

Diffuse Pulmonary Calcification in a Patient With Renal Insufficiency

M.C. Castillo, M.J. Gimeno, B. Carro, J.L. Benito, E. Freile, and J.M. Sainz

Servicio de Radiodiagnóstico, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain.

We report the case of a 37-year-old man with chronic renal insufficiency, on hemodialysis, with no respiratory symptoms but whose chest radiograph showed parenchymal consolidation in the middle and upper lung fields. High resolution computed tomography showed a high-attenuating diffuse alveolar pattern that indicated calcium deposits. Bronchoscopy revealed metastatic calcification on the interalveolar septa and bronchiolar and arteriolar.

The present report, based on radiologic and bronchoscopic findings, describes the pathogenesis and anatomical distribution of the patient's diffuse pulmonary calcification.

Key words: Renal insufficiency. Pulmonary calcification. Metastatic pulmonary calcification. High resolution computed tomography.

Calcinosis pulmonar difusa en paciente con insuficiencia renal

Se describe el caso de un varón de 37 años de edad con insuficiencia renal crónica en hemodiálisis y asintomático desde el punto de vista respiratorio, que presentó una radiografía de tórax con consolidaciones parenquimatosas en campos pulmonares medios y superiores. Los hallazgos de la tomografía computarizada de alta resolución mostraron un patrón alveolar difuso de alta atenuación, indicativo de depósito de calcio. La broncoscopia demostró calcificaciones metastásicas en septos alveolares y paredes de bronquiolos y arteriolas.

Este artículo describe la patogenia y distribución anatómica de las calcificaciones pulmonares difusas basándose en los hallazgos radiológicos y broncoscópicos.

Palabras clave: Insuficiencia renal. Calcinosis pulmonar. Calcificaciones metastásicas pulmonares. Tomografía computarizada de alta resolución.

Introduction

Diffuse pulmonary calcification, also called pulmonary metastatic calcification, is a frequent complication in end-stage chronic renal insufficiency (CRI) treated by hemodialysis. Diffuse pulmonary calcification is a progressive, normally asymptomatic disease but can lead to critical and fulminant respiratory failure.^{1,2}

Calcium deposits in the pulmonary parenchyma can develop both in patients with hypercalcemia secondary to changes in calcium-phosphorus metabolism (especially in the context of CRI) and in patients showing a normal calcium-to-phosphorus ratio in the bloodstream.^{3,4}

Standard digital radiography and high resolution computed tomography (HRCT) offer excellent diagnostic sensitivity in the detection of small calcifications inside the lung.^{5,6}

We describe the case of a 37-year-old male with pulmonary calcification who had no respiratory symptoms but a history of advanced CRI, treated by hemodialysis, and secondary hyperparathyroidism. The diagnosis was based on radiologic findings.

Case Description

The patient was a 37-year old man, ex-smoker, with no signs or symptoms of respiratory disease but with terminal CRI secondary to membranoproliferative glomerulonephritis, diagnosed 20 years ago, which required hemodialysis treatment for 2 years. Eighteen years ago he underwent kidney transplantation followed by 3 episodes of rejection; he received a second transplanted kidney 10 years ago and upon presentation at this time he was suffering another deterioration of kidney function due to rejection. His medical history included high blood pressure, peripheral arterial disease which led to amputation of several fingers, an ischemic left foot, hyperparathyroidism secondary to CRI, and ischemic heart disease with acute inferior myocardial infarction.

He was being treated by hemodialysis, and laboratory studies revealed the following: hemoglobin, 6.9 g/dL;

Correspondence: Dra. M.C. Castillo.
Avda. Cesáreo Alierta, 20, esc. A, 2.º D. 50008 Zaragoza, España.
E-mail: ccastillolario@wanadoo.es

Manuscript received December 3, 2004. Accepted for publication January 17, 2005.



Figure 1. A standard digital posteroanterior radiograph of the thorax showing diffuse interstitial alveolar patterns in both upper lobes.

