Teaching Point
(Section Editor: A. Meyrier)

Sudden onset of adult respiratory distress syndrome (ARDS) in a long standing chronic haemodialysis patient with lung calcification

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Keywords: ARDS; haemodialysis; hyperparathyroidism; lung calcification

Introduction

Patients with end-stage renal failure treated by haemodialysis have a marked increased risk for cardiovascular death. These patients have both an accelerated form of artherosclerosis with calcification in atheromatous intimal plaques and also medial calcification due to Monckeberg’s. In extreme cases soft tissue calcification can lead to calciphylaxis resulting in skin ulceration, amputation and death.

The present case describes a less frequently encountered problem due to vascular and soft tissue calcification, which presents management challenges to the renal physician.

Case

A 57-year-old Northern European Caucasoid man was admitted for an elective parathyroidectomy. He had been on a regular thrice weekly haemodialysis for 14 years due to hypertensive renal disease. Both calcium-based phosphate binders and alfacalcidol had been prescribed since 1992. Due to difficulties with phosphate control, his calcium-based binders were switched to Alucaps® between 1994 and 1998, and then again to Renagel® from July 2001 until the current admission. His intact parathyroid hormone (PTH) levels increased from 12.3 in 1994 (normal < 7) to 42.4 in 1997, to 76.7 in 2000, to 93 pmol/l on admission. At times, during episodes of iatrogenic hypercalcaemia, the PTH fell to around 30 pmol/l. From 1994 until admission for parathyroidectomy, the average serum calcium was 2.60 mmol/l (9.86 mg/dl), phosphate 1.95 mmol/l (5.85 mg/dl), and calcium phosphate product 5.16 mmol²/l² (57.7 mg²/dl²). A dual electron X-ray adsorption (DEXA) scan had shown increasing total body calcium (Table 1) and his lateral spine X-ray showed aortic calcification (Figure 1). The patient was persuaded to accept a surgical parathyroidectomy.

The operation went smoothly but post-operatively, following return to the ward, he was noted to have respiratory difficulty with marked tachypnoea, and a reduced finger probe oxygen saturation of 85%. The potassium had increased to 7.1 mmol/l with a normal ionized calcium of 1.1 mmol/l. A chest X-ray (CXR) was thought to show signs of pulmonary oedema (Figure 2), and he was started on continuous positive airway pressure (+5 cmH₂O) and then commenced on haemodialysis, dialysate composition calcium 1.5 mmol/l, potassium 3 mmol/l and temperature 35°C. Ultrafiltration was attempted, but he became markedly hypotensive, systolic blood pressure fell to 70 mmHg, followed by sudden onset of atrial fibrillation at 130 min⁻¹, which spontaneously resolved following cessation of dialysis. Although the troponin I was elevated at 0.6 μg/l, the only ECG changes were of minor antero-lateral ST wave depression, during the period of atrial fibrillation. He maintained a peripheral oxygen saturation of 95% on 6 l oxygen/minute with a PaO₂ of 14.5 kPa (108 mmHg) and PaCO₂ of 4.82 kPa (36.2 mmHg). A further intermittent haemodialysis was associated with systemic hypotension, necessitating termination, and he was therefore treated by continuous haemofiltration. A cardiac ECHO showed a normal-sized left ventricular cavity, with an ejection fraction of 55% (compared to 60%, 2 years earlier). The estimated mean right atrial pressure was 5 mmHg, with a pulmonary artery systolic pressure of 21 mmHg. An isotopic lung perfusion/ventilation scan excluded major pulmonary embolus. Over the next few days his condition stabilized, continuous haemofiltration was withdrawn and he returned to regular intermittent haemodialysis.
Following recovery and discharge to home he underwent an adenosine heart stress test which did not show any areas of absent or reversible cardiac perfusion. As the CXR appearances remained he had a computerized tomographic (CT) scan of his chest (Figure 3) revealing vascular calcification with ground glass appearance due to interstitial lung calcification. Standard respiratory function tests noted a restrictive pattern with reduced carbon monoxide gas transfer (Table 2, Figure 4).

Discussion

Although this patient had been well dialyzed for 14 years in terms of small solute urea clearance, he had developed secondary hyperparathyroidism with episodes of iatrogenic hypercalcaemia and a persistently elevated calcium phosphate product. He had been in receipt of calcium based phosphate binders for approximately 5 years, aluminium for 4 years and Renagel® for the last 3.5 years. For many years he had refused to consider a parathyroidectomy, but was eventually persuaded.

Following surgery he developed respiratory distress with hypoxia, and this was initially thought to be due to pulmonary oedema, following clinical examination and review of the CXR. However, an attempt to remove

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Fig. 1. Plain lateral abdominal X-ray showing aortic calcification.

