Case Report

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Caplan Syndrome Mimicking Progressive Massive Fibrosis on CT: A Case Report

CT에서 가속화된 진행성거대섬유증으로 오인된 카플란 증후군: 증례 보고

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This report presents a unique case of Caplan syndrome that mimicked accelerated progressive massive fibrosis. The patient, a former coal miner, had been diagnosed with coal worker's pneumoconiosis 15 years prior and had been treated for rheumatoid arthritis for over 20 years. Accelerated progressive massive fibrosis and the development of multiple nodules with cavitation in the basal lungs were subsequently observed on serial CT scans. Here, the CT manifestations of Caplan syndrome are highlighted in a case in which Caplan syndrome mimicked accelerated progressive massive fibrosis.

Index terms Caplan Syndrome; Rheumatoid Nodule; Pneumoconiosis; Multiple Pulmonary Nodules; Arthritis, Rheumatoid

INTRODUCTION

Caplan syndrome, also known as rheumatoid pneumoconiosis, is characterized as the presence of multiple pulmonary nodules in the lung periphery and occurs in individuals with a history of inorganic dust exposure and rheumatoid arthritis (RA) (1). Diagnosing Caplan syndrome in clinical practice remains challenging owing to an overlap of radiological features with those of complicated pneumoconiosis. While there are numerous reports concerning the radiographic manifestations of the disease, there is a scarcity of literature detailing the CT manifestations of Caplan syndrome, especially the development of accelerated progressive massive fibrosis (PMF) on serial CT scans. In this report, we describe a patient with Caplan syndrome who exhibited PMF that worsened over time, with an emphasis on evolving CT findings.

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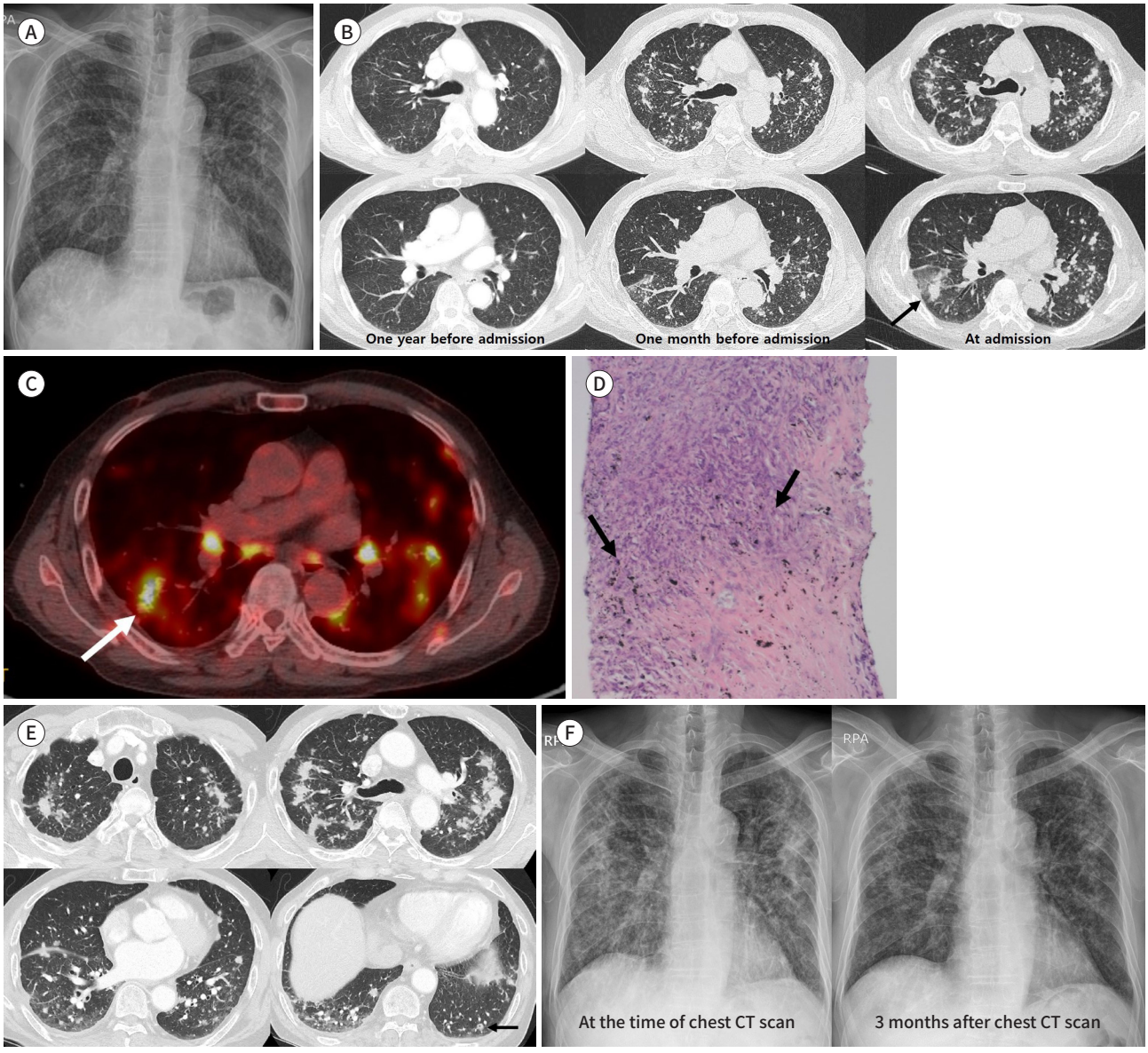
CASE REPORT

