Clinical Case Report

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Primary hyperparathyroidism characterized by diffuse homogeneous metastatic pulmonary calcification

A case report

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Abstract

Rationale: Primary hyperparathyroidism (PHPTI) with respiratory tract symptom is extremely rare. It is caused by autonomic oversecretion of parathyroid hormone (PTH) owing to parathyroid adenoma, hyperplasia, or tumor. The diagnosis of PHPTI often needs to be made based on medical history, clinical manifestation, laboratory tests, and imaging examination. Moreover, no study has reported PHPTI with diffuse metastatic pulmonary calcification (MPC) as the characteristic.

Patient concerns: A 49-year-old female from Zhejiang, China, had a fever of unknown origin, cough with white crude sputum, and asthma after activity for 1 month.

Diagnosis: The computed tomography (CT) examination revealed a homogeneous and diffuse high-density shadow in both lungs. The pathologic examination with CT-guided lung biopsy (left lung puncture) suggested interstitial inflammation of the lung tissue, combined with fibroblast proliferation as well as calcification. B-ultrasonography identified a lump in the right parathyroid gland, with a size of $4.1 \times 1.7 \times 1.9\,cm^3$. Color Doppler sonography indicated rich blood flow inside the lump. Whole-body bone emission computed tomography imaging showed the enhancement of bone metabolism in bilateral lower extremities and a diffuse enhancement of radioactive distribution in both lungs. ^{99m}Tc-methoxyisobutyl isonitrile imaging suggested significantly increased MIBI uptake in the right superior pole of the thyroid gland and indicated adenoma of the right superior parathyroid. The diagnosis of PHPTI was confirmed by postoperative pathology.

Interventions: The patient received a resection of the right parathyroid adenoma.

Outcomes: After surgery, the symptom such as fever, coughing, and white crude sputum were significantly alleviated.

Lessons: This novel case reported the case of a patient with PHPTI having respiratory tract infection as the 1st symptom and diffuse MPC as the symptom characteristic PHPTI, the findings of this case study might improve the recognition of PHPTI on diffuse pulmonary calcification for clinical doctors.

Abbreviations: CRP = C-reactive protein, CT = computed tomography, MPC = metastatic pulmonary calcification, PHPTI = primary hyperparathyroidism, PTH = parathyroid hormone.

Keywords: computed tomography, metastatic pulmonary calcification, parathyroid adenoma, primary hyperparathyroidism

1. Introduction

Primary hyperparathyroidism (PHPTI) is a rare disease in clinic.[1] It is caused by autonomic oversecretion of parathyroid hormone (PTH) owing to parathyroid adenoma, hyperplasia, or tumor.[2] It results in hypercalcemia and hypophosphatemia involving multiple parts of the whole body, but mainly the bone and urinary tract systems. As for the lung, PHPTI involvement is relatively rare,[3] and disperse calcification is the most common symptom in PHPTI. No study to date has reported PHPTI with pulmonary tract infection as the 1st symptom and diffuse metastatic pulmonary calcification (MPC) as the characteristic of PHPTI in the diagnostic procedure. The diagnosis of PHPTI often needs to be made based on medical history, clinical manifestation, laboratory tests, and imaging examination.[4] In this case report, we discussed a patient with PHPTI who had these findings such as respiratory tract infection as the 1st symptom and diffuse MPC as the symptom characteristic, and treated the patient with a resection of the right parathyroid adenoma.

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2. Case presentation

The patient in the present study was a 49-year-old female patient of Chinese Han ethnicity. One month ago, she had cough with white crude sputum but no blood, but she did not pay attention at that time. On March 9, 2016, the patient visited the emergency our hospital due to aggravated cough and sputum combined with vomiting.

Admission examination: The general examination revealed the following results: body temperature 37.2°C, pulse 90 beats/min, breathing 19 times/min, blood pressure 120/82 mm Hg, no lip cyanosis, and no enlargement of superficial lymph nodes or bilateral thyroid; the breath sound of bilateral lungs was low, and no obvious dry or wet rales were heard.

Laboratory examination: The results of routine blood test are shown in Table 1. The results of electrolyte measurement and liver/kidney function for glycolipid metabolism (fasting) are shown in Table 2, and the result of PTH determination is shown in Table 3.