Fig. 2. Post-operative CXR showing bilateral interstitial shadowing predominantly within both middle and lower zones. The heart is enlarged with a cardiac to thoracic ratio of 14:30.

Fig. 3. High-resolution CT of chest showing fairly heavy vascular calcification. Within the lungs, there are multiple symmetrical fairly extensive cloud-like areas of ground glass opacification, within which, particularly superiorly and posteriorly there are few high density foci of calcification.

Table 1. Dual electron X-ray adsorption (DEXA) scan results. Bone mineral content (BMC), lean body mass (LBM), bone mineral density (BMD) g/cm², Lumbar spine (L1–L4)
Fluid with ultrafiltration during haemodialysis resulted in profound hypotension and sudden onset atrial fibrillation. Typically, postoperatively respiratory compromise in the dialysis patient is often associated with excess intravenous fluid administration, acute heart failure due to a peri- or intra-operative myocardial event, or lung collapse. In this case the CXR was interpreted as showing pulmonary oedema. However, the cardiac ECHO measured a normal right atrial filling pressure, with no major left ventricular dysfunction, thereby excluding an acute myocardial infarct and left ventricular failure. The cardiac ECHO measured an increased pulmonary systolic pressure, compatible with both increased lung interstitial pressure and pulmonary arteriolar and or capillary pressures (non-cardiogenic pulmonary oedema). When ultrafiltration was attempted during intermittent haemodialysis, the patient developed sudden onset of atrial fibrillation. Atrial fibrillation is the most common arrhythmia which occurs during haemodialysis in acutely unwell patients with reduced cardiac filling pressures [1]. Further, intermittent haemodialysis was again associated with hypotension, and the patient required a change in dialysis modality to continuous haemofiltration, which was tolerated without cardiovascular instability. Others have reported that intra-dialytic hypotension is more common in patients treated by intermittent than continuous modalities [2].

Vascular and soft tissue calcification in haemodialysis patients has been noted for many years [3]. Previous studies have shown that calcium is not only deposited in the pulmonary vasculature, but also in the smaller bronchi and the interstitium, with deposition within the alveolar septa, resulting in lung fibrosis [4]. The most common type of lung interstitial calcium deposition is the Whi lockite crystal pattern, (CaMg)3(PO4)2, followed by calcium pyrophosphate [5]. Some studies have suggested that lung calcification can be detected in up to 40% of haemodialysis patients [6].

Earlier reports showed that lung calcification was more common in patients with persistently higher serum calcium levels, but no relationship was observed with the duration of haemodialysis, or the serum phosphate concentration, or calcium phosphate product, bicarbonate or pH [5]. Whereas, others noted a relationship not only with hypercalcaemia, but also the prescription of calcium based phosphate binders, duration of vitamin D therapy, peak calcium phosphate product and peak phosphate concentrations [6]. In this patient the serum calcium had been elevated on occasion, and was typically at or above the upper limit of normal. In addition DEXA scanning showed a progressive increase in total body calcium, and skeletal X-rays showed abdominal aortic calcification.

Typically pulmonary symptoms are uncommon, and this patient denied pre-existing exertional dyspnoea. Similarly, CXR findings have been reported to be unusual [8]. Previous reports have suggested a close relationship between pulmonary function tests in terms of changes to vital capacity, diffusing capacity and the severity of lung calcification [5]. However, lung histopathology studies have disputed this, showing that the degree of alveolar septal fibrosis and wall thickening, rather than mere presence of calcium deposits determined the magnitude of functional changes [7].

There is a very rare condition of alveolar microlithiasis, whereby tiny 0.2–5 mm calcified concretions, form in alveolar spaces along with some interstitial fibrosis. This leads to shunting at alveolar capillary bed, and over time the lungs stiffen, become restrictive, resulting in impaired gas transfer, with secondary pulmonary hypertension. In our case the respiratory function tests showed a restrictive flow loop pattern with reduced gas transfer. Unlike alveolar microlithiasis, which is a progressive condition, this patient’s condition should stabilize provided that serum calcium and phosphate can be controlled following parathyroidectomy. Although there are reports from the paediatric haemodialysis field of cardiopulmonary calcification contributing to patient’s death, due to non-cardiogenic pulmonary oedema and respiratory infection [7]. This particularly occurred following mechanical ventilation during general anaesthesia [8].

**Teaching points**

1. Lung calcification can occur in haemodialysis patients due to both calcium deposition in the alveolar septal walls and the pulmonary vessels.
2. In the severest cases this can lead to reduction in pulmonary function, typified by a restrictive pattern with reduction in vital capacity and gas transfer.
3. Patients with lung calcification are more prone to non-cardiogenic pulmonary oedema.

Conflict of interest statement. None declared.

References

Received for publication: 25.11.05
Accepted in revised form: 11.12.05