A 76-year-old man previously diagnosed with both pneumoconiosis and RA was admitted to our hospital and a follow-up CT scan revealed a growing nodule. The patient had been a coal miner for 10 years prior to quitting his job two decades before admission to our hospital. He had been diagnosed with coal worker's pneumoconiosis 15 years prior. Laboratory data indicated elevated C-reactive protein (CRP) (12.04 mg/dL) and rheumatoid factor (RF) (166.6) levels. Chest radiography on admission showed small round nodular opacities with slight high-density dominance in both upper lungs (Fig. 1A). Low-dose CT revealed small nodules (3–26 mm in diameter) in both lungs. These nodules exhibited random and perilymphatic distributions in the peribronchovascular area, predominantly in the bilateral upper lobes. Some of the nodules had conglomerated to form larger nodules and were accompanied with mild fibrotic bands consistent with pneumoconiosis (Fig. 1B). Certain conglomerated nodules showed partial calcification or high attenuation. Slightly enlarged mediastinal lymph nodes with slightly high attenuation (50–70 Hounsfield units) were observed. Scanty pleural effusion was also noted on the right side (not shown). When compared with CT scans taken one month earlier at another hospital, the nodules appeared to be enlarging and conglomerating (Fig. 1B). Even within the month prior to admission, the nodules had significantly increased in size and number (Fig. 1B). Given the relatively rapid progression of the nodules, the patient underwent PET and a CT-guided percutaneous lung biopsy of a 26 mm nodule in the right lower lobe (Fig. 1B, C) to exclude coexisting malignancy. The PET/CT scans indicated that multiple nodules and mediastinal lymph nodes were hypermetabolic (maximum standardized uptake value, 9.1 in a nodule in the right lower lobe) (Fig. 1C). Subsequent histopathological analysis of the lung biopsy specimen revealed necrotizing granulomas with anthracotic centers. Acid-fast bacilli (AFB), polymerase chain reaction for *Mycobacterium tuberculosis*, and Grocott's methenamine silver stains were negative (Fig. 1D). Considering the patient's history, this presentation was initially considered a manifestation of pneumoconiosis. However, after four years, repeat imaging was performed owing to an elevated CRP (12.04 mg/dL) level (Fig. 1E). CT findings indicated that the nodules had further progressed to form irregular masses accompanied with linear fibrotic bands in both upper lobes, resembling PMF. Multiple random perilymphatic nodules with or without cavitation had developed in the basal areas of both lower lobes (Fig. 1E). The pleural effusion had resolved, but mild pleural thickening remained on the right side compared with previous CT scans. Suspecting rheumatoid nodules and Caplan syndrome, specimens from a lung biopsy performed four years prior were reviewed. Necrotizing granulomas appeared to be surrounded with a rim of palisading histiocytes that closely resembled rheumatoid necrobiotic nodules. No pneumoconiotic dust particles were observed. The patient had been receiving oral medications (specifics not known) since being diagnosed with RA 20 years beforehand and was treated with leflunomide and methotrexate following admission to our hospital. Leflunomide treatment was switched to oral tacrolimus after two years. The most recent chest radiograph taken three months after the last CT scan revealed a decrease in the size of the irregular conglomerated masses in both upper lungs (Fig. 1F).