Table 1

Routine blood test (5 classifications).

Item	Result	Reference	Unit
White blood cell count	10.4×10^9↑	$3.5–9.5 \times 10^9$	/L
platelet count	376×10^9↑	$125–350 \times 10^9$	/L
Thrombocytopenia	0.340%↑	0.05–0.282%	
Red blood cell count	2.73×10^{12}	$4.30–5.80 \times 10^9$	/L
Mean corpuscular volume	97.8↑	82.0–100.0	fL
Hematocrit	0.267↓	40.0–50.0%	
Hemoglobin	83↓	130–175	g/L

Table 2

Electrolyte measurement and liver/kidney function for glycolipid metabolism (fasting).

Item	Result	Reference	Unit
Blood potassium	3.13	3.50–5.50	mmol/L
Blood sodium	141.4	135.0–145.0	mmol/L
Blood chloride	107.2	96.0–106.0	mmol/L
Calcium	3.08	2.08–2.60	mmol/L
α-L-Fucosidase	21	0–45	U/L
β2 microglobulin	5.96↑	0.8–3.0	mg/L
High-density lipoprotein	1.07↓	0.83–1.96	mmol/L
Low-density lipoprotein	2.98		
Albumin	31.5↓	65.0–85.0	g/L
Albumin/globulin	0.92↓	1.2–2.4	
Triglyceride	2.53↑	0.45–1.95	mmol/L
Alkaline phosphatase	238↑	45–125	U/L
Homocysteine	16.5↑	0–18.0	μmol/L

Table 3

Parathyroid hormone determination.

Item	Result	Reference	Unit
Parathyroid hormone	572.80↑	<70	pg/mL
Erythrocyte sedimentation rate	29.00↑	0–20	mm/h
Coagulation spectrum			
D-dimer	0.68 mg/L↑	0.00–0.50	mg/L
international normalized ratio	2.58↑	0.84–1.10	
Partial thromboplastin time	48.8↑	22.4–36.7	S
Prothrombin time	28.0↑	15.0–20.5	S
Plasma fibrinogen	4.36↑	1.90–3.90	g/L

Calcitonin + C-reactive protein (CRP) detection showed a CRP level of 44.4 mg/L. Other examinations (pretransfusion) suggested that the patient was positive for hepatitis B virus (HBV) surface antibody and HBV core antibody.

Sputum culture and drug sensitivity analysis (sputum smear): Sputum culture demonstrated leukocytes <25 and epithelial cells more than 10 per low magnification. The flora was normal, with no fungus or *Hemophilus* identified. The sputum smear was also negative for tuberculosis bacteria.

Chest computed tomography (CT) upon hospitalization showed a diffuse distribution of homogeneous patchy shadows in both lungs (Fig. 1A and B). Transbronchial lung biopsy suggested multiple calcium deposits in the alveolar cavity and alveolar septum (Fig. 1C and Fig. 2A). Whole-body bone emission computed tomography imaging indicated the following: enhanced bone metabolism in bilateral lower extremities and diffusively enhanced radioactive distribution in both lungs (Fig. 3A). ^{99m}Tc-MIBT imaging showed significantly increased MIBI uptake in the right superior pole of the thyroid, suggesting the adenoma of right upper parathyroid (Fig. 3B). Ultrasonography identified a hypoechoic mass ($4.1 \times 1.7 \times 1.9$ cm^3) between the posterior side of the right thyroid lobe and the carotid artery, with clear boundaries, irregular shape, and homogeneous echo. Color Doppler suggested rich blood flow in the mass (Fig. 4A–D). Based on the aforementioned results, common diseases of pulmonary calcification were excluded, such as pulmonary trauma, pulmonary infection (tuberculosis, fungi, and so on), alveolar microlithiasis, and silicosis, and the patient was diagnosed with parathyroid adenoma in combination with MPC. After elementary diagnosis, the patient was transferred to the department of surgery and underwent right parathyroidectomy + right thyroid lobectomy + recurrent laryngeal nerve monitoring + recurrent laryngeal nerve exploration under general anesthesia. Postoperative pathology indicated parathyroid adenoma (Fig. 2B), thus confirming the diagnosis of PHPTI. Tumor cells were mainly chief cells. A few cells were eosinophils, with plenty of interstitial blood vessels. After operation, the patient was 1st sent to the intensive care unit and then to the department of respiration for oxygen inhalation, anti-infection, atomization to reduce phlegm and cough, diuresis, subcutaneous injection of Miacalcic, and supplementation of potassium and iron for symptomatic treatment. Further, 15 days after operation, the patient had blood potassium 3.98 mmol/L (3.50–5.50 mmol/L), sodium 136.2 mmol/L (135.0–145.0 mmol/L), chlorine 102.5 mmol/L (96.0–106.0 mmol/L), and calcium 2.11 mmol/L (2.08–2.60 mmol/L). Cough, sputum, and fever disappeared, and the patient was discharged and followed up for observation. CT review was performed 15 months later, and the patchy shadows in both lungs were obviously absorbed (Fig. 5A and B). PTH determination suggested a PTH level of 62.80 pg/mL (<70 pg/mL).

