

## Rapid Progression of Metastatic Pulmonary Calcification and Alveolar Hemorrhage in a Patient with Chronic Renal Failure and Primary Hyperparathyroidism<sup>1</sup>

만성 신부전과 일차성 부갑상선 기능 항진증이 있는 환자에서 빠르게 진행되는 전이성 폐석회화와 폐포출혈<sup>1</sup>

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Metastatic pulmonary calcification (MPC) is common in patients with chronic renal failure. The authors experienced a patient with chronic renal failure and primary hyperparathyroidism by parathyroid adenoma accompanied with rapid progressions of MPC and alveolar hemorrhage. Recent chest radiographs, compared with previous chest radiographs, showed rapid accumulation of calcification in both upper lungs. Following up on the high-resolution CT scan after five years demonstrates more increased nodules in size and ground glass opacity. The patient was diagnosed with MPC and alveolar hemorrhage by transbronchial lung biopsy. We assumed rapid progression of MPC and alveolar hemorrhage in underlying chronic renal failures could be a primary hyperparathyroidism which may be caused by parathyroid adenoma detected incidentally. Therefore parathyroid adenoma was treated with ethanol injections. Herein, we have reported on CT findings of MPC with alveolar hemorrhage and reviewed our case along with other articles.

### Index terms

Computed Tomography, High-Resolution

Lung, Calcification

Lung, Hemorrhage

Parathyroid, Hyperparathyroidism

## INTRODUCTION

Metastatic pulmonary calcification (MPC) tends to be presented in primary or secondary hyperparathyroidism, such as chronic renal failure. CT scan is a good imaging modality for the detection of a small amount of pulmonary calcification, ground glass opacity (GGO), and nodular opacity in upper- and mid-lung fields. For the reason that findings of early stage of MPC are atypical and similar to those of other diseases, such as pulmonary edema and pneumonia, it is hard to detect and diagnose the MPC early (1, 2). Additional imaging modalities and transbronchial lung biopsy may be obvious means for detection

of MPC (1, 3).

We report on an interesting case in which an initial CT scan showed abnormal findings and thus, following up on the CT scan for five years for typical findings of MPC combined with alveolar hemorrhage.

## CASE REPORT

A 50-year-old male diagnosed with end-stage renal disease was admitted with consistent nausea and emesis. He had renal transplantation 14 years ago. After the transplantation, the patient developed chronic rejections and was treated with an im-