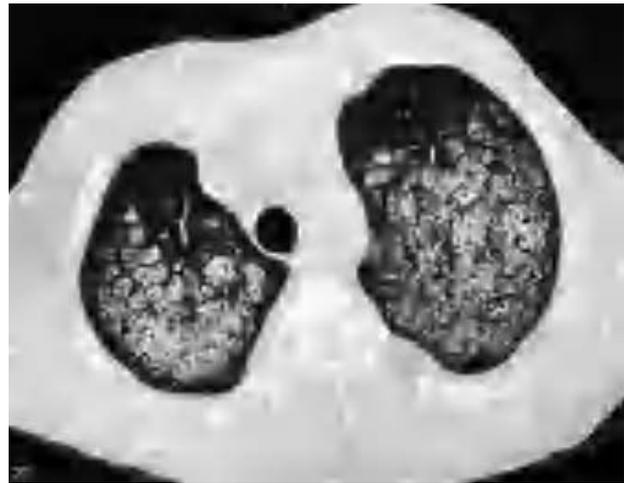


Figure 2. High resolution computed tomography of the thorax showing bilateral moruloid densities (greater than 100 Hounsfield units), consistent with calcified lesions.

hematocrit, 20.9%; leukocytes, 9500/m³ (normal formula); platelet count, 195 000/ μ L; erythrocyte sedimentation rate, 135 mm in the first hour; glucose, 86 g/dL; creatinine, 8.6 mg/dL; urea, 188 mg/dL; sodium, 138 mEq/L; potassium, 4.3 mEq/L; chlorine, 100 mEq/L; calcium, 9.23 mg/dL; phosphorus, 7.83 mg/dL; and parathyroid hormone, 2475 pg/mL.

He was being treated with bisoprolol, atorvastatin, prednisone, allopurinol, oral nitrates, vitamin D, erythropoietin, and cyclosporin.

During clinical examination the patient was conscious and well oriented; hydration was normal and he had no fever. Blood pressure was 190/90 mm Hg. Lung auscultation revealed normal ventilation, and no crepitation, rhonchus, or wheezing. Examination of the abdomen and extremities revealed no relevant findings.

In order to place a permanent catheter for hemodialysis, a standard digital posteroanterior radiograph of the thorax was ordered. The image revealed a diffuse interstitial alveolar pattern in both upper lobes and calcium density (Figure 1). Therefore, although the patient had no fever or respiratory symptoms, HRCT with no intravenous contrast material was ordered. Tomographic findings were the following: increased bilateral density in the pulmonary parenchyma primarily in the middle and upper fields consisting of nodular opacities and/or confluent, moruloid nodules of 3 to 10 mm in diameter (Figure 2). The high density (greater than 100 Hounsfield units) suggested calcification. No loss of volume in the pulmonary parenchyma or signs of acute inflammatory processes were observed, but cavitations were evident in the upper left lobe. Although no mediastinal lymph node involvement was observed, there was diffuse calcification in soft tissue.

Bone scans were also performed, which led to a diagnosis of advanced vascular calcification and articular destruction of the metatarsus and flange of the first and fifth toes of the left foot.

Serological tests were negative for cytomegalovirus and herpes simplex, respiratory syncytial, herpes zoster, hepatitis C and A, and human immunodeficiency viruses; *Coxiella burnetii*; *Rickettsia conorii*; and *Legionella*, *Pneumococcus*, *Aspergillus*, and *Leishmania* species. Both a sputum smear test and a Mantoux test were negative, as were immunological tests with antibodies directed toward rheumatoid factor and

the following antibodies and antigens: bicateary anti-DNA, antibasement membrane, antimitochondrial, anti-smooth muscle, anticardiolipin, antinuclear antigens, anti-neutrophil cytoplasm in both perinuclear and cytoplasmic patterns, and anti-extractable nuclear antigens.

Bronchoscopic examination showed a diffuse pattern of hard, whitish, parallel, linear images in the bronchial tree of both lungs, indicative of metastatic pulmonary calcification.

