

Pulmonary Chondroid Hamartoma With Nontuberculous Mycobacterial Infection

Two Case Reports

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Abstract: Solitary pulmonary nodules (SPNs) can be manifested in a variety of disorders including neoplasms, infection, inflammation, and vascular or congenital abnormalities. In addition, they are often accompanied with other pulmonary pathologic lesions such as consolidations and several pulmonary disorders present as similar pulmonary nodular lesions simultaneously. Diagnostic workup is important for these SPNs; however, many physicians often miss the second diagnosis for multiple pulmonary lesions with SPNs due to lack of clinical suspicion that each pulmonary nodule or pathologic lesion can have each other's diagnosis.

Herein, we report 2 cases of coexistence of pulmonary chondroid hamartoma with nontuberculous mycobacterial (NTM) infection presenting as pulmonary nodules and multiple consolidative lesions. A 60-year-old man was admitted for the evaluation of multifocal pulmonary lesions including SPN with chronic exertional dyspnea. Multiple lung tissues were obtained from each lesion through percutaneous transthoracic needle biopsy (PTNB). At the same time, bacteriologic examination was performed using respiratory samples obtained by bronchoscopy. Based on pathologic and microbiologic results, the patient diagnosed as pulmonary chondroid hamartoma with pulmonary NTM infectious disease. In addition, a 56-year-old woman visited for the evaluation of a small SPN. The SPN was resected surgically for the pathologic examination and turned out to be pulmonary chondroid hamartoma. Interestingly, the diagnostic workup revealed that the patient had Lady Windermere syndrome which is one of features for *Mycobacterium avium* complex (MAC) pulmonary disease. Both

patients were treated with the standard antibiotics against MAC as recommended by the ATS/IDSA guideline.

This is the first report of 2 patients, as far as we know, that chondroid hamartoma and NTM disease develop simultaneously in the lung. This report emphasizes that physicians should endeavor to confirm the individual diagnosis for the various pulmonary abnormal lesions detected at the same time, if necessary through multifocal biopsies for each lesion.

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Abbreviations: CT = computed tomography, HRCT = high-resolution computed tomography, NTM = nontuberculous mycobacterial, PTNB = percutaneous transthoracic needle biopsy, SPNs = solitary pulmonary nodules.

INTRODUCTION

The majority of solitary pulmonary nodule (SPN) cases represent either lung cancers or benign granulomas, and these conditions occur with roughly equal frequency.¹ The most common cause of benign granulomas is tuberculosis; this is particularly true in tuberculosis-endemic regions.²

Hamartoma is defined as an abnormal mixture of tissue elements or an abnormal proportion of a single element, normally present in an organ. Pulmonary chondroid hamartoma is the most common benign neoplasm arising in the bronchial wall and accounts for 7% to 14% of all SPNs.³ Usually they present as asymptomatic SPNs, with gradually increasing in size. Thus, they need to be differentiated from lung malignancies.

The radiographic findings of nontuberculous mycobacterial (NTM) lung disease are variable, depending, in part, on the species. Similar to other granulomatous infections, NTM infection can occasionally result in the formation of an SPN, in which the majority of these lesions were detected incidentally. Although NTM infections can be found as cavitary or bronchiectatic lesions predominantly, they can present as consolidation or infiltration in the lung.⁴

Based on this information, we can guess the overlap of radiologic findings among various pulmonary disorders. However, in clinical practice, physicians often miss the coexistence of 2 diseases due to lack of clinical suspicion. In this report, we describe 2 cases of coexisting pulmonary chondroid hamartoma with NTM.

CASE REPORT

Case 1

A 60-year-old man was admitted for the evaluation of a 1.5 × 1.5-cm-sized SPN on the right upper lobe and a 1.4 × 7.2-cm-sized subpleural consolidation on the left lower

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lobe on a chest computed tomography (CT) (Figure 1). He was an exsmoker of 50 pack-years. He complained mild dyspnea on exertion which had been maintained for several years. However, there was no acute clinical manifestation such as cough, fever, night sweating, and so on. To confirm the diagnosis, we performed percutaneous transthoracic needle biopsy (PTNB) for the SPN and the linear consolidation. Interestingly, one was turned out to be pulmonary chondroid hamartoma, and the other was defined as chronic granulomatous inflammation with necrosis (Figure 2). In addition, *M. intracellulare* was identified in bronchial washing fluid from left lower lobes of the lung, suggesting that the granulomatous inflammation was associated with *M. intracellulare* infection.