Received March 13, 2013; Accepted April 23, 2013

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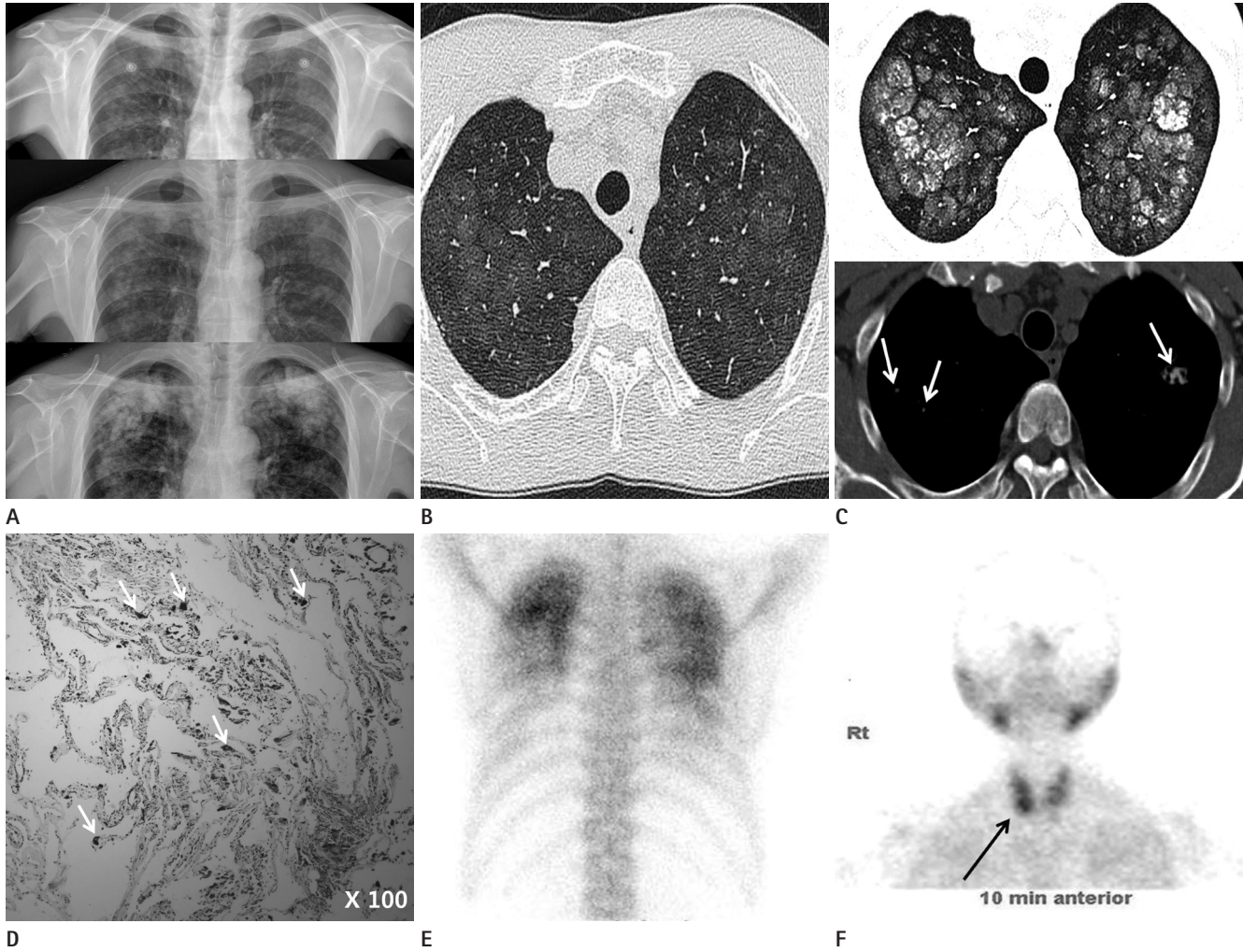
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munosuppressive agent. Since then, he has been dialyzed for seven years. Five years ago, the patient was admitted to our hospital with fever and mild dyspnea. At that time, the laboratory findings indicated leukocytosis and hypercalcemia. Plain radiograph of the chest showed ill-defined nodular opacities in both upper lungs (Fig. 1A).

On this admission, laboratory findings indicated increasing BUN/Cr level of 101.3 (8-20) and 7.31 (0.5-1.3) mg/dL, normal

total Ca/ionized Ca/Mg/P level of 8.83 (8.4-10.2)/4.27 (4-8)/1.91 (1.1-1.7)/4.98 (2.5-4.5) mg/dL, and increasing intact-parathyroid hormone (PTH) level of 1182 (15-68.3) pg/mL.

Chest radiographs for the last six months indicated multiple prominent nodular opacities with calcification and progression of lesion in both upper lung fields (Fig. 1A). In high-resolution CT (HRCT) scans, symmetric centrilobular GGO and prominent calcified nodules that were not seen in previous CT scans



**Fig. 1.** A 50-year-old male with chronic renal failure having metastatic pulmonary calcification.

**A.** Chest radiographs (upper image five years ago, middle and lower images during recent six months, respectively) show more prominent multiple nodules with calcification and rapid progression of metastatic pulmonary calcification in both mid- and upper-lung fields during the recent several months.

**B.** HRCT five years ago shows ill-defined nodules with ground glass opacity in both upper lung fields without calcification.

