CASE REPORT

Lung Calcifications and Chronic Kidney Failure

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Pulmonary calcification is relatively uncommon and typically asymptomatic. A number of diseases are associated with this disorder, including chronic kidney failure, infections, and lung amyloidosis. There are, moreover, a number of conditions, such as hypercalcemia, hyperphosphatemia, alkalosis, and alveolar damage, which predispose a patient to calcification.

We describe a case of pulmonary calcifications associated with chronic kidney failure which had required hemodialysis and a subsequent kidney transplant.

Key words: *Metastatic pulmonary calcifications. Chronic kidney failure. Hemodialysis. Kidney transplant.*

Calcificaciones pulmonares asociadas a insuficiencia renal crónica

La calcificación pulmonar es relativamente infrecuente y por lo general asintomática. Se asocian a ella múltiples enfermedades, como la insuficiencia renal crónica, las infecciones y la amiloidosis pulmonar, entre otras, así como numerosas situaciones que predisponen a su formación, como la hipercalcemia, la hiperfosfatemia, la alcalosis o el daño alveolar.

Presentamos un caso de calcificaciones pulmonares asociadas a insuficiencia renal crónica que había requerido tratamiento con hemodiálisis y posteriormente trasplante renal.

Palabras clave: *Calcificaciones pulmonares metastásicas. Insuficiencia renal crónica. Hemodiálisis. Trasplante renal.*

Introduction

Pulmonary calcifications, which are deposits of calcium in the lung, are associated with several diseases and with certain predisposing conditions. Lung calcification can be either metastatic or dystrophic, with the former referring to calcium deposits in healthy tissue and the latter referring to calcium deposits in damaged tissue. The single most frequent cause of metastatic calcification is chronic kidney failure, particularly if treated with hemodialysis.[1] The disorder is quite unusual, however, so its pathogenesis has yet to be determined. Most patients are asymptomatic, but some may suffer dyspnea—provoked by effort ranging from strenuous to slight—and even chronic respiratory insufficiency. One feature of the disease is that functional impairment increases until ventilation is affected, resulting in hypoxemia and reduced carbon monoxide transfer; this is not always the case, however—the ventilatory disorder in our patient was obstructive, while arterial oxygen pressure remained within normal reference limits. Although chest x-rays tend to be very nonspecific and may even be normal, they sometimes reveal patterns ranging from those reflecting alveolar infiltrates to those associated with bilateral diffuse micronodular lesions. Images are frequently confused with those for other diseases, such as, for example, pulmonary edema or pneumonia. High-resolution computed tomography reveals 3 typical patterns: numerous calcified nodules with a diffuse or limited distribution, poorly defined infiltrates (ground-glass opacities), or regions of dense mass. The most sensitive technique for detecting calcifications appears to be technetium-99m-methylene diphosphonate (99mTc-MDP) scintigraphy,[1] which also has the advantage of being capable of detecting calcification in other organs. Treatment addresses the underlying reason for susceptibility to calcium deposition in the lung. Correction of hypercalcemia, hyperphosphatemia, or hyperparathyroidism may be indicated, or a kidney transplant may be required.

We report the case of a woman with chronic kidney failure who had been on hemodialysis before receiving a kidney transplant 10 years earlier. She was referred to a pneumologist for evaluation of her lung disease (with a bilateral micronodular pattern) and of surgical risk prior to undergoing a second kidney transplant.

Case Description

Our patient was a 63-year-old woman with a history of thalassemia minor, gouty arthropathy, and idiopathic chronic kidney failure (possibly caused by gouty nephropathy, potassium-losing interstitial nephritis, or liquorice intake).

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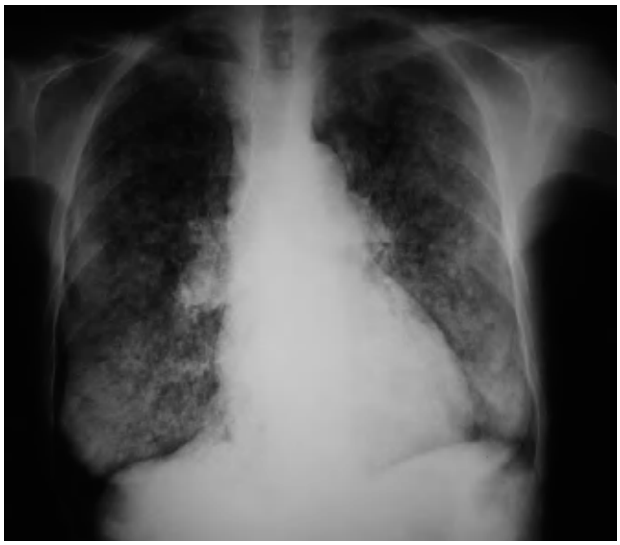

Figure. 1. Chest x-ray of a patient with lung calcifications associated with chronic kidney failure, showing a bilateral diffuse micronodular pattern.

