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Case report

Two cases of cavitary lung cancer with concomitant chronic infectious disease

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ABSTRACT

The existence of a lung cavity on chest radiographs suggests the presence of lung disease, including benign or malignant disease. Lung cancer, tuberculosis, and fungal infection are all known for developing lung cavity. In addition, there are some characteristic findings in the differential diagnosis of cavitary disease, although these cavitary diseases often coexist. Here, we report two cases that presented cavitary lung cancer with concomitant chronic infectious disease. One patient showed pulmonary aspergillosis and lung adenocarcinoma, the other patient showed *Mycobacterium avium* complex lung disease and lung adenocarcinoma. These chronic infectious diseases develop slowly, and clinicians often follow up over several months. To reduce the delay in diagnosis of malignancy, clinicians should aggressively collect the specimens from cavitary lesions and make a correct diagnosis when encountering lung cavity in diagnostic clinical imaging.

1. Introduction

It is well known that some malignant, benign, and infectious lung diseases can lead to cavitary lesions in the lungs [1]. Lung cancer, tuberculosis, nontuberculous mycobacterial (NTM) infections, and fungal infections are especially known to be associated with lung cavity. There are some characteristic findings in the differential diagnosis of cavitary disease. For example, lung cavity with a fungus ball strongly suggests aspergillus infection, and lung cavity with daughter nodules suggests tuberculosis. However, it is often difficult to distinguish the mixture of cancer and infection.

Here, we present two cases of lung cancer detected concomitantly with chronic infectious diseases. These cases support the idea that physicians should pay attention to the possibility of concomitant lung cancer and infectious disease in the assessment of lung cavitary disease.

2. Case presentation

2.1. Case 1. pulmonary aspergillosis + lung cancer

An 82-year-old male patient with chronic kidney disease was referred to our hospital for an abnormal shadow in a chest radiograph. A chest computed tomography (CT) scan revealed lung cavity with a fungus ball in the left lower lobe (Fig. 1A) along with bilateral interstitial pneumonia (Fig. 1B). Values for serum tumor marker of carcinoembryonic antigen (CEA), sialyl Lewis-x antigen, and cytokeratin 19 fragment were 2.7 ng/mL, 38 U/mL and 3.6 ng/mL, respectively. Serum β-D glucan level was 84.4 pg/mL, and an aspergillus galactomannan antigen test was positive. Chronic progressive pulmonary aspergillosis was suspected. Bronchoscopy was challenged to evaluate the details of the fungal infection. The specimens obtained by bronchoscopy showed adenocarcinoma with hematoxylin and eosin staining (Fig. 1C) and filamentous fungus with positive Grocott staining (Fig. 1D). The filamentous fungus was identified as *Aspergillus fumigatus*, and the patient was diagnosed with pulmonary aspergillosis and lung adenocarcinoma. Because of advanced age and poor lung function, he was excluded from receiving surgical treatment and thus received only an antifungal agent with micafungin.

2.2. Case 2. NTM lung disease + lung cancer

An 81-year-old female with a history of colon cancer was referred to our hospital for an abnormal shadow in a chest radiograph. A CT scan revealed a reticulonodular shadow in the middle lobe/lingular segment

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Abbreviations

NTM	nontuberculous mycobacterial
CT	computed tomography
CEA	carcinoembryonic antigen
MAC-LD	*Mycobacterium avium* complex lung disease
PET	positron emission tomography