The patient received a combination therapy of rifampin (450 mg/day), ethambutol (800 mg/day), and clarithromycin (1000 mg/day) for pulmonary NTM disease on a daily basis, and the treatment was scheduled to keep till at least 12 months after the negative conversion of NTM on microbiological examination, as recommended by the ATS/IDSA guideline. Surgical resection was also planned for the pulmonary chondroid hamartoma on the right upper lobe. He had no complications at 10 months follow-up.

Case 2

A 56-year-old woman visited our clinic due to an SPN detected incidentally in high-resolution computed tomography (HRCT) during routine medical checkup. A month ago, she had been diagnosed with pneumonia and treated with an empirical antibiotic regimen of cefpodoxime and roxithromycin. She had completely recovered after the oral antibiotic therapy. Later, she was notified that *M. avium* was identified in sputum expectorated during the diagnostic workup. At the visiting time for the evaluation of SPN, she had no respiratory symptoms and complaints. HRCT revealed that her radiologic findings were focal bronchiectatic change with consolidations in the right

middle lobe and left lingular segment as well as an SPN in the right lower lobe (Figure 3). First of all, to diagnose the SPN histologically, the SPN was resected surgically from the right lower lobe and the pathologic diagnosis of the SPN was chondroid hamartoma (Figure 4), while the patient also underwent the bronchoscopy to obtain the respiratory specimens and the repeated sputum examinations for the diagnosis of pulmonary NTM according to the ATS/IDSA guideline for NTM.⁵ The microbiological examination revealed that *M. avium* was identified again in bronchial washing fluids obtained from the patient. Finally, the workup for her radiologic abnormalities confirmed coexistence of pulmonary chondroid hamartoma with NTM infection. Therefore, she started to take the medication for NTM infection with rifampin (600 mg/day), ethambutol (1000 mg/day), and clarithromycin (1000 mg/day) on a daily basis. According to the ATS/IDSA guideline, the treatment with this regimen was planned to keep till at least 12 months after the negative conversion of NTM on microbiological examination. She had no complications at 12 months follow-up.

DISCUSSION

Hamartoma is an abnormality of growth, first accurately described by Albecht in 1904.⁶ Pulmonary hamartomas are the most common benign tumors of the lung, and they comprise an admixture or overgrowth of various or single normal component(s). Depending on the predominant component, pulmonary hamartomas can be subdivided into various subtypes: chondromatous, leiomyomatous, lymphangiomyomatous, adenofibromatous, and fibroleiomyomatous. Chondroid hamartomas are the most common subtype and have been divided into endobronchial and intraparenchymal lesions. The onset of the tumor is in adulthood, with the peak age incidence in the fourth to sixth decade.⁷ Clinically, they usually present as an asymptomatic SPN. Sometimes, multiple cystic hamartomas are misdiagnosed as pulmonary metastasis.

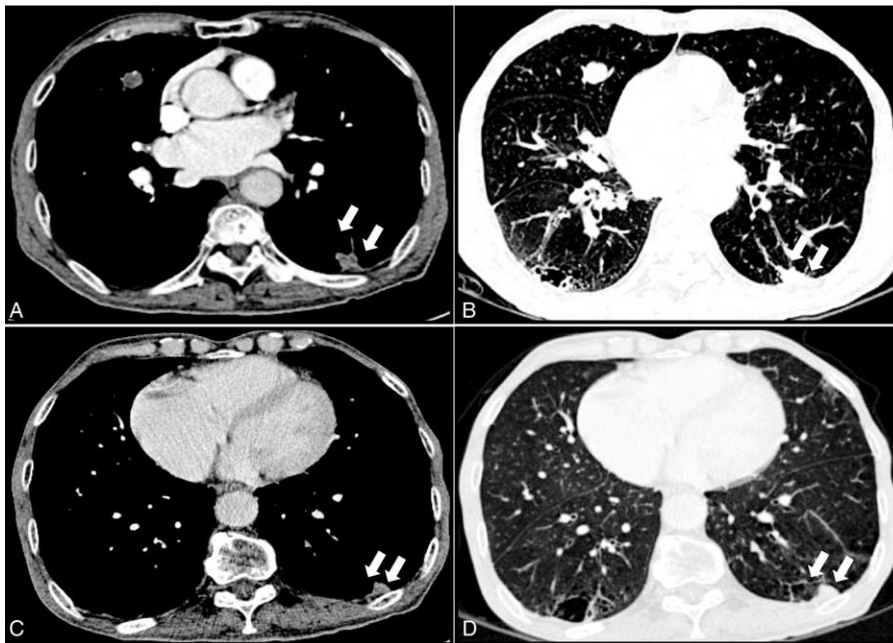


FIGURE 1. CT scan images for a 1.5-cm-sized round, heterogeneous enhanced nodule on the right upper lobe anterior segment and 1.4 × 7.2-cm-sized linear subpleural consolidation (arrows) on the left lower lobe posterior segment are observed (A and C, mediastinal window view, B and D, lung setting view). CT = computed tomography.