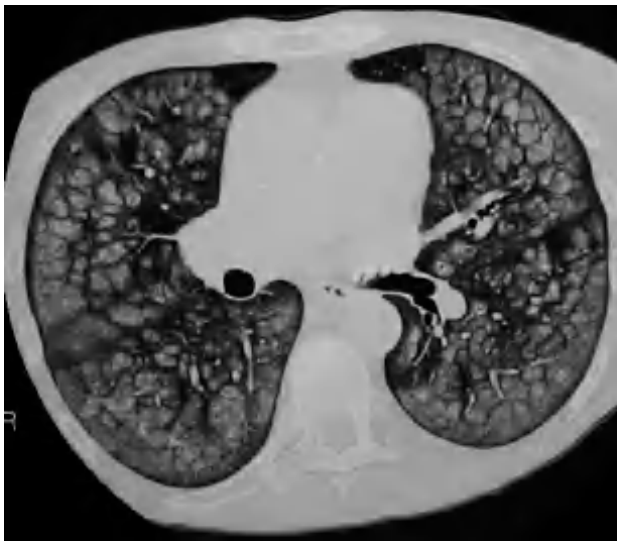

Figure. 2. Computed tomography scan of the chest revealing numerous ground-glass infiltrates and a centrilobular distribution, suggestive of metastatic calcifications.

Hemodialysis commenced in 1992, and in 1993 the patient had a kidney transplant. She required subtotal parathyroidectomy as a consequence of tertiary hyperparathyroidism, and also had paroxysmal atrial fibrillation that was treated with amiodarone. An echocardiographic examination in May 2003 revealed a nondilated left ventricle, with concentric hypertrophy, significant valvular sclerosis with mitral and tricuspid regurgitation, and moderate combined aortic valve disease. Arterial lung pressure was 65 mm Hg. A chest x-ray taken in a preoperative examination for cataract surgery in 2000 revealed bilateral micronodular patterns, and the diagnosis was idiopathic pulmonary fibrosis.

The patient was admitted to hospital on several occasions as a consequence of respiratory decompensation secondary to bronchial infection. The clinical presentation was dyspnea with moderate effort. Because the patient had chronic allograft nephropathy, another transplant was considered and a pneumologist was consulted in order to assess the patient's lung disease and secondary surgical risk. A bilateral diffuse micronodular pattern could be discerned in the chest x-ray, but no loss of lung volume was apparent (Figure 1). Lung function testing revealed moderate airflow restriction and sharply reduced CO transfer. Lung function values (percentage of reference given in parentheses) were forced vital capacity (FVC), 2.20 L (74%) and forced expiratory volume in the first second (FEV_1), 1.37 L (63%). The FEV_1 to FVC ratio was 62%. Functional residual capacity was 88%, residual volume was 110%, total lung capacity was 91%, CO diffusion capacity (DLCO) was 41%, and the ratio of DLCO to alveolar volume was 46%. Arterial blood gas values at rest were 82 mm Hg for PaO_2, 45 mm Hg for $PaCO_2$, 27 mEq/L for bicarbonate, and a pH value of 7.41. A computed tomography chest scan revealed numerous diffuse calcifications located in the soft tissues (mainly subcutaneous tissues), lymph node calcification in the left tracheobronchial region, aortic and mitral valve annulus calcifications, and numerous arterial vascular calcifications. Multiple ground-glass infiltrates—diffuse, widely dispersed and centrilobularly distributed—were apparent in the parenchyma of both lung fields (Figure 2). These findings were suggestive of metastatic calcifications, related to the patient's tertiary hyperparathyroidism which was secondary to chronic kidney failure.