This report was approved by the Institutional Review Board of our institution, which waived the requirement for informed consent (IRB No. 2023-07-070).

Fig. 1. Caplan syndrome in a 76-year-old male.
A. An initial chest radiograph shows diffuse round nodular opacities and mild fibrotic linear opacities in both lungs, predominantly in the upper- to mid-lung zones.
B. Serial chest CT scans demonstrate progressive aggravation of pulmonary nodules (increase in both size and number). Tiny random nodules are observed in the upper lobes, consistent with the findings of coal worker's pneumoconiosis on the CT scan taken one year prior to admission (left images). Low-dose CT scans, performed at admission (right images), show well-defined pulmonary nodules with some conglomeration in the peribronchovascular area, predominantly in the upper lobes. The nodules have progressed compared with CT scans taken one month prior to admission (middle images) and one year prior to admission (left images). A percutaneous lung biopsy was performed for the largest nodule (26 mm in size) in the right lower lobe (arrow).
C. A PET scan shows increased uptake in multiple pulmonary nodules and adenopathy with maximum standardized uptake value, 9.1 in a nodule in the right lower lobe (arrow).
D. Photomicrograph of biopsy specimen shows a necrotizing granuloma with anthracosis surrounded with a rim of active inflammation consisting of palisading histiocytes (arrows) in hematoxylin and eosin staining (× 100).
E. Follow-up chest CT scans performed four years after admission show multiple pulmonary nodules progressing to irregular masses in the upper lobes, resembling progressive massive fibrosis. Multiple random and perilymphatic nodules, some showing cavitation (arrow), have newly developed in the basal areas of both lower lobes.
F. The follow up chest radiograph 3 months after the chest CT scan demonstrates improvement of conglomerated pulmonary nodules.



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DISCUSSION

Caplan syndrome, or rheumatoid pneumoconiosis, is a rare disease that complicates RA. Caplan syndrome is challenging to diagnose clinically because of overlapping radiological manifestations of complicated pneumoconiosis (2). One distinguishing radiographic finding associated with Caplan syndrome is the presence of multiple well-defined nodules ranging in size from 0.5 to 5 cm, which are primarily distributed with peripheral dominance (2). These nodules are typically located at the junction of the outer and middle thirds of the lungs. This appears to be a distinctive feature of nodules in Caplan syndrome, as opposed to coal worker's pneumoconiosis or silicosis where there is an angel's wing appearance on chest radiographs, with nodule distribution at the outer two-thirds of the lung initially but showing slow migration toward the hilum. Another distinctive characteristic is rapid growth of these nodules, which can occur suddenly within a few months. However, they may heal with scarring, remain stable, or grow slowly over several years. Additionally, compared with PMF, Caplan nodules tend to exhibit less scarring, retraction, and central migration (1-3).

