition as a cause of renal impairment. The investigation and management of these patients is discussed. In particular the avoidance of vascular trauma and anticoagulation are stressed.

Case reports

Case 1

A 72-year-old man with a history of controlled hypertension and angina presented with a five day history of fever, malaise, anorexia and claudication. On further questioning he admitted to a four-year history of intermittent digital ischaemia which would resolve spontaneously. On examination peripheral pulses were intact but bilateral carotid and femoral bruits were heard. There was discolouration of his toes. Investigations revealed renal impairment with normochromic normocytic anaemia and a raised plasma viscosity of 1.99. Echocardiography demonstrated mild left ventricular hypertrophy only. Anticoagulation was commenced, but within 10 days there was marked clinical deterioration with extension of digital ischaemia and deterioration of renal function, (urea 31 mmol/l and creatinine 574 μ mol/l). Anticoagulation was withdrawn. An abdominal ultrasound revealed an atheromatous aorta and 9 cm kidneys. A renal biopsy confirmed cholesterol crystal embolisation. His symptoms improved and he was discharged, but died four days later of an acute myocardial infarction.

Case 2

A 69-year-old woman with a five-year history of hypertension, eosinophilia, raised plasma

viscosity, renal impairment (urea 20 mmol/l, creatinine 305 μ mol/l) and abnormal liver enzymes underwent angiography. Subsequently the patient collapsed and became pyrexial. She complained of abdominal pain and developed blue discolouration of the legs but all peripheral pulses were intact. Urinalysis revealed proteinuria and haematuria and there was a normochromic normocytic anaemia with polychromasia and rouleaux formation. Her urea and creatinine rose to 31 mmol/l and 500 μ mol/l, respectively. Urgent laparotomy revealed an ischaemic but viable bowel. No bowel resection was performed. She was commenced on intravenous heparin pending histological examination of an intraoperative renal biopsy. Subsequently she developed profuse melaena and despite withdrawal of heparin, blood transfusion, and inotropic support the patient died. Renal histology confirmed cholesterol embolisation (figure). Post-mortem examination revealed a dilated aorta from the arch to a level just below the renal arteries with severe atheroma. There was an associated dissection with almost total occlusion of the right renal artery. There was also evidence of coronary artery disease and cholesterol crystal embolisation to the spleen.

Figure Photomicrograph of a small muscular artery in the kidney showing cholesterol embolisation (case 2). The section fortuitously passes through a vascular bifurcation, the usual site of imaction of emboli. One limb of the bifurcation is patent; the other is largely occluded by cholesterol crystals, represented after histological processing by needle-shaped clefts. H&E $\times$ 125

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Case 3

A 62-year-old man was admitted for a routine arteriogram to investigate renal impairment (urea 12 mmol/l, creatinine 269 μ mol/l), hypertension and symptoms of claudication. There was a long history of poorly controlled hypertension, transient ischaemic attacks on two occasions and a previous repair of a ruptured abdominal aneurysm. The blood pressure was 200/100 mmHg and fundoscopy revealed grade 2 hypertensive retinopathy. All peripheral pulses were present, but there were bilateral carotid, femoral and renal artery bruits. The blood film revealed polychromasia and rouleaux formation and plasma viscosity was 1.96. Cholesterol and triglyceride were 7.9 mmol/l and 2.3 mmol/l, respectively. An abdominal ultrasound showed a small left kidney and a 4.3 cm suprarenal aortic aneurysm. The arteriogram revealed widespread atheroma, right renal artery stenosis and the previously discovered aneurysm. Renal biopsy of the left kidney revealed acute tubular necrosis and cholesterol embolisation. There has been no further deterioration in the patient condition and no further intervention is planned.

Case 4

A 65-year-old woman with a history of rheumatic heart disease and angina underwent cardiac catheterisation. The patient was readmitted the following week with pleuritic chest pain and pyrexia. Anticoagulation with heparin and warfarin was started for a presumed pulmonary embolus although the ventilation/perfusion scans were subsequently normal and warfarin was withdrawn. The patient then developed acute renal failure and, despite full supportive treatment, died. At post-mortem, examination of the kidneys revealed hypertensive nephropathy, acute tubular necrosis and cholesterol crystal embolisation. There was also evidence of a recent acute myocardial infarction.