Discussion

Metastatic pulmonary calcifications are associated with specific diseases and with certain conditions that predispose a patient to the deposition of calcium. These diseases can be distinguished according to whether the etiology is benign (for example: chronic kidney failure requiring hemodialysis; orthotopic liver transplantation; primary, secondary, or tertiary hyperparathyroidism; exogenous administration of calcium and vitamin D; hypervitaminosis D; osteopetrosis; or Paget disease) or malignant (for example: parathyroid cancer; multiple myeloma; lymphoma or leukemia; squamous-cell hypopharyngeal carcinoma; synovial sarcoma; breast cancer; or choriocarcinoma) (Table). Conditions that predispose a patient to the formation of lung calcifications include hypercalcemia and alkaline blood pH, although calcifications do not usually form when these conditions occur in isolation.[1]

In the case of hypercalcemia, there is no correlation between serum calcium concentrations and calcification.[2,3] Calcification may occur if there is an underlying dysfunction in calcium metabolism, even at normal levels of calcium. Calcium salts tend to precipitate in an alkaline environment, however, and the release of hydrogen radicals creates an alkaline environment in the organs that are most likely to develop calcification, namely, the stomach, kidneys, heart, and lungs. Blood pH in the lungs is more alkaline than in the other organs as a consequence of carbon monoxide exchange. The fact that calcification occurs particularly in the lung apices, where there is a higher ventilation-perfusion ratio (which leads to greater PaO_2 and lower $PaCO_2$, and consequently, a higher pH) has been commented by Chan et al[1] in their review of the subject, as also by other authors.[4,5]

Chronic kidney disease requiring hemodialysis is the condition most frequently associated with metastatic

Causes of Pulmonary Calcification*

I. Metastatic
- A. Benign causes
  - Chronic renal insufficiency on hemodialysis
  - Orthotopic liver transplantation
  - Primary hyperparathyroidism
  - Excess exogenous administration of calcium and vitamin D (milk-alkali syndrome)
  - Hypervitaminosis D
  - Osteopetrosis
  - Osteitis deformans (Paget disease)
- B. Malignant causes
  - Parathyroid carcinoma
  - Multiple myeloma
  - Lymphoma/leukemia
  - Hypopharyngeal squamous cell carcinoma
  - Synovial sarcoma
  - Breast cancer
  - Choriocarcinoma

II. Dystrophic
- A. Granulomatous disorders
  - Histoplasmosis
  - Coccidioidomycosis
  - Tuberculosis
  - Sarcoidosis
- B. Viral infections
  - Postvaricella pneumonia
  - Smallpox handler's lung
- C. Parasitic infections
  - Paragonimiasis
  - Pneumocystosis
- D. Amyloidosis
- E. Pulmonary vascular calcifications
  - Vascular grafts
  - Pulmonary hypertension
  - Congenital high flow
  - Hemosiderosis
- F. Coal worker's pneumoconiosis
- G. Silicosis

III. Idiopathic
- A. Pulmonary alveolar microlithiasis

*Source: Table adapted from Chan et al. See Chan et al[1-3] for the original source.

pulmonary calcifications.[1-3] In our particular case 4 factors predisposed the patient to calcifications: *a)* acidosis (which can increase bone resorption of calcium and phosphate, resulting in an increase in blood concentrations of these minerals); *b)* secondary, and subsequently tertiary, hyperparathyroidism (which can also increase bone calcium and phosphate resorption); *c)* intermittent alkalosis resulting from the hemodialysis sessions; and *d)* reduced glomerular filtration of phosphate (which contributes to increased blood calcium and phosphate levels). For our patient, these factors, together with the findings of additional examinations, supported a diagnosis of lung calcifications associated with chronic kidney failure —rather than the initial diagnosis of idiopathic pulmonary fibrosis.

The patient was referred to the pneumology service because of the possible surgical risk associated with a second transplant. In this case, although the surgical risk would be greater, the most appropriate treatment would be to correct the chronic allograft nephropathy by means of another kidney transplant.

In conclusion we wish to emphasize the unusualness of this case. Although the disease is rare, it should be taken into consideration if a patient has any of the diseases described in the table. Should this disorder be suspected for a patient with respiratory symptoms, and given that the x-ray findings will often appear normal, we recommend a high-resolution computed tomography chest scan or 99mTc-MDP scintigraphy.

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