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Case Report

A rare case of synchronous mycobacterium tuberculosis, aspergillosis and lung adenocarcinoma in a patient

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Abstract: Pulmonary tuberculosis, pulmonary aspergillosis and lung cancer are amongst the most common causes of pulmonary cavities; however, concurrence of all three in a patient is rare. We report a case of a 52-year-old woman presented with chronic cough and intermittent blood-stained sputum who has been diagnosed as pulmonary tuberculosis 6 months earlier before admission with failed initial anti-tuberculosis therapy. CT-guided biopsy targeted at the periphery lower lobe cavity of the right lung was carried out to diagnose choronic cavitary pulmonary aspergillosis, nevertheless, 3 month anti-fungal therapy with voriconazole failed. Thus, the bronchoscopy was performed again, lung adenocarcinoma was diagnosed and the treatment with gefitinib was effective. Our case is a rare one presenting with the synchronous Mycobacterium tuberculosis, aspergillosis infection and lung adenocarcinoma in a patient. Physicians should be aware of malignancy when previous therapeutic effect for pulmonary cavity is poor.

Keywords: Pulmonary cavity disease, pulmonary tuberculosis, pulmonary aspergillosis, lung neoplasm, PET-CT

Introduction

Pulmonary cavities are defined as 'gas-filled space that develops within pulmonary consolidation, a mass or a nodule' [1], and are frequent manifestation of a wide variety of pathological process involving the lung. Either infectious diseases or non-infectious diseases may produce cavities in the lung. Lung cancer, mycobacterium tuberculosis or aspergillosis infection are three major causes of pulmonary cavity [2], however, the synchronous of lung neoplasm, tuberculosis and aspergillosis has rarely been seen. In this article, we present a case of pulmonary cavity with proven diagnosis of tuberculosis, aspergillosis and lung adenocarcinoma.

Case report

In September 2014, a 52-year-old woman present with severe cough and intermittent blood-stained sputum was admitted to the respiratory department of Xinqiao hospital. She had been diagnosed as pulmonary tuberculosis with acid-fast bacillus positive in sputum smear, and took initial anti-tubercular treatment (2HREZ/4HRE Regimen) 6 months earlier in local health care center. The thoracic CT (2014-2-4, **Figure 1A**) showed there is a nodule in the upper lobe and thin-walled cavity in the periphery lower lobe. She had declared slightly improvement after anti-tuberculosis treatment for 2 month and return to local health care center for subsequent visit. Chest CT scan showed focal absorption of right lower lobe cavity and slightly development of the upper lobe lesion (**Figure 1B**). Phlegm acid-fast bacillus turned negative. In order to eliminate the patient's concern, a bronchoscopy and a CT-guided fine needle biopsy were conducted. The histological manifestation inclined to be chronic inflammation (no tumor cell has been seen) and the patient was suggested to continue anti-tubercular treatment till admission. During this period, chest radiography was performed for follow-ups.