**C.** HRCT scan (upper image) at last admission shows poorly defined nodular opacities and ground glass opacities. Mediastinal window image with no contrast injection (lower image) demonstrate definite nodular calcifications (arrows) compared with the previous CT scan.

**D.** H&E stained section of the lesion obtained by bronchoscopic biopsy shows calcium deposits as black spots in the alveolar wall and bronchiolar wall (arrows).

**E.**  $^{99m}\text{TcO}_4$  bone scan shows localized radiotracer accumulation representing metastatic pulmonary calcification in both upper lung fields.

**F.**  $^{99m}\text{Tc}$ -MIBI parathyroid scan shows localized hyperdense accumulation demonstrating adenoma at the right lower pole of the thyroid (arrow).

Note.—HRCT = high-resolution CT, MIBI = methy-isobutyl-isonitrile

were observed in both upper lung fields (Fig. 1B, C). Diffuse ground-glass opacity and interlobular septal thickening were also noted. Neither mediastinal lymphadenopathy nor pleural change was seen.

Bronchoscopy was performed and bronchoalveolar lavage (BAL) analysis showed hemosiderin laden macrophages, indicating hemorrhage. Transbronchial lung biopsy demonstrated dystrophic calcification (Fig. 1D) and was negative for cytomegalovirus (CMV) infections.

He was treated with prednisone for alveolar hemorrhage as suspected in CT and BAL analysis. Chest radiographs showed clearer lung fields with regression of multiple nodular opacities.

Additional  $^{99m}\text{TcO}_4$  bone scan was performed for evaluation of pulmonary calcification and disseminated accumulation of calcifications was observed on both upper lungs (Fig. 1E).  $^{99m}\text{Tc}$ -methyl-isobutyl-isonitrile (MIBI) scan was performed for detection of the abnormal parathyroid gland and showed localized nuclear hyper-dense accumulation and delayed washouts in the inferior portion of the right thyroid gland (Fig. 1F). The patient was diagnosed with pulmonary metastatic calcification due to primary hyperparathyroidism. The patient was discharged after ethanol injection of the right parathyroid nodule. The nausea and emesis disappeared and the laboratory findings were changed as follows; BUN/Cr (19.6/2.45 mg/dL), normal ranged total Ca/ionized Ca/Mg/P (9.67/4.75/1.42/3.55 mg/dL), and decreasing intact-PTH (919 pg/mL). Follow-up chest radiographs showed persistent nodular opacity in both upper lungs and no progression of lung lesions.

## DISCUSSION

MPC is the deposition of calcium in the walls of the alveoli and small blood vessels in normal tissue. MPC can occur in diseases such as primary and secondary hyperparathyroidism, chronic renal failure (CRF), hemodialysis, or renal transplantation, intravenous calcium therapy, vitamin D intoxication, infiltrative disease such as sarcoidosis, and bone destruction such as metastasis (1, 4). In an earlier report, MPC was present in 60-80% of patients with chronic renal failure (1, 3). MPC can occur in patients with chronic renal failure; however, coexistence of other diseases, such as opportunistic infections, can also occur easily due to chronic rejections, similar to our case.

Distribution of abnormal pulmonary lesions predominantly in the upper lung zones is very interesting. Apices of both lungs are more alkaline than other regions of lungs due to higher ventilation/perfusion ratio (5). Alkaline apices tend to make it easier for calcium salt to precipitate.

Chest radiograph is insensitive for detecting the MPC. Although dual-energy digital radiography has been shown to be more sensitive than chest plain radiograph, the HRCT scan is more useful than any other imaging modality (2, 6). As mentioned earlier, CT scan was a good detection tool for recognizing the pulmonary calcification and characteristics of MPC (1). Hartman et al. (1) reported that HRCT scan showed various patterns of MPC. The first pattern is that multiple nodular opacities in upper- and mid-lung fields have possibilities of accompanied calcification. The second pattern includes the GGO and patch opacity in diffuse areas of the lung. It also shows the presence of calcification in the vessel of the chest wall. Pulmonary opacity and calcification of vessels are characteristics of MPC. Calcification was not an evident finding in MPC.

