The silver lining: pleural calcification in an end-stage renal disease patient with tertiary hyperparathyroidism

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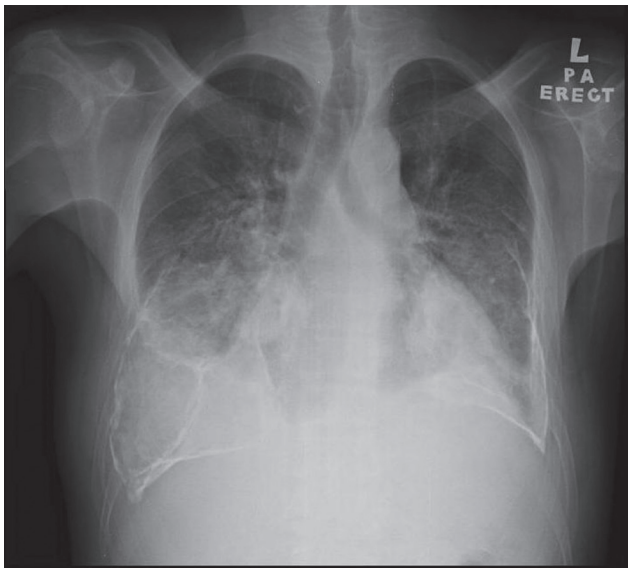
A 40-year old man with end-stage renal failure secondary to diabetic nephropathy had been on regular haemodialysis for the past seven years. He was poorly compliant with a low phosphate diet and had developed tertiary hyperparathyroidism. On August 2018 his intact parathyroid hormone was 1320pg/ml (normal range 10–65pg/ml) and ultrasonography of his neck revealed multiple enlarged parathyroid glands. He was subsequently referred for parathyroidectomy.

A chest X-ray during his preoperative assessment revealed calcifications over his pleura (Figure 1). Further history revealed that he had been having progressively worsening breathless and a non-productive cough for the previous year. He smoked 20 cigarettes daily for 20 years before stopping six years previously. There was no history of asbestos or talc exposure. Examination revealed findings consistent with bilateral pleural effusion over the bases. CECT of the thorax confirmed bilateral chronic, calcified pleural collections (Figure 2). Changes suggestive of pulmonary arterial hypertension, such as dilated heart chambers and an enlarged pulmonary trunk measuring 3.44cm were also found. Lung function tests revealed severe restrictive and obstructive airway disease. We were unable to obtain any samples of his pleural fluid due to the loculated nature of the pleural effusion.

The patient had been hospitalised seven years previously for fluid overload and bilateral pleural effusion. The diagnostic thoracocentesis at that time was traumatic, resulting in blood-stained samples which were unsuitable for biochemistry studies and cell count measurements. However, it yielded gram-negative rods, suggesting the infectious nature of the pleural effusion. Cytology was negative for malignant cells and no acid-fast bacilli were present.

Figure 1 Patient's chest X-ray demonstrating bilateral pleural calcification.



The aetiology of extraskeletal calcification can be broadly divided into either metastatic calcification, whereby calcium deposits on normal tissues, or dystrophic calcification whereby calcification occurs in previously injured tissues.[1]

Metastatic calcification is commonly associated with disorders of calcium-phosphate metabolism, including chronic renal failure, hyperparathyroidism and malignancy such as multiple myeloma.[1,2] pH plays a central role in the pathogenesis of calcification. In patients with chronic renal failure, especially those on regular dialysis, the underlying mechanism is thought to be related to the leaching of calcium and phosphate from the bones as a result of acidosis and

