

Progressive pulmonary calcification after successful renal transplantation

Masanori Yasuo MD, PhD*, Tsuyoshi Tanabe MD*, Yoshimichi Komatsu MD*,
Kenji Tsushima MD, PhD**, Keishi Kubo MD, PhD*, Kyoko Takahashi MD**,
and Satoshi Kawakami MD, PhD***

* First Department of Internal Medicine, Shinshu University School of Medicine,

** Second Department of Internal Medicine, Shinshu University School of Medicine,

***Department of Radiology, Shinshu University School of Medicine,

Matsumoto, Nagano, JAPAN

Correspondence: Masanori Yasuo

1st Department of Internal Medicine

Shinshu University School of Medicine

3-1-1 Asahi, Matsumoto, Nagano, Japan

Telephone: +81 263 37 2631, Fax: +81 263 36 3722

E-mail address: yasumasa@hsp.md.shinshu-u.ac.jp

Abstract

In 2005, a 46-year-old female consulted our department for an evaluation of a chest radiographic abnormality. She had undergone a successful living renal transplantation in 1999 after being treated by dialysis for four years. A chest computed tomographic scan revealed progressive bilateral fluffy, poorly defined small nodules and the bronchoscopic study revealed a unique linear and nodular lesion pattern. Based on the findings of these modalities, we confirmed the diagnosis of metaplastic pulmonary calcification. This is the first report of these bronchoscopic findings and submucosal calcification in a case of metastatic pulmonary calcification.

Key words: metastatic pulmonary calcification, renal transplantation, tracheobronchial calcification, bone scintigraphy, multi planer reconstruction of the computed tomography

Introduction

Metaplastic pulmonary calcification is known to occur as a complication of chronic renal failure [1-3]. The process is usually seen in the case of untreated renal failure, failed renal transplantation, and during hemodialysis treatment. According to postmortem examinations, about 60% to 80% of patients who received chronic hemodialysis [1, 2], and all patients who received a failed renal transplantation [4] were seen to have pulmonary calcification. The mechanism of this disease is considered to be metastatic, with deposits of a calcium magnesium phosphate complex accumulating in both normal interstitial tissue and bronchovascular tissue in the lung [5]. Because a chest radiograph is not very effective for detecting metastatic pulmonary calcification [1, 6], and no detectable serum markers have yet been reported [1, 2], the premortem diagnosis has thus been considered to be difficult. On the other hand, the ^{99m}Tc bone-imaging agent and high resolution chest computed tomography (HRCT) have also been reported to be useful for the diagnosis of this disease [3, 6]. At present, only two reports have described progressive metastatic pulmonary calcification following a successful renal transplantation [5, 7]. These two reports do not indicate whether the pulmonary calcification was present in the pre-transplant period, as detected by recent radiographic modalities [5, 7].

We herein describe a case of progressive metastatic pulmonary calcification after a successful renal transplantation, which confirms the findings of both pre- and post-transplant chest CT studies. We also obtained unique CT and bronchoscopic findings, and identified the calcification of the bronchus and lung, and the falx cerebri by ^{99m}Tc bone-imaging techniques.

Case Report

In 2005, a 46-year-old female consulted our department for evaluation of a chest radiographic abnormality. The patient had been noted to have proteinuria as a young adult. The patient was diagnosed to have IgA nephropathy and chronic renal failure in 1995. She was treated by continuous ambulatory peritoneal dialysis for four years. In 1997, she underwent a total parathyroidectomy and autotransplantation of the parathyroid glands for the treatment of secondary hyperparathyroidism. She had sought renal transplantation from 1996. She began to be treated by chronic hemodialysis from January 1999, and she received a living renal transplantation from her brother in July 1999. After undergoing a parathyroidectomy, neither calcium nor phosphorus serum abnormalities were observed. The serum parathyroid hormone level was also normal. Her chest radiograph findings also became normal. However, her chest CT scan,