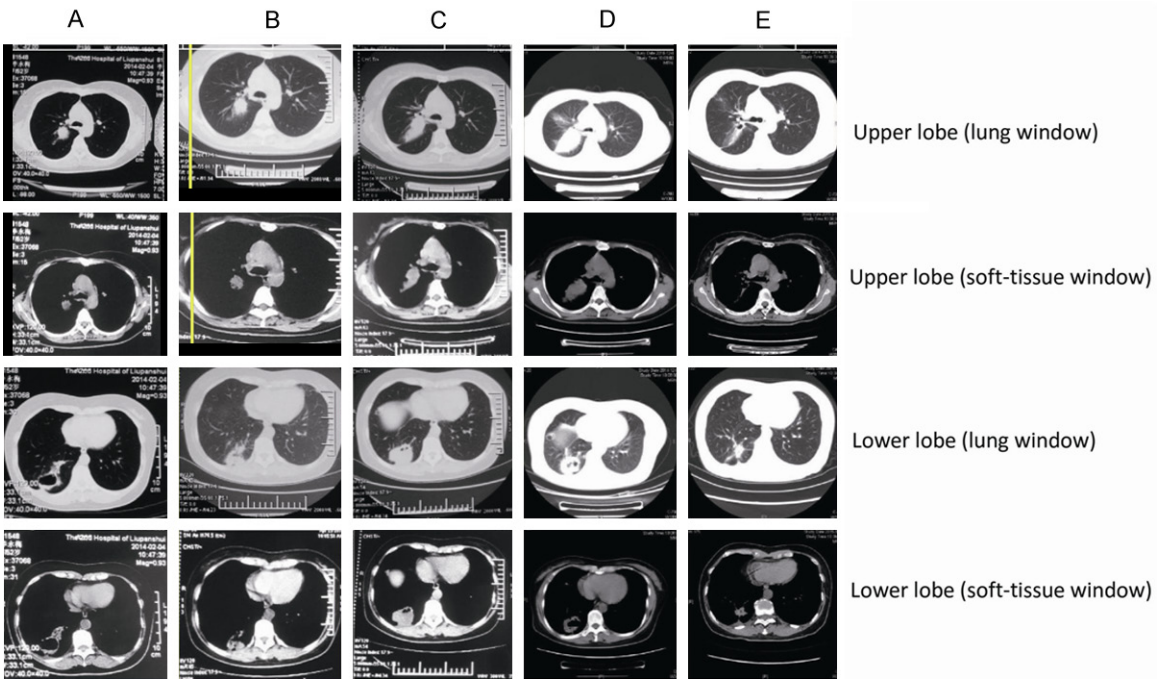

Figure 1. CT images showing the development of the lesions (a nodule in the upper lobe and a cavity in the lower lobe).

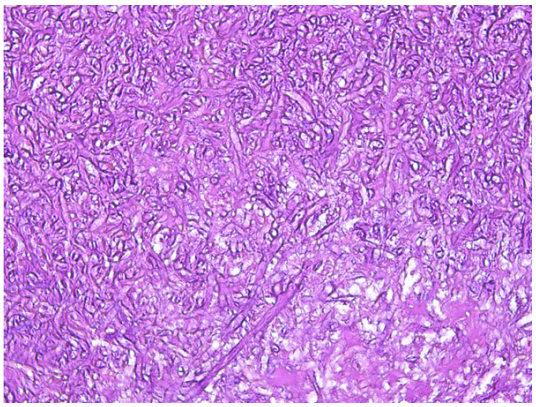

Figure 2. Histology of CT-guided biopsy in the lower lobe showing typical aspergillus organisms with septate hyphae.

The patient was nonsmoker, and there was no history of any other illness. Physical examination did not reveal any abnormality. The following investigations were done: serum CEA was slightly elevated (7.8 ng/ml), Sputum culture for bacteria was negative, Sputum for Acid Fast Bacillus was negative, sputum for direct fungal stains was positive and Tuberculin test was positive. Thoracic CT showed a progression of upper lobe lesion that complicated with a possible obstructive pneumonia, and the lower lobe cavity became eccentric thick-walled cavity with necrosis which is obvious in the soft-tissue window (**Figure 1C**). Bronchoscopy was conducted, there was a slightly narrowing of lower lobe basal segment lumen, no neoplasm was seen under bronchoscopy and no tumor cells were found in Bronchoalveolar lavage. CT-guide fine needle biopsy targeted at the periphery lower lobe cavity was performed, the histological showed typical aspergillus organisms with septate hyphae (**Figure 2**). The patient was suggested to perform a PET/CT for further differential diagnosis with malignancy disease and was refused by the patient. She was then diagnosed as chronic cavitary pulmonary aspergillosis (CCPA) and voriconazole was prescribed. As for now, antitubercular treatment was changed to second-line Regimen. Follow-up as an outpatient, she declared symptoms were not significantly improved during the treatment.

