
CASE REPORT

Metastatic Calcification

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ABSTRACT

A patient with metastatic calcification is presented and the contributions of plain film, computed tomography, and bone scintigraphy in the diagnosis are discussed. The patient had a long history of end-stage renal failure, and was previously receiving peritoneal dialysis and calcium supplements. His serum calcium level had been persistently elevated for several years without correction. Recently, the patient complained of generalised bone pain and dyspnoea. Chest radiography at presentation showed diffuse pulmonary calcification. He was subsequently referred for a bone scan examination to exclude osteomyelitis given his markedly elevated alkaline phosphatase levels. Widespread distribution of abnormal radiotracer uptake in multiple organs was seen at technetium 99m hydroxymethylene diphosphonate bone scan, consistent with metastatic calcification. Further biochemical and histological investigations revealed persistent hypercalcaemia and hyperparathyroid bone disease, while non-enhanced computed tomography scanning and high-resolution computed tomography scanning of the thorax showed characteristic chest wall vascular calcification and parenchymal calcification.

Key Words: Calcification, Computed tomography, Hypercalcemia, Hyperparathyroidism, Metastasis, Pathologic, Radionuclide imaging

INTRODUCTION

Metastatic calcification is defined as the deposition of calcium salts in previously normal tissue due to abnormal biochemistry with disturbances in the calcium or phosphorus metabolism.¹ Common causes of metastatic calcification include hyperparathyroidism, chronic renal disease, massive bone destruction in widespread bone metastases, and increased intestinal calcium absorption.

CASE REPORT

A 45-year-old man presented with dyspnoea and generalised bone pain at a renal clinic in Hong Kong. He had a history of chronic renal failure and had been receiving peritoneal dialysis, antihypertensive therapy and calcium supplements since March 1998. In April 2001, he had undergone cadaveric renal transplant

surgery in China. After the operation, he continued to attend the outpatient renal clinic in Hong Kong for monitoring his renal function and immunosuppressive drug therapy.

Physical examination at presentation was largely unremarkable. Total serum calcium was elevated (2.78 mmol/L; normal range, 2.05-2.55 mmol/L), as was serum alkaline phosphatase (450 IU/L; normal range, 50-120 U/L), which was bony in origin. The serum calcium and alkaline phosphatase levels had been similarly elevated when measured in July 1999. Chest radiography in May 2001 for persistent dyspnoea showed diffuse pulmonary parenchymal calcification and consolidation (Figure 1). He was treated for pneumonia in the early post-transplantation period. However, there were no clinical signs of fever at that time. Subsequent chest radiographs had shown no change in findings.

A whole body bone scan was requested to investigate the current symptom of generalised bone pain. It showed multiple sites of abnormal soft tissue uptake, including the stomach, heart, and lungs (Figure 2). There was also increased soft tissue uptake in both thighs. Intense

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Figure 1. Chest radiography shows bilateral high-density consolidation, which was unchanged on follow-up chest radiography.

accumulation of radiotracer in the native kidneys was also considered abnormal in view of the history of end stage renal failure. The transplanted kidney was present in the right iliac fossa. Single photon emission computed tomography (SPECT) of the lower thorax showed increased uptake in the left ventricular myocardium and both lungs (Figure 3). The scintigraphic findings were consistent with metastatic calcification. A non-enhanced CT scan of the thorax confirmed high-density consolidation in both lungs. Calcification was also seen in the vessels of the chest wall (Figure 4). A selected axial CT section of the thighs detected extensive vascular calcifications (Figure 5). Diffuse, patchy, 'ground-glass' opacities, high-density consolidation, and ill-defined centrilobular nodular opacities were evident with high resolution computed tomography (HRCT) of the thorax (Figure 6).

Bone and skeletal muscle biopsies were also performed and revealed hyperparathyroid bone disease and metastatic calcification, respectively. Parathyroid hormone (PTH) assay showed a markedly elevated PTH level (38.3 pmol/L; normal range, 1.1-7.7 pmol/L). The patient's calcium supplement was stopped and intravenous biphosphonate infusion was given to control calcium levels. The patient declined to undergo surgical exploration for tertiary hyperparathyroidism. His serum calcium levels were continuously monitored.