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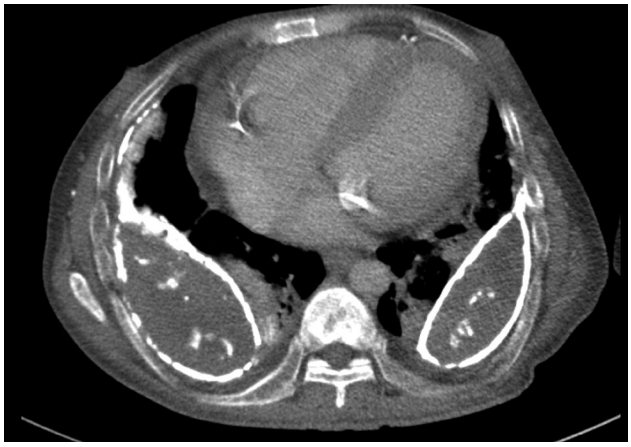
Figure 2 CT Thorax demonstrating bilateral chronic, calcified pleural collections.



secondary hyperparathyroidism.[1,2] The reduced glomerular filtration rate further promotes hyperphosphataemia.[2] The intermittent postdialytic alkalosis would then favour precipitation of calcium salts.[1] Interestingly, even though elevated calcium-phosphate products are the primary driver of the calcification process, metastatic calcification may also occur with normal or even low calcium levels, suggesting other significant contributing factors.[2] Uraemia is thought to alter protein configurations and it is speculated that sensitisation by exogenous Vitamin D makes tissues more liable to calcification.[1,3]

Metastatic calcification in chronic diseases most commonly occurs in soft tissue and blood vessels.[2,4] Even though visceral organ involvement may be rarely apparent clinically, it has been well described in literature, especially in the lungs.[3] The calcium salts in metastatic pulmonary calcification often deposit in the alveolar walls, and to a lesser extent in bronchial walls, pulmonary arteries, and veins.[5] It deposits rarely on the pleura with few cases reported in the literature. Other visceral organs that may be affected, albeit less commonly, include the stomach, heart and kidneys.[2] It is interesting to speculate that the lung may be more liable to calcification compared to other visceral organs because of its role in carbon dioxide removal, resulting in a more alkalotic local environment which promotes calcium salts precipitation.[1] Likewise, the secretion/excretion of hydrogen ions in the stomach and kidneys may also be implicated.[1] Dystrophic calcification, on the other hand, occurs when damaged tissues undergo calcification. Environmental exposure to agents such as asbestos is commonly associated with pleural plaques which may then calcify.[6] Other possible aetiologies of pleural calcification include malignancy, tuberculosis and infectious pleural disease.[1] The underlying pathophysiology of dystrophic calcification is related to cell necrosis which leads to an increase in intracellular calcium. These free calcium ions then bind to free fatty acids from degraded phospholipids, resulting in an initial nidus of calcification.[1]

As our patient had a history of an infectious process in his lungs and subsequently developed end-stage renal failure and tertiary hyperparathyroidism, one may speculate that the underlying mechanism of his pleural calcification had been initiated by dystrophic calcification and propagated by metastatic calcification.

References

1 Chan ED, Morales DV, Welsh CH et al. Calcium deposition with or without bone formation in the lung. *Am J Respir Crit Care Med* 200; 165: 1654–69.
2 Kuzela DC, Huffer WE, Conger JD. Soft tissue calcification in chronic dialysis patients. *Am J Patho*l 1977; 86: 403–24.
3 Davies MR, Hruska KA. Pathophysiological mechanisms of vascular calcification in end-stage renal disease. *Kidney Int* 2001; 60: 472–9.
4 Kraus MA, Kalra PA, Hunter J et al. The prevalence of vascular calcification in patients with end-stage renal disease on hemodialysis: a cross-sectional observational study. *Ther Adv Chronic Dis* 2015; 6: 84–96.
5 Conger JD, Hammond WS, Alfrey AC et al. Pulmonary calcification in chronic dialysis patients. Clinical and pathologic studies. *Ann Intern Med* 1975; 83: 330–6.
6 Albelda SM, Epstein DM, Gefter WB et al. Pleural thickening: its significance and relationship to asbestos dust exposure. *Am Rev Respir Dis* 1982; 126: 621–4.