

## Scientific Letter

### Pulmonary Calcifications: A Reflection of Renal Impairment



#### *Calcificaciones pulmonares: reflejo de una alteración renal*

Dear Editor,

Pathological pulmonary calcifications (PC) can be generally divided into metastatic (MPC) and dystrophic (DPC) calcifications, depending on whether the calcium deposition occurs on healthy lung tissue or on a previously injured lung.<sup>1,4</sup>

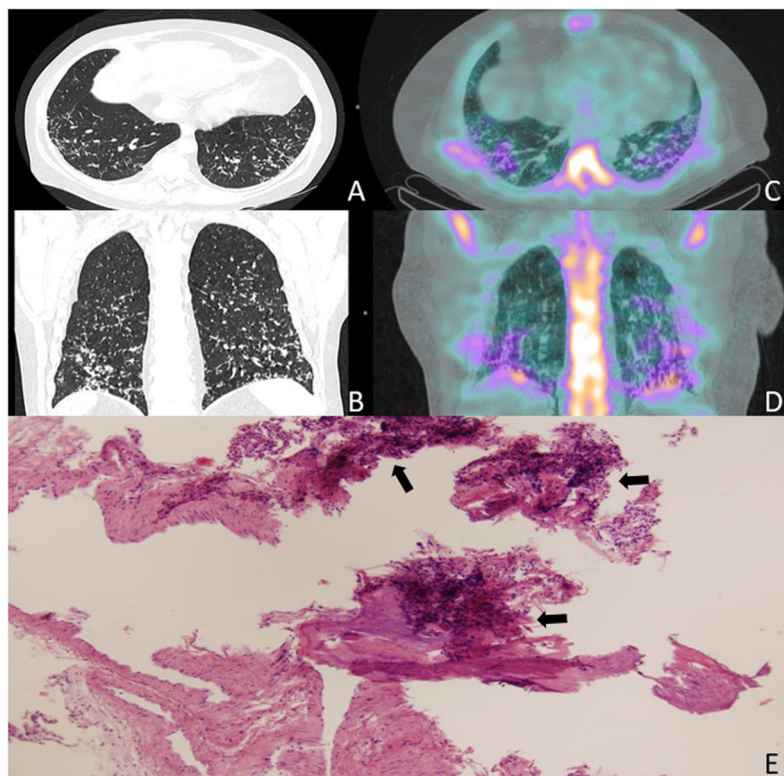
We present the case of a 48-year-old male with advanced chronic kidney disease (CKD), who received his first kidney transplant from a deceased donor in 1993. In 2019, after many years of hemodialysis, he underwent a second kidney transplant due to graft dysfunction.

In 2004, he was referred to the Pulmonology clinic after a computed tomography (CT) scan incidentally revealed interlobular

septal thickening, bilateral diffuse interstitial infiltrates, and peribronchovascular calcified micronodules, predominantly in the lower lobes (Fig. 1). Analytically, serum calcium and phosphorus levels were usually within normal limits, but notable findings included hyperparathyroidism, with levels up to 227 pg/mL, that persists after the improvement of renal function.

At the respiratory level, the patient was asymptomatic and had normal pulmonary function tests (PFTs) results. Considering his nephrological history and radiological findings, MPC was suspected, and periodic follow-up was decided.

During 20 years follow-up, a progressive decline of the diffusion capacity of carbon monoxide (DLCO) was observed, with the last measurement showing 71% of the reference value, while the rest of the parameters remained within normal limits. In addition, radiological findings showed a slow increase in the number of nodules and slight subpleural reticulation, leading to the decision to perform cryobiopsy. The analysis of the obtained sample confirmed



**Fig. 1.** (A and B) Chest CT scan showing bilateral micronodular calcifications predominantly in the lower lobes. (C and D) Scintigraphy with Tc99m-HDP showing increased radiotracer uptake in the posterior basal segments of both lower lobes. (E) Pathology: fragments of lung parenchyma and stroma with a focus of calcification (indicated with arrows).

the presence of a calcification focus, with no other abnormalities in the analyzed parenchyma (Fig. 1).