Figure 2. Whole body bone scan shows multiple sites of abnormal extra-skeletal uptake including the stomach, heart, lungs, bilateral native kidneys, and increased soft tissue uptake in both thighs. The transplanted kidney showed faint uptake (right lower quadrant of the abdomen).

DISCUSSION

The exact pathophysiology of the calcifying mechanism in metastatic calcification is not well understood, although it is thought to relate to serum calcium and phosphorus concentrations.^{2,3} Tissues comprising an alkaline environment are more susceptible to calcification, and therefore common sites of calcification include the lungs, gastric mucosa, and kidneys. This condition contrasts with that of dystrophic calcification, in which deposits occur in damaged tissue in the presence of normal calcium metabolism. Metastatic calcification can occur in various soft tissue structures, such as muscle, subcutaneous tissue, heart, and peripheral vessels, as well as the thyroid, liver, spleen, and

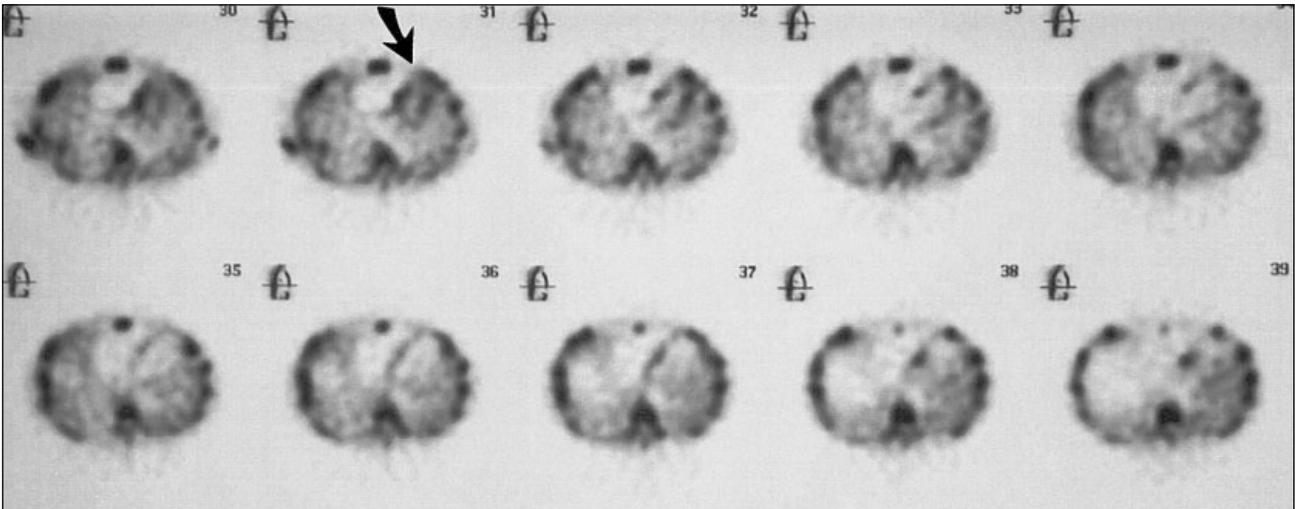


Figure 3. Single photon emission computed tomography of the lower thorax demonstrates accumulation of radiotracer in the left ventricular myocardium (arrow) and both lungs.

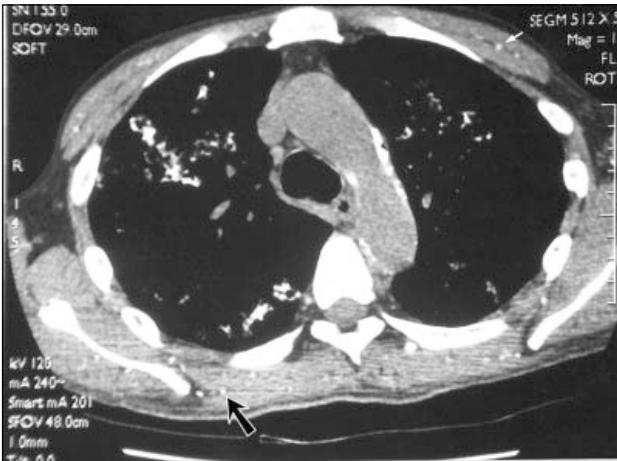


Figure 4. Non-enhanced computed tomography scan of the thorax demonstrates a patchy area of calcification in both lungs and calcified vessels in the chest wall (arrows).

