# A Case of Secondary Hyperparathyroidism with Metastatic Pulmonary Calcification: Discussing Treatment Options

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***Cite this article as:*** Mütiş Alan A, Fırat Şentürk E, Toker Dinçer Z, et al. A case of secondary hyperparathyroidism with metastatic pulmonary calcification: discussing treatment options. *Cerrahpaşa Med J.* 2024;48(3):298-301.

## Introduction

Metastatic calcification occurs as a metabolic disorder where calcium accumulates in tissues outside their normal locations.[1,2] The lung is predominantly one of the main areas of metastatic calcium accumulation, primarily in the alveolar walls, but also in bronchial walls, pulmonary arteries, and vessels.[3] Metastatic pulmonary calcification (MPC) is often asymptomatic, but suspicion is important when unexplained respiratory symptoms and radiological findings are detected in dialysis patients. A thoracic CT identified lung calcification in a 27-year-old male patient receiving peritoneal dialysis is presented, as well as the treatment strategy for pulmonary calcifications in dialysis patients.

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

## Case Report

A 27-year-old male patient with granulomatosis with polyangiitis (Wegener's granulomatosis) presented to the outpatient clinic with a cough. He has had chronic kidney disease (CKD) since 2019. Between January 2020 and February 2023, the patient's parathyroid hormone (PTH) levels varied between 154 and 549 pg/mL. Throughout this period, vitamin D analogs were given to normalize the PTH levels within the acceptable range. However, calcimimetics could not be used due to low calcium levels. His blood pressure was 125/72 mm Hg, pulse rate was 90 beats per minute, body temperature was 36.4°C, and peripheral oxygen saturation was 97% (on room air), indicating stable vital signs. On physical examination, 2+ pretibial edema was detected, and no breath sounds were heard in the lower left lung. Laboratory results were as follows: serum creatinine 11.9 mg/dL (0.7-1.2 mg/dL), calcium 6.7 mg/dL (8.4-10.2 mg/dL), phosphorus 7.6 mg/dL (2.5-4.5 mg/dL), albumin 3.32 g/dL (3.5-5.0 g/dL), C-reactive protein 11.9 mg/L (0-5.0 mg/L), hemoglobin 8.8 g/dL (13.6-17.0 g/dL), and parathormone 3111 pg/mL (15-65 pg/mL). Calcium, phosphorus, and parathormone levels are indicated in Figures 1 and 2. Since being diagnosed with small-vessel vasculitis, hemodialysis treatment has been administered for 3/7 days. For the past year, peritoneal dialysis has been initiated due to recurrent catheter infections and infective endocarditis. A posteroanterior (PA) chest X-ray showing prominent opacities in the right lobe of the lung. Thorax computed tomography (CT) showed that centrilobular ground-glass density areas and calcifications were observed in both lungs, prominent in the upper lobe of right lung (Figure 3A-D). Bronchoalveolar lavage was performed on the patient. No hemosiderin-laden macrophages were observed, and no malignancy was detected. The culture results showed no microorganism growth. The lesions were considered as metastatic calcification due to his history of CKD. In a patient with low calcium, high phosphorus, and elevated parathormone levels, SHPT was considered the primary diagnosis. In neck ultrasonography, a well-circumscribed hypoechoic nodular lesion (parathyroid hyperplasia?) measuring 9 × 5 mm was detected in the lower pole of the left thyroid gland. Parathyroid scintigraphy revealed a minimal increase in activity in the same region (Figure 4A and B). In this case, due to high phosphorus levels, low calcium levels, and metastatic calcifications, active vitamin D and calcimimetic treatment could not be administered. Parathyroidectomy (PTx) was planned for the patient. However, PTx could not be performed due to his poor overall condition, and the patient subsequently died.