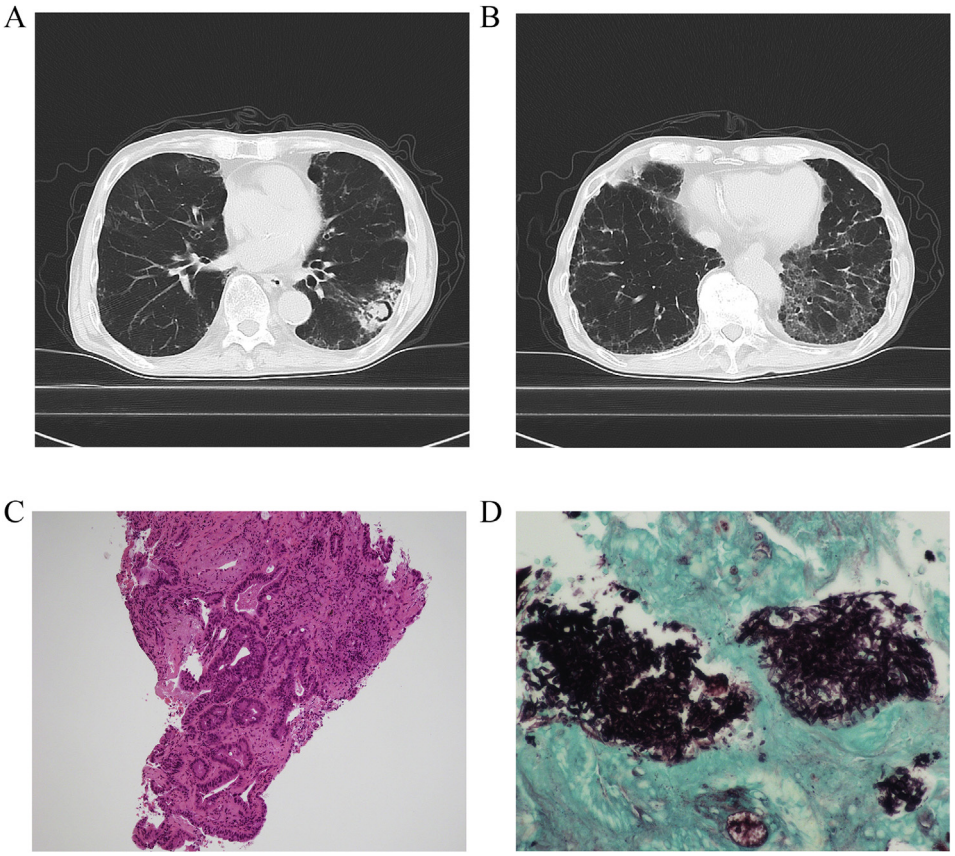

Fig. 1. Chest computed tomography scan image for case 1 showed lung cavity with a fungus ball in the left lower lobe (A). Interstitial pneumonia was also detected in the bilateral lower lobes (B). Specimens obtained via bronchoscopy revealed the aggregation of malignant cells with irregular papillary and tubular structure, suggesting adenocarcinoma (C, hematoxylin and eosin staining, × 100). The filamentous fungus with positive Grocott staining was detected in the same specimens, suggesting pulmonary aspergillosis (D, Grocott staining, × 100).

(Fig. 2A). Cavity formation with daughter nodules was detected in the middle lobe (Fig. 2B), and the patient was suspected to have NTM lung disease. She had difficulty in expectorating sputum and was recommended to undergo bronchoscopy at the initial assessment, but she refused. After 6 months of follow-up, she was considered for surgical resection of the right middle lobe and was referred to a thoracic surgeon. At this time, serum tumor marker of CEA was 1.8 ng/Ml, and serum β-D glucan level was 17.0 pg/mL. The patient underwent lobectomy of the right middle lobe. The specimens showed adenocarcinoma on hematoxylin and eosin staining (Fig. 2C) and epithelioid granulomas with focal necrosis, which suggested mycobacterial infection (Fig. 2D). *Mycobacterium avium* was detected in the culture of the resected lung specimen. She was diagnosed with *Mycobacterium avium* complex lung disease (MAC-LD) and lung adenocarcinoma. After surgical resection, she received combination therapy with clarithromycin, ethambutol, and rifampicin for the MAC-LD.

3. Discussion

Several studies suggest a relationship between the wall thickness of the pulmonary cavity and whether it is benign or malignant [2,3], with a maximum wall thickness of 4 mm or less suggesting benign disease, wall thickness of 5–15 mm suggesting equivalency, and wall thickness greater than 15 mm suggesting malignant disease [2]. In accordance with this previous report, wall thickness of the cavities in our two patients had a relatively thin wall (case 1: 2.6 mm, case 2: 2.2 mm), thus it was suggested to be benign. Honda et al. mentioned that the presence of satellite nodules, consolidation, and ground-glass attenuation indicated a benign cavity [3]. In the present cases, both patients had a thinner cavity wall and chronic infections, as expected. Nonetheless, they were found to have concomitant lung cancer. Although wall thickness and the existence of a fungus ball are useful references in the diagnosis of fungal infections, they are not sufficient to diagnosis the presence or amount of air-fluids and do not correlate with benignity or malignancy [2].

Recently, positron emission tomography (PET)-CT scanning has been more commonly used clinically for the diagnosis and extension of malignant diseases. PET-CT scanning has demonstrated a high performance for evaluating malignant disease, but the differential diagnosis of whether the disease is malignant or not is challenging. A previous meta-analysis showed the heterogeneity of diagnosing lung nodules by using PET-CT, especially regarding the diagnosis of endemic infectious lung disease regions [4]. In accordance with this meta-analysis, it is difficult to determine benignity or malignancy. Furthermore, clinicians often hesitate to employ PET-CT scans because of the high cost.

Another clinical important parameter in evaluation of cavitary disease is the course of disease progression (acute or chronic). The insidious progression of cavitary disease usually suggests benignity. In the present cases, both cases showed slowly progression of lung involvement, although both cases had malignant disease. This illustrates the need for physicians to stay mindful of exceptions; it is also underlines the importance of considering the potential for the existence of an underlying disease. For instance, granulomatosis with polyangiitis is rare, but is an important underlying disease in the differentiation of lung cavity. It is also important to consider the patient's residential area [5]. For example, endemic infectious diseases develop only in limited