After the resection of the right parathyroid adenoma, the symptom of the patient such as fever, coughing, and white crude sputum were significantly alleviated.

3. Discussion

The PHPTI is a parathyroid disease-induced autonomic overproduction and secretion of PTH, further leading to hypercalcemia, hypophosphatemia, and hypercalciuria.[5] The etiology of PHPTI is yet to be clarified, but the disease mainly

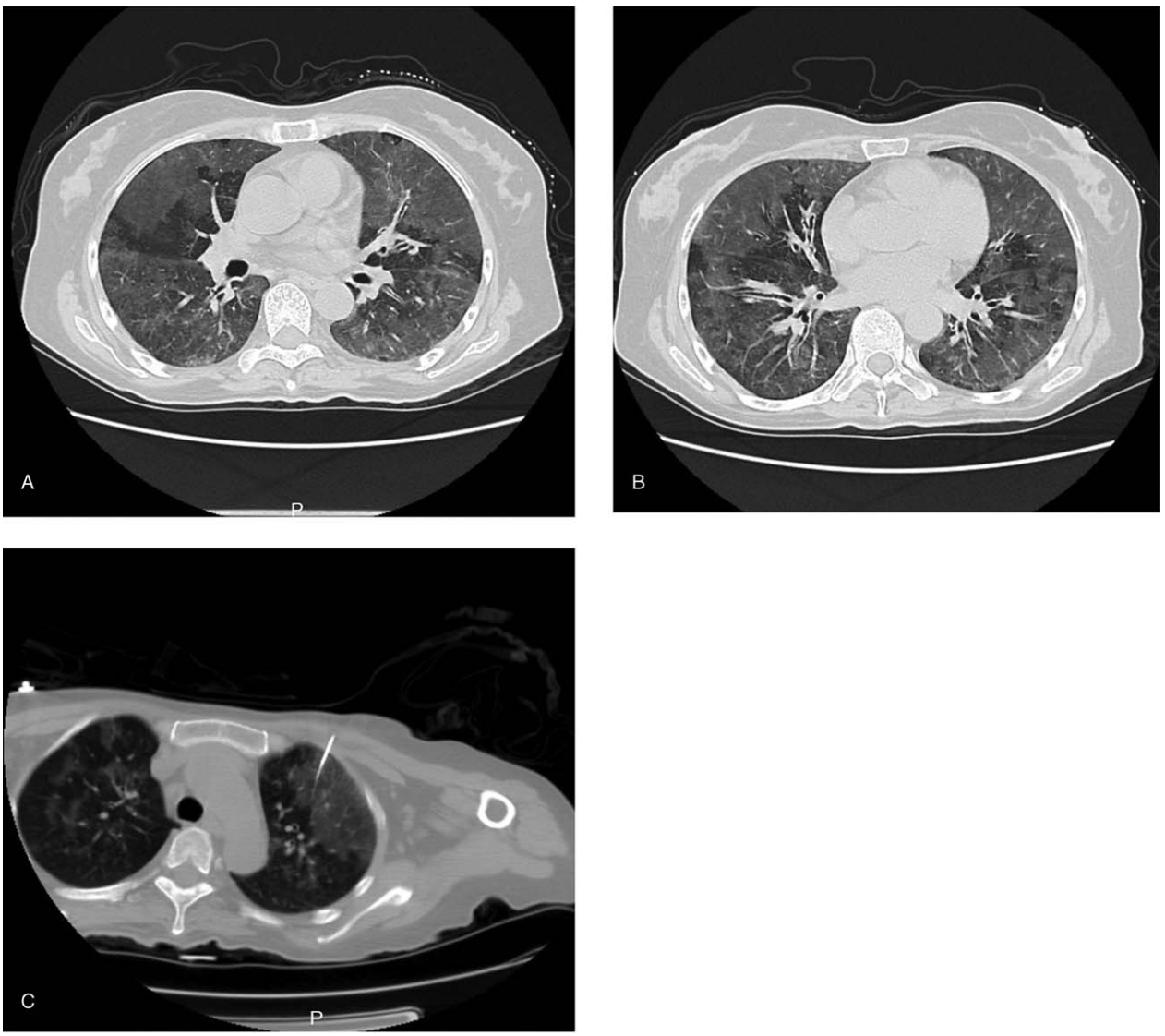

Figure 1. Chest computed tomography of both lungs upon hospitalization. (A and B) Diffuse distribution of homogenous patchy shadows. (C) Multiple calcium deposits in the alveolar cavity and septum.

includes adenoma (80–90%), hyperplasia (15–20%), and adenocarcinoma (1%). The clinical manifestation of PHPTI is complicated. Most patients develop recurrent urinary calculi and bone lesions, while some may also have hypercalcemia-induced neuromuscular excitability, such as fatigue, weakness, nausea, vomiting, constipation, abdominal distention, and so forth.[6] Still, other patients may develop metastatic calcification in joints, myocardium, arterial wall, gastric mucosa, and lung, with related symptoms.[7] Previous studies rarely reported patients with parathyroid adenoma, who also showed respiratory tract symptoms caused by diffuse MPC, because MPCs are mostly patchy and hence do not affect the respiratory function.[8]

The ^{99m}Tc-MIBI dual-phase scintigraphy helps in localizing thyroid lesions. The sensitivity and specificity of this technique are 90.7% and 98.8%, respectively.[9] Surgery is the only effective treatment for PHPTI.[10]

In 1947, Mulligan proposed the concept of MPC for the 1st time, claiming that chronic high levels of calcium and phosphate would cause calcium deposits in the lung tissue, further resulting in secondary calcium metabolic abnormalities but no soft tissue injury.[11] MPC most likely occurs when the calcium–phosphorous product is more than 70, but it may also occur in patients with a normal calcium–phosphorous product. The most common causes include chronic renal failure, primary or secondary hyperparathyroidism, and destructive bone damage.[12]

Usually, MPC does not cause clinical symptoms, but a few patients may develop dyspnea or even respiratory failure. The lung tissue might be hardened and the alveolar septum widened and further fibrillated because the increase in blood calcium could lead to the deposition of calcium salts in normal alveoli, alveolar septum, bronchial wall, and pulmonary vascular wall. Dyspnea might be associated with restrictive dysfunction and