On Dec 9, the patient was admitted again for persistent low-grade fever. Serum CEA was elevated (14.7 ng/ml). Thoracic CT showed a rapid progression of disease in the upper lobe and slightly absorption in the lower lobe (**Figure 1D**). Bronchoscopy was conducted again, the lumen of upper lobe posterior segment was narrow

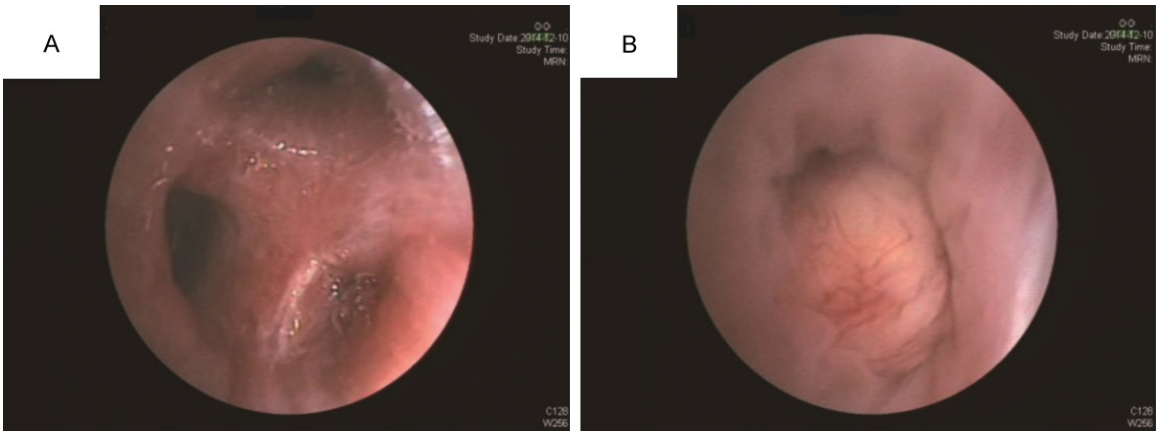

Figure 3. Bronchoscopy showing narrowing of upper lobe posterior segment lumen (A) and the neoplasm in the lower lobe lateral basal segment (B).

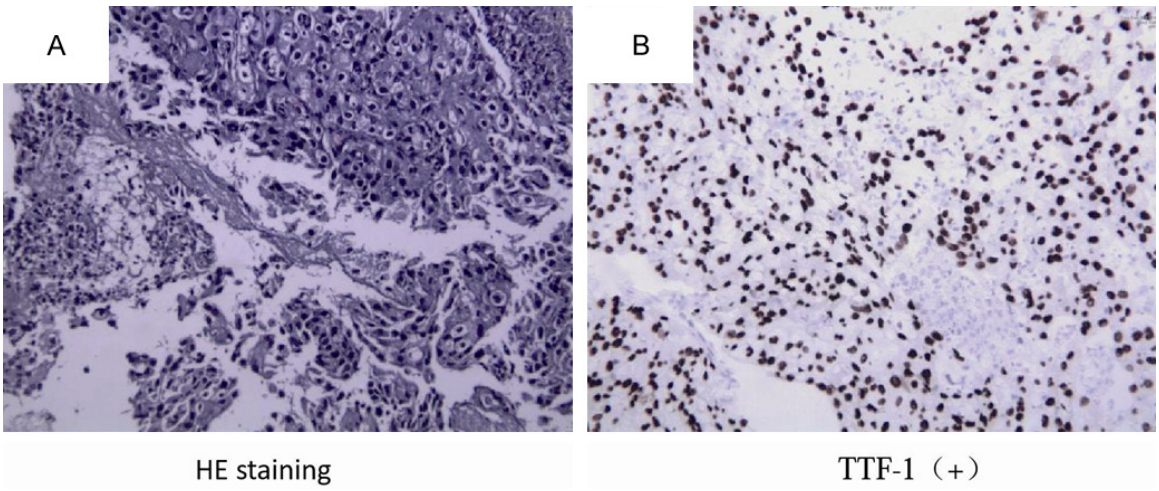

Figure 4. A. HE staining of the tissue via bronchoscopic biopsy; B. Tumor cells reactive for TTF-1.