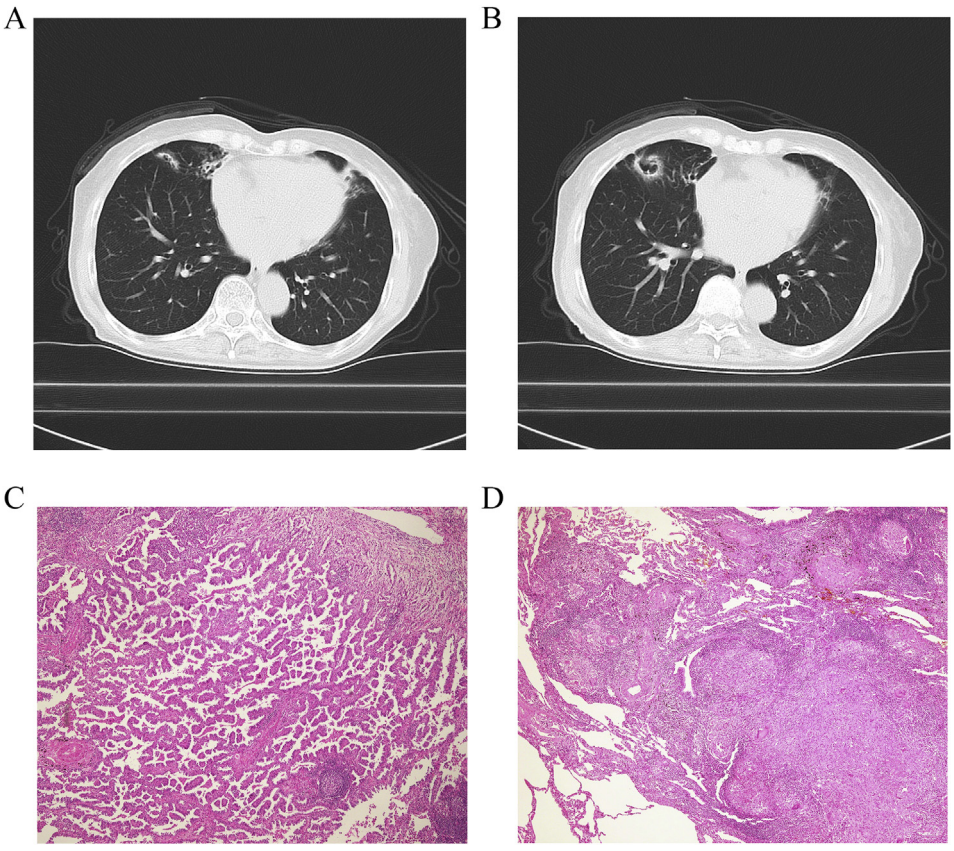

Fig. 2. Chest computed tomography scan revealed reticulonodular shadow in the middle lobe/lingular segment (A). Cavity formation with daughter nodules was also detected in the right middle lobe (B). Specimens taken by surgical resection revealed malignant cells with papillary and tubular structure. Epithelioid granulomas with focal necrosis were located around the bronchus (C, D, hematoxylin and eosin staining, × 100).

areas. In Japan, histoplasma, blastomycosis, and coccidioidomycosis are rare and thus are less suspected when physicians encounter the cavitary disease in the absence of recent overseas travel. In general, measuring serum tumor markers can support the differential diagnosis of malignant disease. Nevertheless, in the present two cases, there was no elevation of tumor markers. This emphasizes the need for physicians to consider that serum tumor markers are not always elevated in the early stage of cancer.

4. Conclusions

We encountered two rare cases of cavitary lung with concomitant chronic infectious disease. Lung cancer and chronic infectious diseases occasionally coexist in patients with lung cavitary diseases. Physicians should consider a potential malignancy when they diagnose cavitary lung disease. In practice, we should try to evaluate the cavity by bronchoscopy or CT-guided biopsy as possible when we encounter lung cavity.

Declarations of interest

There are no conflicts of interest to declare.

Role of the funding source

There is no funding support for this case report.

Ethical approval and consent

Our institution does not require ethical approval for case reports. This submission was approved by the patients, from whom we obtained written consent.

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References

[1] J.H. Ryu, S.J. Swensen, Cystic and cavitary lung diseases: focal and diffuse, Mayo Clin. Proc. 78 (2003) 744–752.
[2] J.H. Woodring, A.M. Fried, V.P. Chuang, Solitary cavities of the lung: diagnostic implications of cavity wall thickness, AJR Am. J. Roentgenol. 135 (1980) 1269–1271.
[3] O. Honda, M. Tsubamoto, A. Inoue, T. Johkoh, N. Tomiyama, S. Hamada, N. Mihara, H. Sumikawa, J. Natsag, H. Nakamura, Pulmonary cavitary nodules on computed tomography: differentiation of malignancy and benignancy, J. Comput. Assist. Tomogr. 31 (2007) 943–949.
[4] S.A. Deppen, J.D. Blume, C.D. Kensinger, A.M. Morgan, M.C. Aldrich, P.P. Massion, R.C. Walker, M.L. McPheeters, J.B. Putnam, E.L. Grogan, Accuracy of FDG-PET to diagnose lung cancer in areas with infectious lung disease: a meta-analysis, J. Am. Med. Assoc. 312 (2014) 1227–1236.
[5] L.B. Gadkowski, J.E. Stout, Cavitary pulmonary disease, Clin. Microbiol. Rev. 21 (2008) 305–333 table of contents.