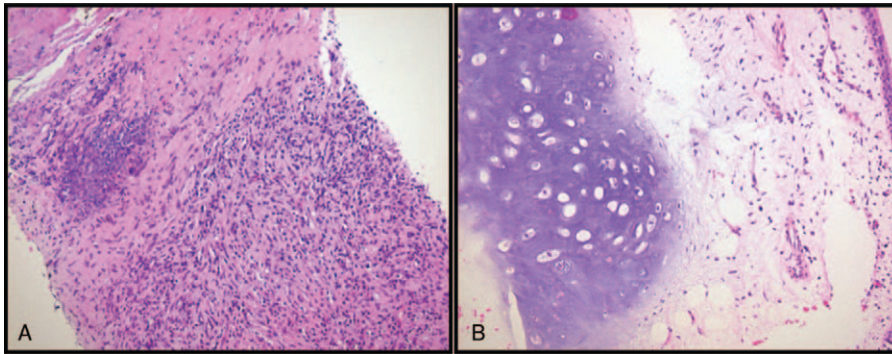


FIGURE 2. Microscopic features of chondroid hamartoma and chronic granulomatous inflammation. (A) Chronic granulomatous inflammation, consisting of aggregation of epithelioid cells, surrounded by lymphocytes. And necrosis is also present (H&E stain, ×40). (B) Prominent chondroid component is located underneath the respiratory epithelium (H&E stain, ×100). H&E = Hematoxylin & Eosin.

Pulmonary NTM infections often occur in the context of preexisting lung disease, especially chronic obstructive pulmonary disease (COPD), bronchiectasis, pneumoconiosis, cystic fibrosis, and previous tuberculosis.⁵ In particular, bronchiectasis is the most well-defined underlying structural lung disease linked to develop pulmonary NTM diseases. A recent report has demonstrated that 20% of cystic fibrosis patients and 10% of primary ciliary dyskinesia patients have NTM recovered from respiratory specimens.⁵ In addition, an NIH study has noted a higher incidence of cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations (36%) in patients with pulmonary NTM diseases compared with a matched control population.⁸ As a result, the clinical manifestations of NTM lung disease are often similar to those of the underlying disease such as bronchiectasis. These include cough, fatigue, malaise, fever, weight loss, dyspnea, hemoptysis, and chest discomfort. These same symptoms are also present in patients with NTM lung disease who do not have preexisting pulmonary disease. In addition, the NTM lung disease is often diagnosed by the identification of NTM on respiratory specimens in cases under evaluation for pulmonary tuberculosis.

As for the prognosis, to date, the natural history of the development of NTM lung disease and/or bronchiectasis remains incompletely understood.⁹ However, some studies have suggested that coexisting cavitary lung disease and COPD are adverse prognostic factors for response to the treatment for NTM infection.¹⁰

The radiographic findings of NTM lung disease are variable, depending on the mycobacterium species. Findings

consistent with pulmonary NTM infection on chest radiograph or HRCT scan include nodular or reticulonodular infiltrates, cavities, multifocal bronchiectasis, and/or multiple small nodules. Therefore, the radiologic features are in broad spectrum which can cover the other pulmonary nodular diseases. This overlap makes us realize the need for the differential diagnosis and the possibility for coexistence of various pulmonary disorders. However, in many cases, physicians are apt to make a single diagnosis on the combined radiologic features such as nodules and bronchiectasis.

As for the overlap of radiologic findings between pulmonary NTM and hamartoma, since the majority of hamartomas exhibit coin lesions, that is, round nodule with clear margin, on CT scan and chest x-ray with variable size,¹¹ whereas pulmonary NTM has a variety of radiologic features. The radiologic image shared by both diseases seems to be a round nodular lesion which makes the physicians confuse to diagnose them.