## Discussion

Metastatic pulmonary calcification is generally associated with both systemic and local alterations in phosphocalcic metabolism. The most common cause is CKD-Mineral and Bone Disorder (CKD-MBD), but other causes include primary hyperparathyroidism,

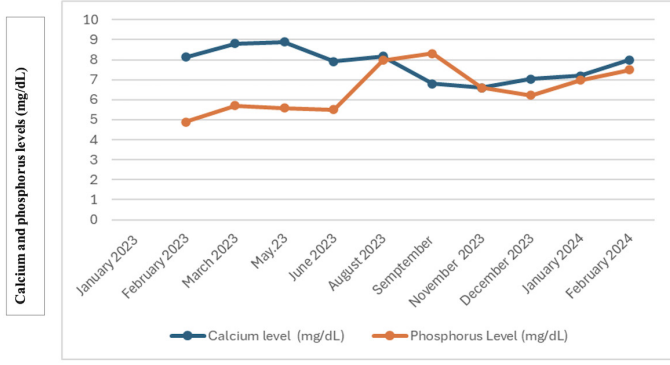


**Figure 1.** Calcium and phosphorus levels between January 2023 and February 2024.

**Received:** July 10, 2024 **Revision requested:** November 23, 2024
**Last revision received:** October 29, 2024 **Accepted:** November 23, 2024
**Publication Date:** December 18, 2024
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**DOI:** 10.5152/cjm.2024.24028

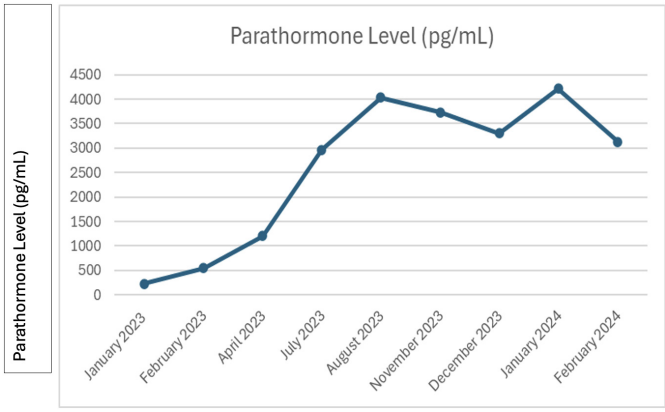


**Figure 2.** Parathormone levels between January 2023 and February 2024.

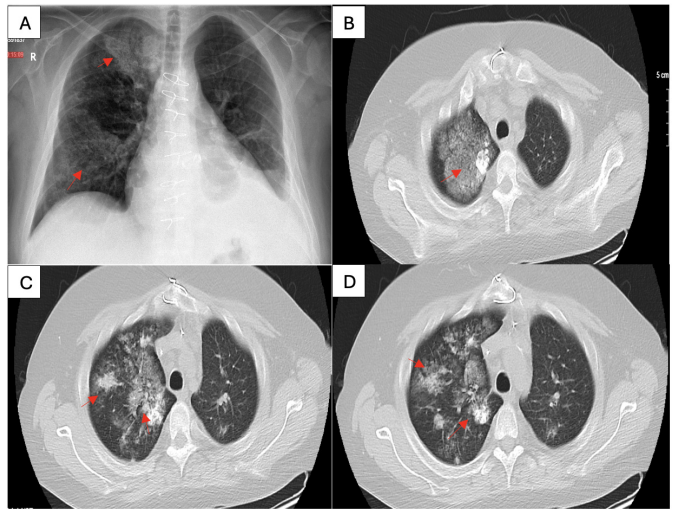


**Figure 3.** (A) In PA chest X-ray showing prominent opacities in the right lobe of the lung (red arrows). (B–D) Thorax CT showed that centrilobular ground-glass density areas and calcifications were observed in both lungs, prominent in the upper lobe of right lung (red arrows).

kidney transplantation, hypervitaminosis D, and malignant diseases such as myeloma.[4] Since a chest X-ray is not sensitive enough to detect small amounts of calcium, high-resolution CT[5] is the most sensitive and effective test for diagnosing this condition. Lung biopsy is rarely performed.[4]