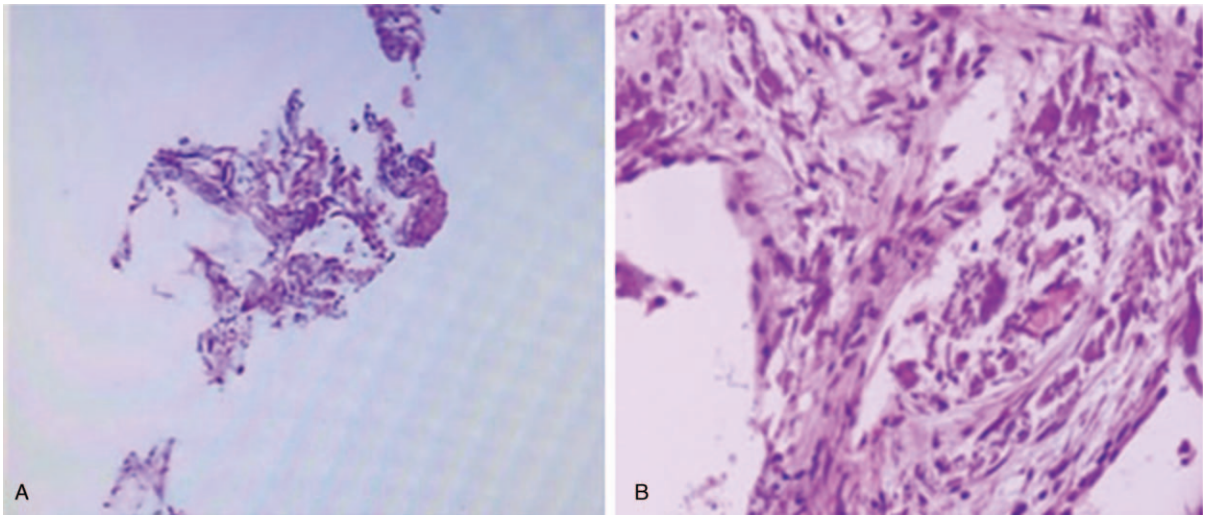

Figure 2. TBLB pathology. (A) Multiple calcium deposits in the alveolar cavity and septum before operation. (B) Parathyroid adenoma indicated by postoperative pathology.

diffusion impairment caused by the excessive deposition of calcium salts in the lungs.[12] The patient in this case study had postactivity asthma, which might be related to excessive pulmonary calcium deposition, further resulting in dysfunctions of ventilation and diffusion. Therefore, early diagnosis and treatment of the primary disease would be of great significance to improve the symptom and prognosis of patients with MPC.

The imaging of MPC lacks specificity. On X-ray examination, the disease manifests as scattered patchy shadows with restricted distribution, whereas on chest CT, it manifests as disperse patchy shadows or ground-glass opacity.[13] Sometimes, it may also show multiple, diffuse, calcified nodules distributed in the interstitial or basal segment of the lung, but diffuse pulmonary calcification is less commonly seen.[14] In this case report, the patient developed diffuse homogeneous calcification in both lungs, which was different from previous studies, and thus reported as a special case.

The patient in this study had clear etiology and was diagnosed with PHPTI based on the results of auxiliary examinations.