Following this finding, it was decided to complete the study with a nuclear imaging with technetium-99m-hydroxymethylene diphosphonate (Tc99m-HDP), where an increased radiotracer uptake in the lower lobes was observed, coinciding with the areas of the micronodular pattern (Fig. 1).

With all this, the initial suspected diagnosis was confirmed. He currently remains asymptomatic and continues to be monitored in follow-up visits.

The differential diagnosis of PC is broad and includes MPC secondary to CKD, liver transplantation, and malignancies associated with hypercalcemia.<sup>1,5</sup> CPM is closely related to alterations in calcium-phosphorus metabolism and pH. It is a long-term complication in patients with CKD, due to decreased glomerular phosphate filtration, metabolic acidosis, and secondary hyperparathyroidism, which stimulate bone resorption of calcium and phosphate, contributing to an increased calcium-phosphorus product. However, a direct correlation between CPM and serum levels of the ionic calcium-phosphorus product has not always been demonstrated. Even with normal values, as in our case, calcifications can occur. These calcium salts tend to precipitate under alkaline conditions, making organs with alkaline surfaces, such as the lungs, kidneys, and stomach, more susceptible to calcification. The intermittent alkalosis that occurs during each hemodialysis session creates an additionally favorable environment for the precipitation of calcium salts in soft tissues. In addition, the use of vitamin D supplementation in patients with CKD may contribute to calcification because it increases calcium absorption and precipitation. Furthermore, azotemia can alter the configuration of tissue proteins, making them more prone to calcifications.<sup>1,2,4</sup> Our patient presents all the previously mentioned risk factors, which reinforces the clinical suspicion of CPM.

The clinical manifestations are usually minimal, and PFTs are often normal, as seen in our case. However, cases of acute respiratory failure with rapidly progressive lung parenchyma involvement have been described, simulating pneumonia or pulmonary edema.<sup>1,2</sup>

Chest CT is a relatively sensitive tool for detecting calcifications. In MPC, three main patterns can be identified: centrilobular ground-glass opacities, dense confluent consolidations, and small calcified nodules. These patterns typically predominate in the upper lobes, likely due to greater alkalinity in the apices.<sup>4,5</sup> Another common finding is the calcification of vascular structures. However, in this case, there was none, and the nodules predominated in the lower lobes. Our patient exhibited reticulation, which, although infrequent, has been described in other cases adjacent to inflammatory and/or fibroproliferative processes.<sup>3,4</sup>

Scintigraphy with Tc99m-HDP helps to distinguish doubtful cases, being more sensitive in detecting calcifications and ectopic ossifications. Lungs affected by MPC show greater uptake of radioactive isotopes, as in our case.<sup>1,4</sup>

Clinical management is aimed at correcting hyperphosphatemia and renal function. MPC may improve over time if the underlying electrolyte abnormalities are treated. However, there have been cases where MPC persists or progresses despite correct treatment.<sup>1,4,5</sup> The reason for progression is unclear, although occult tertiary hyperparathyroidism may be responsible for some of these cases. In severe cases associated with primary or tertiary hyperparathyroidism, parathyroidectomy is indicated.<sup>4</sup>

In conclusion, MPC represents a condition that should be considered in patients with CKD. Although it is relatively rare and often asymptomatic, it is crucial to be aware of this condition to make a correct diagnosis and provide appropriate treatment for these patients.

### Informed consent

Informed consent was obtained from the patient for the publication of his clinical data and the use of diagnostic images.

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### Authors' contributions

X. Gao responsible for the design and implementation of the study, for the analysis of the results and for writing of the manuscript. M.J. Bernabé performed bronchoscopy and cryobiopsy. C. Gamila Wakfie-Corieh contributed to the analysis of nuclear imaging results. A. García Egido performed and interpreted the anatomopathological study. C. Matesanz López conceived of the presented idea and supervised the work.

### Conflicts of interest

The authors have no conflict of interest to declare.

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