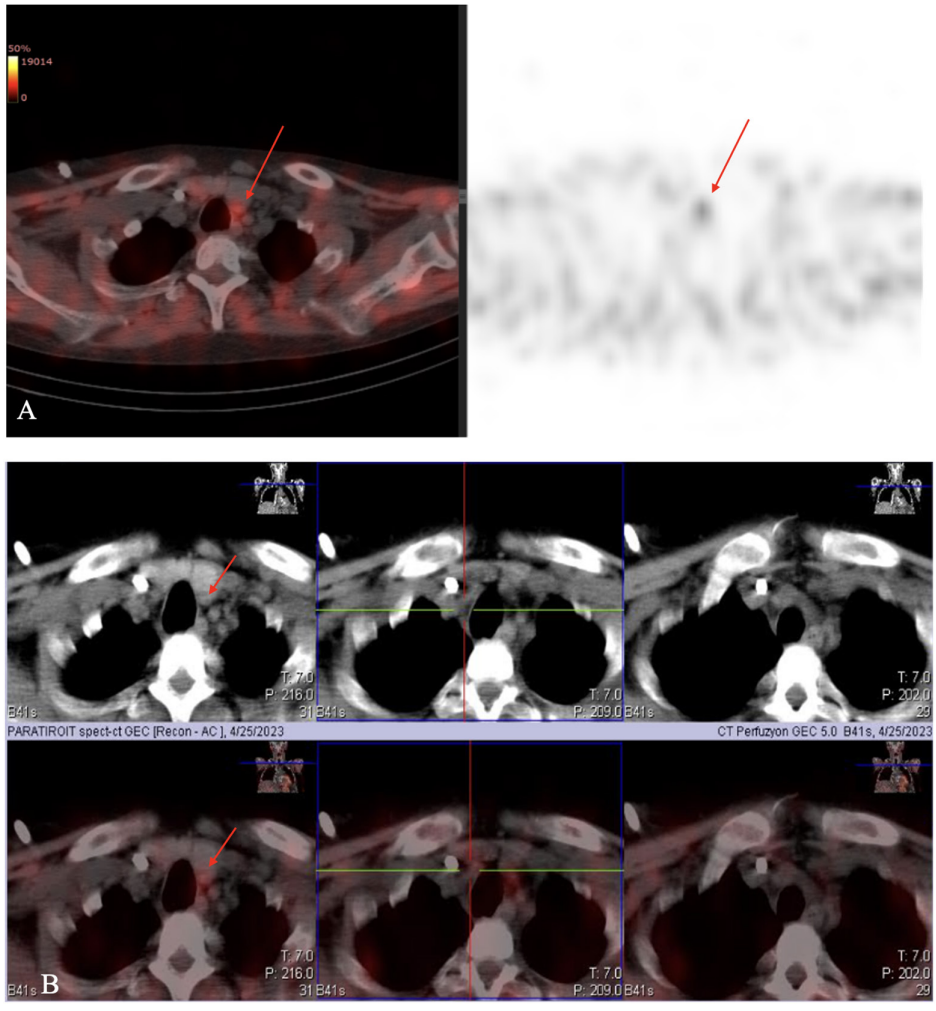


**Figure 4.** (A, B) Parathyroid scintigraphy showing minimal uptake in a millimetric focus located in the posterior lower pole of the left thyroid lobe, which exhibited no washout in the late images.