Additional  $^{99m}\text{TcO}_4$  bone scan can assist in diagnosis of MPC.  $^{99m}\text{Tc}$ -MIBI and ultrasonogram of the thyroid is useful for detection of abnormal calcium abnormalities. In addition, transbronchial lung biopsy may be an obvious means for detecting the MPC (1-3).

In our case, HRCT findings have changed from centrilobular GGO and nodular opacities predominating in both upper lung fields to increased opacity, size, and numbers of nodules predominating in apices with remaining GGO. Because many pulmonary diseases may display similar findings on CT scan, these findings are non-specific. In our case, the patient took an immunosuppressant agent after his organ transplantation. Therefore, we had to exclude CMV pneumonia and other opportunistic infections (7). In addition, alveolar hemorrhage was considered the reason for detecting the hemosiderin laden macrophages in the BAL fluid where HRCT findings were similar to the HRCT findings of alveolar hemorrhage, which includes patchy or diffused ground-glass opacity, consolidation and interlobular septal thickening. After administering the steroid which is considered the golden standard therapy for alveolar hemorrhage, the GGO on the chest radiograph was regressed. It should be taken into account that alveolar hemorrhage accompanied with MPC can occur in patients with CRF (7, 8).

In most cases, development of MPC occurs slowly or remains at an asymptomatic state. It may also lead to fulminant calcification or rapid respiratory failure combined with other conditions, such as infectious pneumonia, et cetera. However, our case depicted slow development and rapid progression of MPC during a period of several months. Primary hyperparathyroidism by parathyroid adenoma may provoke MPC. Therefore, regular follow-up and close observation for the patient with MPC is important (2, 6). Regular checks of CT scan and additional bone scans can help us to differentiate MPC from other infectious diseases and to diagnose and detect progressions of MPC earlier.

Our case is very interesting and educative in that hypercalcemia with coexistence of chronic rejection after renal transplantation and primary hyperparathyroidism showed slow and rapid changes of MPC for five years and MPC with alveolar hemorrhage caused confusion of accurate diagnosis. We had to regard infectious lung diseases and pulmonary complication of chronic renal failure. We have to account for infectious lung diseases and pulmonary complications of chronic renal failures.

In conclusion, it is our responsibility to perform early diagnosis of MPC in patients with CRF and to determine various findings and changeable imaging patterns under various hormone levels combined with pulmonary lesions.

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# 만성 신부전과 일차성 부갑상선 기능 항진증이 있는 환자에서 빠르게 진행되는 전이성 폐석회화와 폐포출혈<sup>1</sup>

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전이성 폐석회화는 만성 신부전 환자에서 흔하다. 저자들은 신장 이식의 만성 거부로 인한 신부전과 우연히 발견된 부갑상선 선종에 의한 일차성 부갑상선 항진증이 동반된 환자에서 빠르게 진행되는 전이성 폐석회화와 폐포 출혈의 증례를 경험하였다. 예전과 비교하여 최근 흉부 일반 촬영 사진들에서 양측 상폐야에서 빠르게 석회화가 진행됨을 알 수 있었다. 호흡기 증상을 확인하기 위해 시행한 5년 추적 검사 CT에서 결절의 크기와 간유리 음영이 증가하였고 폐포 중심성 석회화를 확인하였다. 기관지를 통한 조직 생검으로 전이성 폐석회화와 폐포 출혈이 확진되었고 우연히 발견된 부갑상선 선종이 원인일 것으로 추정되는 일차성 부갑상선 항진증이 진단되었다. 에탄올 주입으로 치료하였다. 저자들은 폐포 출혈이 동반된 전이성 폐석회화의 증례 보고와 함께 다른 보고들을 소개하고자 한다.

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