The pathologist detected deposits on the interalveolar septa, bronchiolar walls, and arterioles.

The patient refused spirometric testing that would have enabled evaluation of his lung function (which suggested a restrictive pattern).

All indications—from the HRCT of the thorax, bronchoscopic examination, and pathology—suggested that the pulmonary condition was secondary to calcium deposition in the parenchyma associated with hyperparathyroidism secondary to CRI.

Discussion

We describe the case of a kidney transplant patient on hemodialysis who was under study for high density pulmonary infiltrates in both upper lobes. Such pulmonary parenchymatous calcification could be indicative of various processes: infection, silicosis, diffuse pulmonary amyloidosis, alveolar proteinosis, idiopathic pulmonary hemosiderosis, alveolar microlithiasis, metastases of malignant sarcoma or adenocarcinoma or, finally, diffuse pulmonary metastatic calcification.⁷⁻⁹ Owing to the patient's favorable clinical picture and the negative serological tests, we ruled out diagnoses of infectious lung diseases—especially viral pneumonia, histoplasmosis, and tuberculosis.

A possible diagnosis might have been diffuse pulmonary amyloidosis, which is characterized by nodular calcification (especially subpleural and in the middle fields), hilar lymph node involvement, septal thinning, and ground-glass opacities. However,

bronchoscopic findings and the patient's clinical picture did not suggest amyloid accumulation.^{7,10}

Alveolar proteinosis, in turn, is characterized by intraalveolar accumulation of proteinaceous material with diffuse, bilateral, predominantly basal involvement but no calcification; symptoms are clearly apparent upon clinical examination: cough, dyspnea, fever, weight loss, and restrictive lung function pattern.⁸ Our patient did not present these symptoms.

Although the patient had very low hematocrit and hemoglobin values due to his CRI, a diagnosis of pulmonary hemosiderosis was ruled out since no signs of hemoptysis or alveolar macrophages were present.

Alveolar microlithiasis is characterized by the presence of predominantly basal, paracardial calcified nodules inside the alveoli—but less than 1 mm in diameter. For that reason, this diagnosis was ruled out.¹¹

Calcification associated with hypercalcemia is called metastatic calcification and involves the transport of large amounts of calcium from one site in an organism (such as bone) to another, where the calcium precipitates out. Calcium deposits accumulate predominantly in sites where acid is secreted (hydrochloric acid in the stomach, uric acid in the kidneys, and the anhydride of carbonic acid in the lungs) since the calcium precipitates upon alkalization of the pH.

Pulmonary metastatic calcification occurs most often in the apexes of the lungs owing to the regional differences in pH: at the apexes the ventilation—perfusion ratio brings about a pH of about 7.50, whereas in the bases pH is 7.39. The alkaline pH of the apex favors the deposition of calcium salts in the alveolar membrane, which thins out, leading to changes in diffusion capacity.

Our patient's clinical picture suggested a diagnosis of diffuse pulmonary calcification (also called metastatic pulmonary calcification), since this disease is characterized by calcium deposits in the small vessels of the alveolar wall and diffuse calcium infiltrates in soft tissue. Diffuse pulmonary calcification is often the consequence of changes in calcium-phosphorus metabolism and frequently occurs in patients with CRI although cases have also been reported associated with hyperparathyroidism¹² (an increased secretion of parathyroid hormone that mobilizes calcium and phosphorus and increases tubular reabsorption of calcium), vitamin D intoxication, milk-alkali syndrome, sarcoidosis, massive bone destruction due to malignant metastasis, osteomyelitis, or tuberculosis.¹³

According to Morkos⁵ plain chest radiography and especially digital chest radiography can be sufficient for detecting diffuse pulmonary calcification that forms zones of confluent or nodular opacities that have a density consistent with calcification. Calcification can also present with diffuse interstitial involvement.¹⁴ However, Lingam et al⁷ concluded that HRCT is the

most effective technique, and Hartman et al¹⁵ even found that diffuse pulmonary calcification could be diagnosed by this technique alone. Both groups of authors describe 3 possible patterns of calcification: a diffuse distribution of nodules, patchy areas of ground-glass opacity, and zones of lobar parenchymatous attenuation.