The majority of patients with renal failure and asymptomatic non-progressive MPC do not require any medical treatment. However, it is recommended to treat symptomatic patients.[6,7] As a treatment approach, maintaining calcium and phosphorus levels within the normal range is recommended as the primary strategy, although there is no clear treatment recommendation.[10]

Secondary hyperparathyroidism, a common and significant complication of CKD, significantly contributes to increased cardiovascular morbidity and mortality, hospitalizations, fractures, and the risk of extra-skeletal calcification in dialysis patients.[9] Kidney Disease Improving Global Outcomes (KDIGO) CKD-MBD 2017 guideline recommends using calcitriol or vitamin D analogs, calcimimetics, or a combination of calcimimetics and calcitriol or vitamin D analog to lower PTH in CKD stage 5D patients with high or gradually increasing PTH levels. Parathyroidectomy is recommended in CKD stage 3-5D patients with severe hyperparathyroidism that does not respond to medic al/pharmacological treatment.[11] Additionally, if accompanying disorders such as persistent hypercalcemia or hyperphosphatemia, tissue or vascular calcification including calciphylaxis, and/or worsening osteodystrophy are present, PTx should be considered.[11]

Preoperative imaging evaluations of enlarged parathyroid glands (PTGs) during PTx for SHPT are important to ensure their complete removal. Preoperative imaging methods include ultrasonography (USG), CT, and 99mTc-Sestamibi (MIBI) scintigraphy.[12] Ultrasonography (USG) is the first-line method to image the PTGs, especially to determine the size and location of the glands in the neck region. However, it may be limited in detecting hyperplastic glands in SHPT and may have restricted use in identifying ectopic glands. Computed tomography effectively identifies the 4 primary and ectopic PTGs, but it rarely observes the PTGs located in the thymus and thyroid gland. While MIBI scintigraphy effectively identifies ectopic PTGs in the mediastinum and upper neck, false positives and false negatives compromise its diagnostic precision. Ultrasound exhibits the highest sensitivity at 91.5%, while MIBI scintigraphy demonstrates the lowest sensitivity at 56.1%. The sensitivity of the combination of ultrasound and CT, as well as the combination of ultrasound, CT, and MIBI scintigraphy, was 95.0% and 95.4%, respectively. Furthermore, a meta-analysis revealed that the sensitivity and specificity of MIBI scintigraphy were 58% and 93%, respectively. Histological confirmation of hyperfunctioning parathyroid glands post-PTx was the gold standard for the resected glands.[13,14]

The surgical intervention may involve a mix of total or subtotal PTx, transcervical thymectomy, and autograft. Subtotal PTx entails the excision of 3.5 PTGs while preserving 40–80 mg of PTG tissue.

Generally, it is preferable to preserve normal-looking PTGs to prevent recurrence. The evidence evaluating surgical interventions for SHPT is scarce. A study from the American College of Surgeons National Surgical Quality Improvement Program revealed similar complications, reoperations, readmissions, and 30-day death rates between subtotal and complete PTx with autotransplantation.[15]

Total PTx is preferred for patients requiring long-term dialysis, but special attention is needed for cardiovascular events. Nevertheless, for patients with SHPT who are awaiting a kidney transplant in the near future, subtotal PTx may be indicated.[16,17] In this case, if surgery had been feasible, a subtotal PTx would have been the appropriate approach.

In this case, due to the presence of metastatic calcification in the lungs, along with hyperphosphatemia and hypocalcemia, active vitamin D or analogs and calcimimetic treatment were not applied to the patient. The decision for PTx was made due to the PTH level being >800 pg/mL for 6 months and the development of resistant hyperphosphatemia and tissue calcification.

**Availability of Data and Materials:** The data that support the findings of this study are available on request from the corresponding author.

**Informed Consent:** Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – A.M.A., S.T.; Design – A.M.A., M.T.D.; Supervision – M.T.D., A.M., S.T., N.S.; Resources – A.M.A.; Materials – A.M.A.; Data Collection and/or Processing – A.M.A., E.F.S., Z.T.D., M.M., E.M.; Analysis and/or Interpretation – A.M.A.; Literature Search – A.M.A., M.T.D.; Writing Manuscript – A.M.A.; Critical Review – M.T.D, S.T.; Other – A.M.A.

**Declaration of Interests:** The authors have no conflict of interest to declare.

**Funding:** The authors declared that this study has received no financial support.

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