In our cases, the case 1 patient had a linear nodular consolidation which is an uncommon presentation in NTM on the left lower lobe and underlying severe emphysematous changes. The case 2 patient had ill-defined multiple consolidations on the right middle lobe with typical focal bronchiectatic changes without any other underlying lung disease, so-called Lady Windermere syndrome.¹² Moreover, both of them had an SPN with clear margin and similarity to granuloma, interestingly confirmed as pulmonary hamartomas through pathologic analyses. Both pulmonary hamartoma and NTM lung disease can manifest the same or similar radiologic findings, SPNs, however, the therapeutic approach is different; one is medical

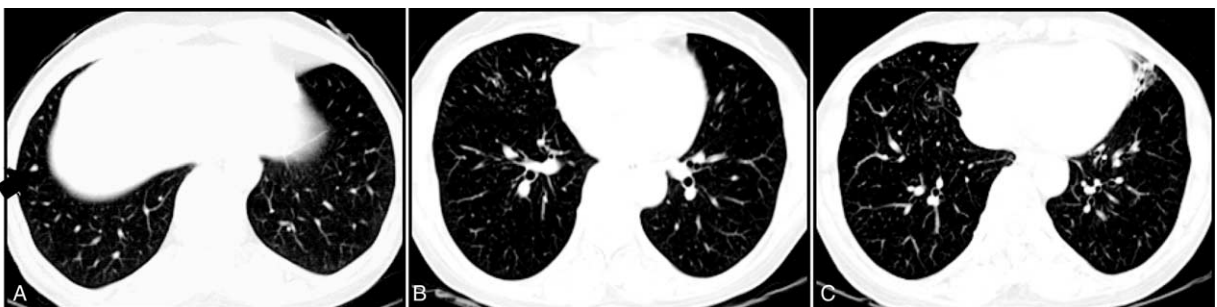


FIGURE 3. A 5-mm-sized SPN (arrow) is shown on the right lower lobe (A). There are focal consolidations with bronchiectatic changes on the right middle lobe (B) and left lingular segments (C). SPN = solitary pulmonary nodule.

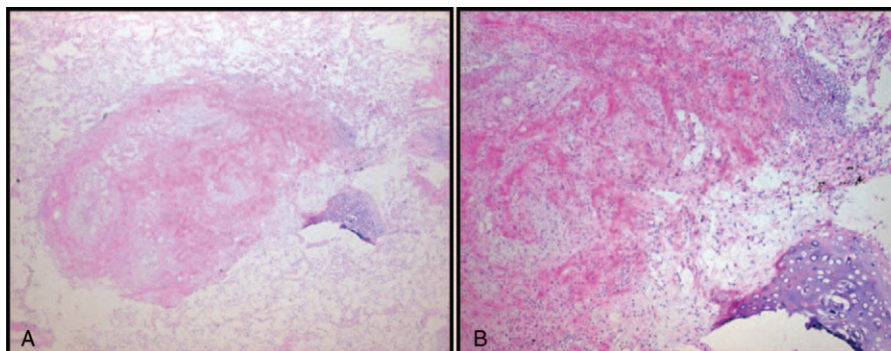


FIGURE 4. Microscopic features of chondroid hamartoma of the lung. (A) Tumor component is identified within the normal lung alveolar structures (H&E stain, $\times 40$). (B) Most of the tumor was composed of proliferating connective tissue. Mature cartilaginous tissue was also identified (right lower side) (H&E stain, $\times 100$). H&E = Hematoxylin & Eosin.

therapy and the other is surgery. Since the majority of hamartomas exhibit the benign prognosis, it may be overlooked to distinguish them developed simultaneously; however, we should remember the importance of correct diagnosis for persistent pathologic lesions unresolved by treatment and the minimal potential of benign tumor to be malignant.

In summary, we report 2 interesting and similar cases of coexistence of pulmonary chondroid hamartoma with NTM infection for the first time. On the basis of our experiences with these rare conditions, we would like to emphasize that physicians should have clinical suspicion for the radiological overlap among various pulmonary diseases and consider multifocal biopsies or surgical resections for the differential diagnosis between single disease and coexisting diseases showing similar radiological features.

ETHICAL REVIEW AND PATIENT CONSENT

The Institutional Review Board (IRB) of Chonbuk National University Hospital has stated that it is not necessary to achieve IRB approval for this case report and this report requires obtaining patient consent because this study is dealt with only the patient's medical record and related images, retrospectively. Written informed consent of this case report and accompanying images was obtained from the patient for the publication.

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