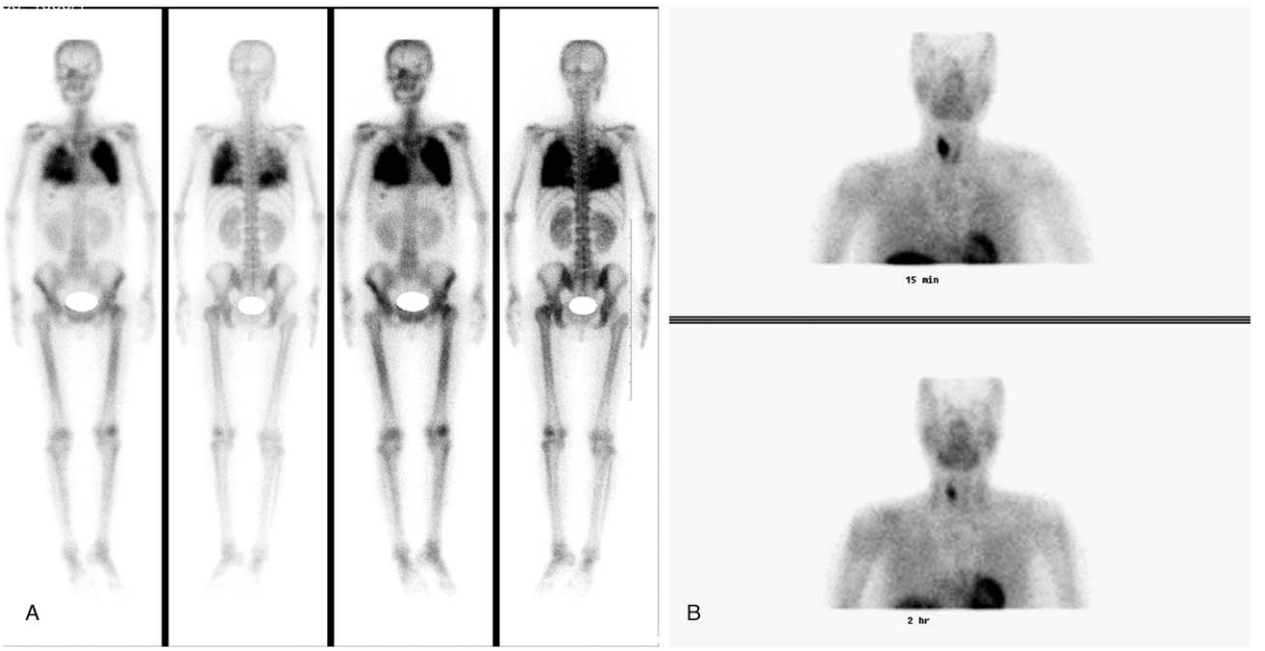

Figure 3. Preoperative whole-body bone emission computed tomography imaging and ^{99m}Tc-MIBI scintigraphy. (A) Enhancement of bone metabolism in bilateral lower extremities, and diffuse enhancement of radioactive distribution in both lungs. (B) Significantly increased MIBI uptake in the right superior pole of the thyroid.

