Systemic cholesterol crystal embolisation with pulmonary involvement: a fatal combination after coronary angiography

T J Walton, N J Samani, R Andrews

Cholesterol crystal embolisation (CCE) is a poorly recognised multisystem disorder resulting from the exposure of ulcerated atherosclerotic plaque to circulating blood. CCE results in a clinical syndrome which can closely resemble vasculitis, commonly involving the kidneys and peripheries. The lungs, however, are usually spared. The authors report a case of fatal CCE with significant lung involvement.

CASE REPORT

A 64 year old man presented with a history of peripheral cyanosis, dyspnoea, and haemoptysis. Ten months previously he suffered a myocardial infarction, followed by exercise induced chest pain. Coronary angiography was performed six weeks before admission, at which time renal function was normal. Three weeks after angiography the patient developed painful blue toes (fig 11) and episodic dyspnoea. An appointment with a vascular surgeon was arranged. Two days before admission he developed haemoptysis. On admission he was pyrexial, oxygen saturation was 96% on air, and auscultation revealed bibasal inspiratory crackles. Although cyanosis was present on the toes of both feet, all peripheral pulses were present.

Haematological analysis revealed a normochromic normocytic anaemia, with a normal leucocyte and platelet count. The erythrocyte sedimentation rate was raised at 102 mm/hour. Serum urea concentration was 15.4 mmol/l, and serum creatinine was 234 µmol/l. Levels of serum immunoglobulins and glomerular basement membrane antibody were normal, and an autoantibody screen was negative. Urine, blood, and sputum culture revealed no growth, and there were no acid-fast bacilli. A chest radiograph showed bilateral pleural effusions, perihilar alveolar shadowing, and increased vascular markings. An echocardiogram revealed mild mitral regurgitation and mildly impaired left ventricular function. Intravenous frusemide (furosemide), cefuroxime, and heparin were started. After review by a vascular surgeon, peripheral arteriography was performed, revealing atheroma in the aorta and iliofemoral segments, but there was no distal embolus or stenosis. Serial chest radiography demonstrated persistent bilateral alveolar shadowing, which was unchanged by diuretics. Purpuric spots appeared on both legs. His renal function declined, the anaemia worsened, and an eosinophilia (0.59–0.89 × 10^9/l) developed. At this point a clinical diagnosis of cholesterol embolism was made. The patient failed to improve and died 33 days after admission. A postmortem examination showed ulcerated atheromatous plaque in the thoracic, abdominal, and common iliac arteries. Sections from the spleen and both kidneys revealed multiple atheromatous emboli (fig 2). A solid pulmonary oedema was noted, but there was no evidence of embolus or obvious macroscopic infarction. Multiple sections of the lung failed to show the presence of cholesterol emboli in the branches of the pulmonary or the bronchial arterial trees.
**DISCUSSION**

CCE may occur spontaneously but is more commonly precipitated by invasive vascular procedures.\(^1\) The incidence of patients presenting with features of CCE after cardiac catheterisation is reported to be less than 2%.\(^2\) In patients in whom symptoms are present, there may be a temporal delay of up to eight weeks. Abdominal viscera, kidneys, and lower limbs are commonly involved, often associated with a systemic inflammatory response manifest by fever, anaemia, and high erythrocyte sedimentation rate.\(^3\) Eosinophilia is also described. Gastrointestinal involvement presents with abdominal pain and haemorrhage, while multiple renal atheroemboli cause a protracted, stepwise deterioration in renal function, often associated with accelerated hypertension.\(^4\) Livedo reticularis, “blue toes,” and purpura reflect cutaneous small vessel involvement. The definitive diagnosis of CCE requires the demonstration of bioconvex needle shaped cholesterol clefts in the lumen of blood vessels, a finding that may be essential in differentiating CCE from vasculitis.\(^5\) The mortality rate associated with CCE is high. Most case series report an overall mortality of between 60% and 80%.

Respiratory symptoms have been rarely reported in the context of CCE. To date, five cases of CCE with respiratory symptoms have been reported, in which all five patients died.\(^6\) Haemoptysis and dyspnoea are most commonly described. The pathogenesis of pulmonary involvement in CCE is unclear. Two theories have been proposed: either that pulmonary features result from the direct deposition of atheroemboli in the lungs,\(^7\) or that systemic inflammation associated with CCE results in de novo production of pulmonary lesions.\(^8\) Pulmonary atheroembolism was first reported in the context of an aortocaval fistula complicating aortic aneurysm repair.\(^9\) More recently, Sabatine et al described a 69 year old man who presented with progressive dyspnoea, haemoptysis, and renal failure.\(^1\) Open lung biopsy revealed the presence of atheroemboli in both the bronchial arterial and pulmonary arterial circulatory beds. Our case represents the second to report an absence of pulmonary cholesterol crystals in patients presenting with haemoptysis and CCE. Hillion et al described a 47 year old man with haemoptysis, purpura, and renal failure.\(^2\) A high titre of circulating immune complexes was demonstrated in vivo, along with diffuse CCE at postmortem. No pulmonary atheroemboli were evident, however, and alveolar haemorrhage was attributed to immune complex deposition. Immune complexes were not demonstrated in our case, nor was there evidence of alveolar haemorrhage or infarction. A cause for the lung involvement in our case is not immediately apparent, though it is conceivable that adult respiratory distress syndrome, and possibly pulmonary oedema, may have played a part.

Cholesterol crystal embolisation is a rare but serious multisystem disorder complicating invasive arterial procedures, and one which medical staff performing such procedures should be aware of. It should be considered in any patient presenting with cutaneous features and renal failure in the period of up to eight weeks after an invasive vascular procedure. Lung involvement is uncommon but when present appears to confer an extremely poor prognosis.

**Learning points**

- Cholesterol crystal embolisation is a poorly described multisystem disorder with a high mortality.
- It can occur up to eight weeks after invasive arterial procedures.
- Common features include abdominal pain and bleeding, renal failure, and purpura.
- It should be considered in the differential diagnosis of vasculitic disorders.
- Pulmonary features, usually haemoptysis and dyspnoea, are rare, but when present are usually fatal.

**REFERENCES**