While most distinguishing features can be primarily observed on radiographs, there is a paucity of comprehensive studies or case series on CT findings that could aid in diagnosis of Caplan syndrome. Few studies have described the CT appearance of the disease, with nodules characterized as large or cavitary, often with a background of small or miliary pneumoconiotic nodules (4, 5). These nodules can also cavitate or calcify and coalesce into larger nodules or masses (similar to PMF findings) (6). CT findings concerning nodules in Caplan syndrome commonly include cavitation of the nodules and their peripheral or apical locations, making it difficult to distinguish them from superinfected tuberculomas (4-7). When mycobacterial infection occurs in conjunction with pneumoconiosis, radiological abnormalities such as newly developed cavities associated with large, progressive consolidation, and the development of pleural effusion have been observed (7). To differentiate between these conditions, it is essential to consider the typical clinical features and perform comparisons using periodic sequential radiographs.

In our case, serial CT scans over five years revealed rapid progression of random and perilymphatic nodules, which had coalesced to mimic PMF acceleration. Distinguishing features became more evident as the disease progressed. Multiple peripheral/subpleural nodules had developed in the lower and basal lungs. Cavitary nodules had also emerged during this process, and unilateral pleural effusion was observed. These features resembled those of rheumatoid nodules rather than those of pneumoconiosis.

Rheumatoid nodules generally develop in the later stages of RA, and approximately 90% of individuals with rheumatoid nodules are RF-positive, although this does not necessarily correlate with RA progression or severity. Rheumatoid nodules in extrathoracic areas, such as the forearms and fingers, tend to form at sites of repetitive irritation and trauma, initiating the aggregation of inflammatory products, including RF complexes and cytokines. It remains unclear whether pneumoconiosis predisposes individuals to autoimmune diseases. However, in silicosis, it has been hypothesized that indigested silica dust can destroy macrophages, requiring recruitment of more macrophages, potentially leading to chronic immune activity and fibrosis. Similarly, pneumoconiosis is associated with increased levels of autoantibodies, im-

mune complexes, and immunoglobulins, including RFs (1).

The rapid progression of rheumatoid nodules in the extraarticular areas, known as accelerated rheumatoid nodulosis, has been reported in patients with chronic RA treated with methotrexate, etanercept (anti-tumor necrosis factor-α), and leflunomide (8, 9). However, the pathogenic mechanisms underlying accelerated rheumatoid nodulosis remain unclear. A reverse phenomenon has been noted in patients with RA whose joint inflammation improved with methotrexate but who experienced worsening subcutaneous rheumatoid nodules (8). When Caplan syndrome was first described in 1953, accelerated rheumatoid nodulosis (recognized in 1986) was unknown. The relationship between the rapid development of nodules in Caplan syndrome and patient medication history requires further investigation. When pneumoconiotic nodules exhibit rapid progression during follow-up without evidence of infection, RA may be considered, and an assessment of patient medication history is warranted. The likelihood of pneumoconiosis progression can also be differentiated even in the absence of further exposure, younger age, and the initial severity of pneumoconiosis on chest radiographs (10).

In conclusion, in Caplan syndrome, nodules can manifest as accelerating forms of PMF on serial chest CT. Along with the increasing size and conglomeration of PMF masses, critical findings for discriminating PMF include the development of pulmonary nodules, with or without cavitation, in the basal lungs as the disease progresses. The emergence of pleural effusion may contribute to the diagnosis of Caplan syndrome. Serial CT can provide valuable assistance in the diagnosis of diagnosing Caplan nodules in patients with pneumoconiosis.

Author Contributions

Conceptualization, H.J.Y.; investigation, B.J.; resources, H.J.Y.; supervision, H.J.Y.; writing—original draft, B.J.; and writing—review & editing, H.J.Y.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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CT에서 가속화된 진행성거대섬유증으로 오인된 카플란 증후군: 증례 보고

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본 증례 보고에서는 가속화된 진행성거대섬유증으로 오인된 카플란 증후군을 소개한다. 환자는 15년 전 탄광부진폐증을 진단받고 20년 이상 류마티스관절염 치료를 받은 자로 연속적인 CT 검사에서 진행거대섬유증의 진행과 함께 폐기저부에 동공을 동반한 다발성 폐결절이 관찰되었다. CT상 가속화된 진행성거대섬유증 소견으로 오인할 수 있는 카플란 증후군 증례를 보고하고자 한다.

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