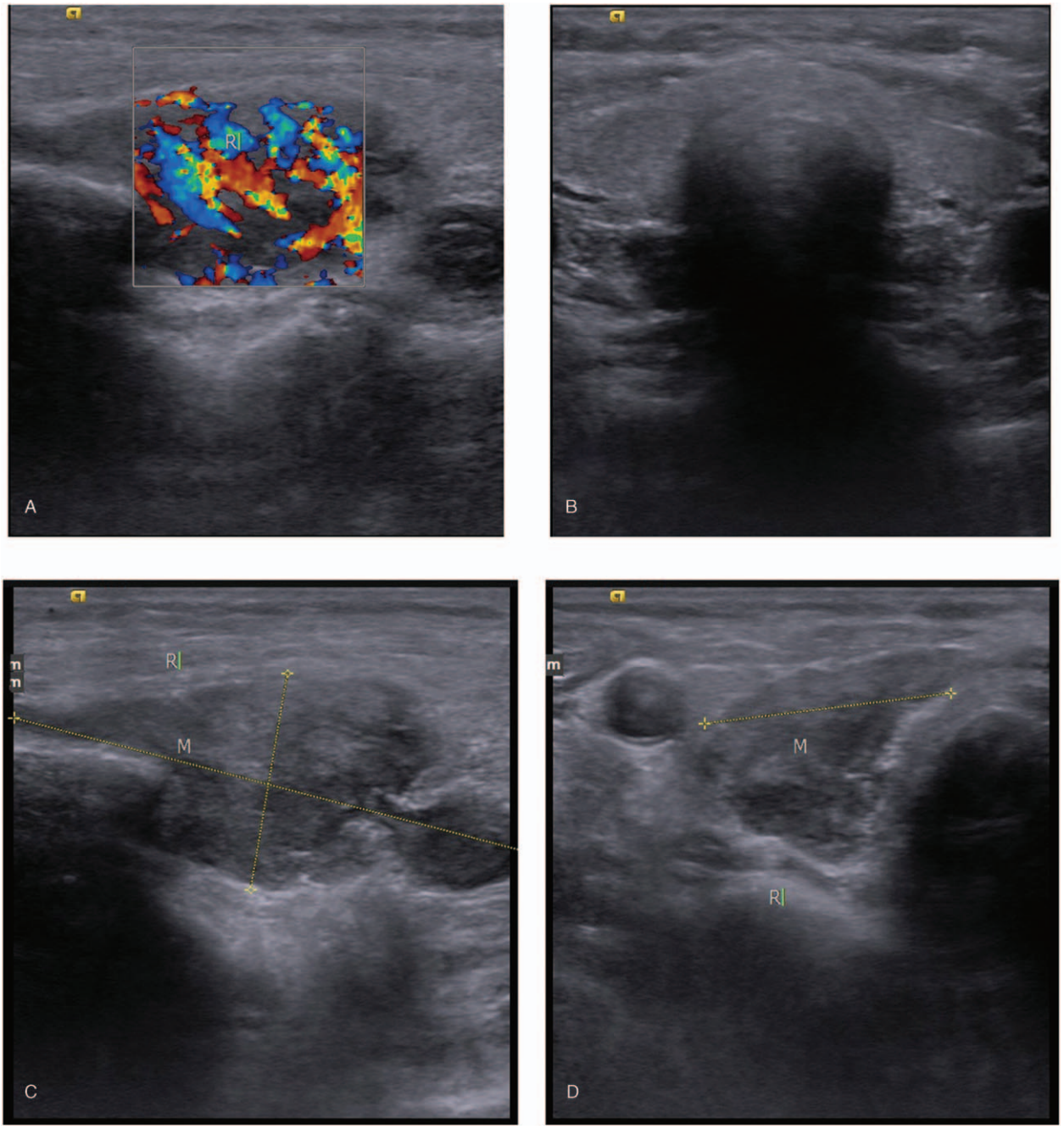

Figure 4. Preoperative color Doppler. (A–D) The hypoechoic mass between the posterior side of the right thyroid lobe and the carotid artery, and rich blood flow signals could be identified within the mass from different orientations.

Pathologic diagnosis after surgical resection suggested parathyroid adenoma. Oversecretion of PTH led to high calcium and low phosphate levels. The patient had a calcium–phosphorus product within the normal range. However, tuberculosis, silicosis, and other common diseases were excluded based on the pathology of bronchoscopic lung biopsy, massive calcific deposition in the alveolar cavity and septum, and disperse patchy shadows in both lungs revealed by CT imaging. Further, considering the imaging results of ^{99m}Tc-MIBI bone scintigraphy, the patient was definitely diagnosed with parathyroid adenoma in combination with MPC.[12,15]