Case 5

A 65-year-old woman known to suffer from noninsulin-dependent diabetes, hypertension, angina, and mild aortic regurgitation was admitted for a routine cardiac catheterisation. On examination blood pressure was 230/90 mmHg, all peripheral pulses were normal and she had signs of mild aortic regurgitation. Investigations were unremarkable except for urea 7 mmol/l, creatinine 149 μ mol/l, triglyceride 2.94 mmol/l, and cholesterol 6.58 mmol/l. Cardiac catheterisation revealed severe stenosis of right coronary and circumflex arteries. Following the cardiac catheter she developed a 'vasculitic' rash and her renal function deteriorated with a urea of 20 mmol/l and creatinine 226 μ mol/l. The diagnosis of cholesterol embolisation was suspected, however, renal biopsy was not performed when subsequent investigations revealed a single functioning kidney. Her renal function spontaneously recovered over the next three months without intervention.

Discussion

The syndrome of cholesterol crystal embolisation usually affects elderly males with a history of hypertension and arterial disease (see box). Smoking is a major risk factor for cholesterol crystal embolisation because it accelerates atherogenesis and alters platelet and endothelial function.^{6,7} Presentation is non-specific with multisystemic symptoms and may masquerade as polyarteritis nodosa, systemic lupus erythematosus, Wegner's syndrome, and Churg-Strauss syndrome (see boxes).^{8,9} The course of the disease may be episodic (following angiography, vascular surgery, anticoagulation or thrombolysis), spontaneous, gradual or a combination.

Laboratory findings are also non-specific and include raised plasma viscosity, reduced complement, leucocytosis, eosinophilia, normochromic normocytic anaemia, proteinuria, leucocyturia, and haematuria. The characteristic histological features are biconvex, needle-shaped clefts, (cholesterol crystals are dissolved in routine fixation) within and occluding small arteries, often with an associated cellular response (figure). Other features include arteritis and glomerulonephritis.¹⁰⁻¹³ The characteristic histological lesions can be missed because of the patchy nature, although diagnostic yield may be increased by use of skin and/or muscle biopsies,¹⁴ and by focusing on arterial branching. The pathophysiology is poorly understood, but embolisation occurs when cholesterol plaques become denuded of their epithelial lining or protective overlying thrombus. These emboli go on to cause partial or total occlusion of vasculature with its associated inflammatory/immunological reactions and ischemic vasoconstriction. Since the abdominal aorta is the most common location of atheroma, the kidneys, visceral organs, and skin of the lower extremities are more fre-

Cholesterol crystal embolisation

Risk groups

- elderly males
- history of hypertension and arterial disease
- smokers

Cholesterol crystal embolisation

- skin features
- retinal embolisation
- renal failure (50%)
- pancreatitis

Cholesterol crystal embolisation

Skin features

- livedo reticularis of lower body
- focal digital ischaemia (purple toe syndrome)
- nodules, cyanosis, purpura, ulceration, gangrene, petechiae

quently affected. Other factors such as episodes of haemodynamic instability, dissection of an artery, or the use of nephrotoxic contrast media may be important in aetiology of renal failure in some patients.

The reported mortality rate is high,^{8,15,16} although probably this represents an overestimate as subclinical cases may go unrecognised. The cause of death is usually cardiac, renal, or multifactorial. Previous studies have suggested that the presence of thoracic aneurysms or the use of corticosteroids (six and nine patients, respectively, out of 221) is associated with 100% mortality.⁸ There is also evidence to suggest that anticoagulation tends to precede life-threatening systemic embolisation.¹⁶⁻¹⁸ In one study 11 patients out of 30 died following anticoagulation for cholesterol crystal embolisation.⁸

All the five patients reported above had significant risk factors for atherosclerosis with symptoms of significant arterial disease. Cholesterol crystal embolisation was pre-

cipitated or aggravated by either anticoagulation and/or vascular trauma. The two surviving patients had not received anticoagulation.

In summary, the diagnosis of cholesterol crystal embolisation should be suspected in the presence of unexplained non-specific symptoms in patients with known risk factors for atherosclerosis, especially if related to anticoagulation or following vascular trauma. Histological confirmation is improved by biopsies of skin/muscle, especially if there is associated livedo reticularis. The mainstay of management is supportive, to control blood pressure, dialysis if required and the avoidance of corticosteroids and invasive procedures. Anticoagulation should be avoided if at all possible. An awareness of the potential for cholesterol crystal embolisation is essential if the disease is to be prevented and where possible non-invasive techniques should be used in place of angiography, especially in patients with diffuse atherosclerosis.

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