Others have described cases such as that of the present report, in which calcification is present in bronchial walls, trachea, small vessels, and soft tissue.^{3,4,7}

Finally, it is important to be able to recognize the radiologic patterns of diffuse pulmonary calcification in any patient with CRI since, together with the findings of bronchoscopy and pathology, such patterns are sufficient for establishing a diagnosis.

REFERENCES

1. Kuhlman FE, Ren H, Hutchins GM, Fishman EK. Fulminant pulmonary calcification complicating renal transplantation: CT demonstration. *Radiology*. 1989;173:459-60.
2. Santiago Villalobos R, Rodríguez Becerra E, Borderas Naranjo F, Martín Juan J. Calcificación pulmonar metastásica: una rara causa de enfermedad pulmonar intersticial. *Arch Bronconeumol*. 2003; 39:184-6.
3. Murrís-Espin M, Lacassagne L, Didier A, Voigt JJ, Cisterne JM, Giron J, et al. Metastatic pulmonary calcification after renal transplantation. *Eur Respir J*. 1997;10:1925-7.
4. Ulmer E, Borre H, Sandoz P, Mayr M, Dalquen P, Solèr M. Diffuse pulmonary nodular infiltrates in a renal transplant recipient. *Chest*. 2001;20:1394-8.
5. Morkos SK. Regarding metastatic pulmonary calcification in renal failure. *Br J Radiol*. 2002;75:711-2.
6. Miyoshi I, Saito T, Kobayashi M, Taguchi H. Pulmonary calcinosis in adult T-cell leukaemia. *Br J Haematol*. 2004;126:164.
7. Lingam RK, Teh J, Sharma A, Friedman E. Metastatic pulmonary calcification in renal failure: a new HRCT pattern. *Br J Radiol*. 2002;75:74-7.
8. Romagnoli M, Mourad G, Serre I, Senad JP, Paradis L, Godard P, et al. Diffuse pulmonary calcinosis without calcium metabolism abnormalities in a renal transplant recipient. *Eur Respir J*. 1997;10:958-60.
9. Poletti V, Costabel U, Casoni GL, Bigliuzzi C, Drent M, Olivieri D. Rare infiltrative lung diseases: a challenge for clinicians. *Respiration*. 2004;71:431-43.
10. Jeong YJ, Lee KS, Chung MP, Han J, Chung MJ, Kim KI, et al. Amyloidosis and lymphoproliferative disease in Sjögren syndrome: thin-section computed tomography findings and histopathologic comparisons. *J Comput Assist Tomogr*. 2004;28:776-81.
11. Castellana G, Lamorgese V. Pulmonary alveolar microlithiasis. World cases and review of the literature. *Respiration*. 2003; 70:549-55.
12. Támez Pérez HE, Forsbach Sánchez G, Colunga González F, García FC. Diffuse pulmonary calcinosis in a case of primary hyperparathyroidism. *Rev Invest Clin*. 2000;52:98-100.
13. Weber CK, Friedrich JM, Merkle E, Prummer O, Hoffmeister A, Mattfeldt T, et al. Reversible metastatic pulmonary calcification in a patient with multiple myeloma. *Ann Hematol*. 1996;72:329-32.
14. Zompatori M, Rimondi MR, Fantone F, Monetti N, Franchi R, Canini R. The high-resolution computed tomographic study of metastatic pulmonary calcifications. A case report. *Radio Med (Turino)*. 1994;87:515-8.
15. Hartman TE, Muller N, Primack SL, Johkoh T, Takeuchi N, Ikezoe N, et al. Metastatic pulmonary calcification in patients with hypercalcemia: findings on chest radiographs and TC scans. *AJR Am J Roentgenol*. 1994;162:799-802.