which was performed in the pre transplantation evaluation, revealed diffuse ground glass opacity in the bilateral lung fields (Fig. 1a). After the renal transplantation, no serum or hematological abnormality, including that of the parathyroid hormone level, was detected, and she was maintained on a daily dose of 3 mg of FK506 and 2.5 mg of prednisolone. Her chief physician planned a general survey because several years had passed since her renal transplantation. A chest CT study was performed in 2005. The CT revealed a diffuse ground glass opacity in the bilateral lung fields, and some high density areas were also seen in the bilateral upper lung fields (Fig. 1b). These findings had progressed in comparison to the CT study performed in 1999 (Fig. 1a). The ground glass opacity appeared as a centri-lobular group of fluffy, poorly defined small nodules by HRCT (Fig. 1c). Furthermore, multiplanar reconstruction (MPR) of the CT scans revealed severe tracheobronchial cartilaginous calcification (Fig. 1d). Pulmonary function studies showed both a mild restrictive component and some decrease in the diffusing capacity. A fiberoptic bronchoscopic examination demonstrated a unique linear appearance and some nodular white bulges (Fig. 2a), and a biopsy of the nodular lesion demonstrated submucosal calcification (Fig. 2b). A transbronchial lung biopsy revealed alveolar wall calcification (Fig. 2c). The diagnosis of metastatic pulmonary calcification was made. Since bone scintigraphy has been reported to be potentially

useful in the detection of this disease [3], we performed ^{99m}Tc bone scintigraphy. As expected, the findings of a scintigraphic study showed an intense uptake in both lungs (Fig. 3a). Furthermore, the agent accumulated in the falx cerebri (Fig. 3a, arrow), as was noted when we examined the brain with a CT scan. The CT study revealed a massive calcification of the falx cerebri (Fig. 3b). The patient continues to have no pulmonary symptoms at the present time.

Discussion

A case of progressive metastatic pulmonary calcification is herein presented. To our knowledge, this is only the third case of progressive pulmonary calcification in a successful renal transplant recipient, and this was the first case in which the progression was clarified by a CT study, before it was detected by a chest roentgenographic study. Furthermore, the MPR of the CT findings and associated bronchoscopic findings were also described for the first time.

Soft tissue calcification including pulmonary calcification tends to be identified in dialysis patients significantly more frequently than in nondialysis patients [2]. Although the soft tissue calcification most frequently involves the heart, lungs, stomach, and kidneys [2], the lung is the most frequent visceral site of metastatic calcification [8].

The cause for the calcium deposition is still not fully understood, but several potential causes have been discussed. The secretion of free hydrogen ions is an important local factor. Three of the above most frequently involved organs are concerned with the secretion of free hydrogen ions. This secretion creates an alkaline milieu in which calcium salts may precipitate. This is the reason why it has been postulated that acidosis in the interdialytic interval leaches calcium from bone which is then deposited in soft tissue during the post dialysis alkalosis in dialysis patients [8]. Furthermore, an imbalance of the calcium and phosphorus metabolism may induce metastatic calcification. Chronic renal failure, unsuccessful renal transplantation, primary and secondary hyperparathyroidism and D hypervitaminosis are well known causes of this disease. No correlation has been observed with levels of parathyroid hormone, calcium, creatinine, alkaline phosphatase or albumin, history of parathyroidectomy, duration of hemodialysis, and with the type of dialysate [9]. The present case has not demonstrated a calcium-phosphorus imbalance since undergoing a successful renal transplantation, however, pulmonary calcification appeared to be worsening in this patient. Because this case is only the third case to demonstrate progressive pulmonary calcification occurring after a successful renal transplantation, the precise mechanism of this disease progression remains unknown.

In many of the previous reports, especially those published before the 1980's, the premortem diagnosis of this disease was reported to be difficult [1, 2]. Since that time, however, the usefulness of several radiological modalities has been reported, such as the use of ^{99m}Tc bone-imaging agents and HRCT. Coolens et al reported that scintigraphy can be useful, especially in the diagnosis of early pulmonary calcifications because of the high frequency of radiographically-negative, and scintigraphically-positive results [3]. Hartman et al described seven metastatic pulmonary calcification patients [6]. In that study, all of the patients had positive findings on chest CT studies, and fluffy, poorly defined small nodules were the most common findings in HRCT [6]. In the present case, HRCT showed fluffy, poorly defined small nodules, and also the ^{99m}Tc bone-imaging agent accumulated substantially in the bilateral lung fields. A bone scintigraphic study also revealed an accumulation in the falx cerebri, while a brain CT study demonstrated the massive calcification of the falx cerebri. In addition, the HRCT findings in our case resembled those of hypersensitivity pneumonitis, a differential diagnosis relatively easy to confirm based on other clinical findings. In our case, the pulmonary calcification was initially detected before the patient underwent renal transplantation.