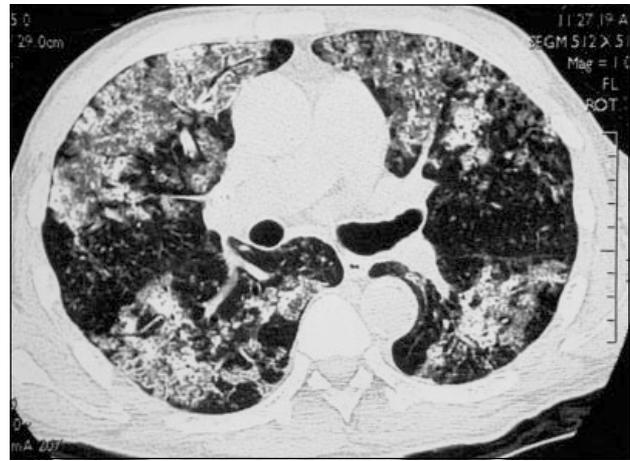


Figure 6. High-resolution computed tomography scan of the thorax shows patchy areas of parenchymal consolidation, diffuse areas of 'ground-glass' attenuation, and centrilobular nodular opacities.

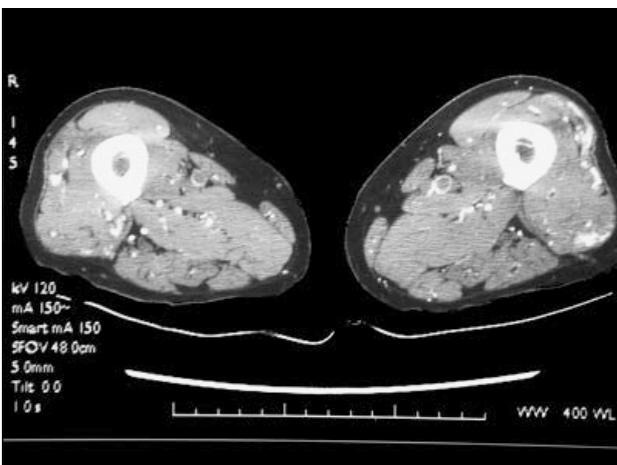


Figure 5. Non-enhanced axial computed tomography scan of the thighs showing extensive vascular calcifications corresponding to the increased uptake in the soft tissue of the lower limbs seen on bone scan.

pancreas.⁴ The clinical symptoms of metastatic calcification are non-specific and thus the diagnosis may be overlooked. Symptoms can include mood disturbances, generalised bone pain, peptic ulcer symptoms, polydipsia, and polyuria.

Chest radiographs may show arterial and soft tissue calcifications but lack specificity and sensitivity with respect to identifying metastatic calcification. CT scanning of the thorax is very sensitive in detecting minute calcific foci. Small, calcified nodules are the most common findings on CT examination of patients with metastatic calcification. In addition, calcification in the vessels of the chest wall is said to be characteristic. Other findings include patchy areas of parenchymal consolidation and diffuse areas of 'ground-glass' attenuation at HRCT scanning.⁵

Bone scintigraphy is one of the most useful methods for detecting metastatic calcification as it can illustrate systemic deposits.⁶ Uptake of radiotracer can usually be found in the lungs, kidneys, stomach, heart, liver, thyroid, and skeletal muscle. Some cases of pulmonary metastatic calcification demonstrated by bone scintigraphy are not readily identified on CT scan. Conversely, if the calcified tissue is already end-stage and 'burnt out', no active extraction of radiotracer will occur on scintigraphic assessment,⁷ and metastatic calcification may only be detected by plain radiography. Plain film radiography and CT findings reflect the amount of calcium deposit in the tissue, while bone scintigraphy depicts the active process of calcium phosphate mobilisation. Therefore, the use of both CT and bone scintigraphy offers greater accuracy in reaching the diagnosis.

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