The PHPTI with respiratory tract infection as the 1st symptom and diffuse MPC as the characteristic is rarely seen and can be easily misdiagnosed with lung diseases. If patient 1st developed respiratory tract symptoms and showed multiple diffuse calcification in both lungs, the possibility of MPC should be considered. Parathyroid adenoma could be excluded if further examinations of parathyroid are performed.

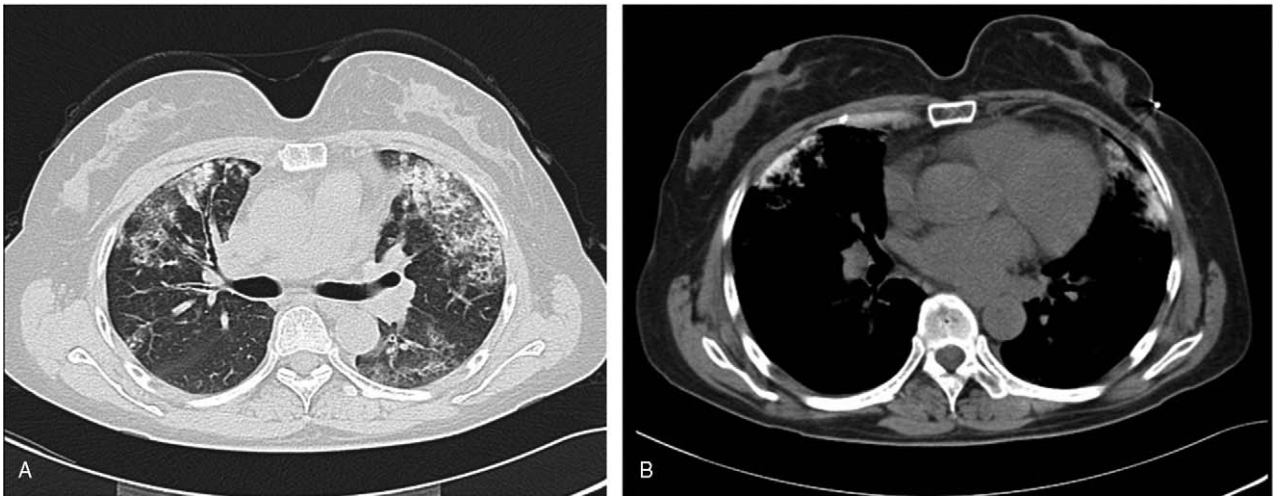

Figure 5. Chest computed tomography performed 15 months after discharge. (A and B) Significantly absorbed patchy shadows.

Author contributions

Investigation: Yuzhu Jia, Lihua Wang, Guangzhao Yang, Guoqun Mao, Yougen Cheng, Yulin Cao.
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Writing – review & editing: Yuzhu Jia, Lihua Wang, Guangzhao Yang, Guoqun Mao, Yougen Cheng, Yulin Cao.

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