Because about 80% of hemodialysis patients tend to have metastatic pulmonary

calcification [2], her pulmonary calcification before transplantation was not surprising. However, the pretransplant CT findings were useful for comparison purposes with the post transplantation findings of the CT study. To our knowledge, no reports to date have described the bronchoscopic findings and the presence of central airway calcifications in such a patient. In our case, severe tracheobronchial cartilaginous calcification was revealed by MPR of chest CT scans and both a unique linear appearance and some small nodular white bulges were revealed by a fiberoptic bronchoscopic examination. The lesion identified by bronchoscopy was proven to be submucosal calcification by a transbronchial biopsy. Likewise, alveolar wall calcification was identified by a transbronchial lung biopsy.

Usually, the majority of such patients are asymptomatic during their clinical course. In contrast, some patients have been reported to demonstrate fulminate respiratory failure [10]. Although our patient did not have any pulmonary symptoms for more than seven years, we nevertheless began to administer appropriate treatment during her clinical course.

In summary, we herein reported a case of progressive metastatic pulmonary calcification who was able to successfully undergo a renal transplantation. The unique bronchoscopic findings, and the pre and post transplant CT findings were obtained.

Although a premortem diagnosis has been reported to be difficult to establish in this disease, recent imaging modalities may therefore be useful both for accurately making a premortem diagnosis and for planning the clinical follow-up and further care.

References

1. Conger JD, Hammond WS, Alfrey AC, Contiguglia SR, Stanford RE, Huffer WE.
Pulmonary calcification in chronic dialysis patients. Clinical and pathologic studies.
Ann Intern Med **83**: 330-336, 1975.
2. Kuzela DC, Huffer WE, Conger JD, Winter SD, Hammond WS. Soft tissue
calcification in chronic dialysis patients. *Am J Pathol* **86**: 403-424, 1977.
3. Coolens JL, Devos P, De Roo M. Diffuse pulmonary uptake of ^{99m}Tc
bone-imaging agents: case report and survey. *Eur J Nucl Med* **11**: 36-42, 1985.
4. Fairshter RD, Vaziri S, Farooqui S, Martin D. Pulmonary pathology in renal
transplant recipients. *Int J Artif Organs* **7**: 327-330, 1984.
5. Breitz HB, Sirotta PS, Nelp WB, Ott S, Figley MM. Progressive pulmonary
calcification complicating successful renal transplantation. *Am Rev Respir Dis*
136:1480-1482, 1987.
6. Hartman TE, Muller NL, Primack SL, et al. Metastatic pulmonary calcification in
patients with hypercalcemia: findings on chest radiographs and CT scans. *AJR Am J*
Roentgenol **162**: 233-238, 1994.

7. Murriss-Espin M, Lacassagne L, Didier A, et al. Metastatic pulmonary calcification after renal transplantation. *Eur Respir J* **10**: 1925-1927, 1997.
8. Neff M, Yalcin S, Gupta S, Berger H. Extensive metastatic calcification of the lung in an azotemic patient. *Am J Med* **56**: 103-109, 1974.
9. Sanders C, Frank MS, Rostand SG, Rutsky EA, Barnes GT, Fraser RG. Metastatic calcification of the heart and lungs in end-stage renal disease: detection and quantification by dual-energy digital chest radiography. *AJR Am J Roentgenol* **149**: 881-887, 1987.
10. Mootz JR, Sagel SS, Roberts TH. Roentgenographic manifestations of pulmonary calcifications. A rare cause of respiratory failure in chronic renal disease. *Radiology* **107**: 55-60, 1973.

Figure Legends

Figure 1 a; Chest computed tomography (CT) in 1999. A diffuse ground-glass opacity was seen in the bilateral lung field. b; A chest CT study performed in 2005. The diffuse ground-glass opacity had progressed, and calcification was seen in the bilateral upper lung fields. c; A high resolution chest CT scan demonstrated diffuse fluffy, poorly defined small nodules. d; Multi-planar reconstruction of the CT scans clearly revealed severe tracheobronchial cartilaginous calcification.

Figure 2 a; The bronchoscopic findings demonstrated a unique linear appearance and some nodular white bulges (arrows). b; The transbronchial biopsy showed submucosal calcification (*). c; The transbronchial lung biopsy showed alveolar wall calcification.

Figure 3 a; ^{99m}Tc bone scintigraphy showed intense bilateral lung and falx cerebri (arrow) accumulation. b; A brain CT scan demonstrated massive calcification of the falx cerebri.