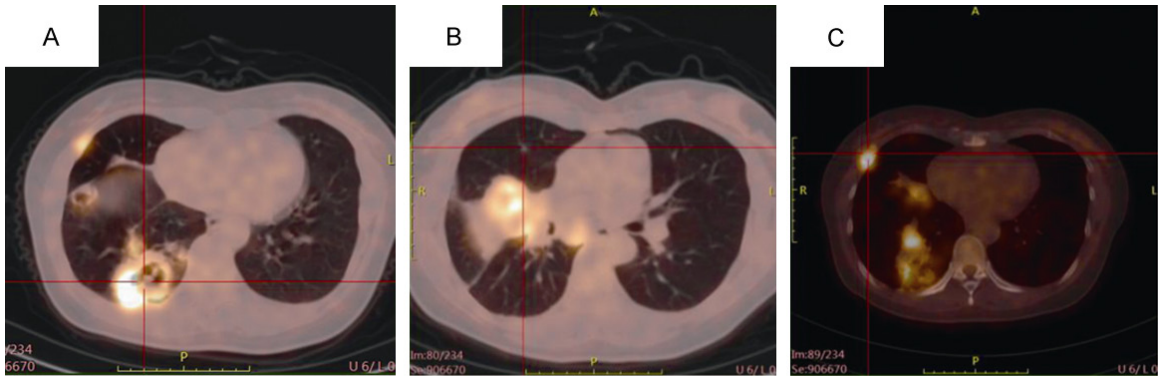

Figure 5. PET-CT scan of the thorax showing high 18F-FDG value in the upper lobe nodule (B) and lower lobe cavity (A), and a solitary nodular implant in the right rib (C).

and neoplasm was seen under bronchoscopy in the lower lobe lateral basal segment (**Figure 3**). Histology indicated that the tumor was adenocarcinoma (**Figure 4**). EGFR mutation test

was positive (exon 19). The patient was diagnosed with bronchial adenocarcinoma stage IV (TNM classification $T_2N_2M_1$, stage IV)) with right rib involvement (**Figure 5**), and gefitinib treatment with 250 mg/once per day was prescribed for targeted therapy. The patient had significant alleviation of clinical symptoms and improvement of thoracic CT image in the latest follow-up (**Figure 1E**).

Discussion

Pulmonary cavities with nodules are common radiological appearances of various etiologies. Pulmonary tuberculosis, pulmonary aspergillosis and lung cancer are amongst the most common causes of pulmonary cavities. The CT morphological feature of a cavitation that suggests malignancy include wall thickness over 4 mm at the thinnest part, irregular inner and outer margins, associated soft tissue mass with or without infiltration of the thoracic wall and enlarged lymph node. Occasionally, a cavitated lung cancer may have thin walls [2]. Tuberculosis, however, may present a typical cavitary lesions located in the apical and posterior segments of the upper lobes and the superior segments of the lower lobes. The cavity walls may be thick or thin, with or without air-fluid levels [3]. As for aspergillosis, the most frequent findings reported were single or multiple thick-walled cavitary upper lobe lesions [4].

As signs, symptoms and radiologic findings can be masked by pre-existing disease, diagnosis of lung cancer superimposed on pulmonary TB or pulmonary aspergillosis is difficult and, in most cases, delayed until an advanced stage. We reported a case of 52-year-old female non-immunodeficiency patient being treated for pulmonary TB that in the sixth month of treatment presented with cough and blood-stained sputum, signs and symptoms interpreted as secondary to the TB itself. Since the beginning of TB treatment acid-fast bacilli was being persistently detected in sputum smears and became negative after 2 month treatment, documenting adequate response. However, the non-response and growth of upper lobe nodule was suggestive of further examination. Biopsy targeted at the periphery cavity in the lower lobe of the right lung revealed the existence of aspergillus. Pulmonary aspergillosis, comprising of noninvasive semi-invasive, invasive and allergic bronchopulmonary aspergillosis, is more frequently observed in patients with immunodeficiency or diabetes mellitus. In our case, the patient tends to be chronic cavitary-pulmonary aspergillosis (CCPA) for semi-invasive characteristics according to the diagnostic criteria [5]. Nam et al, reported CCPA tends to affect persons with abnormal pulmonary defense mechanisms as a result of underlying lung disease, and tuberculosis ranks the first [6]. This makes sense that the comorbidity of CCPA with pre-existing tuberculosis. However, this is not the end of story, after 3 month of oral voriconazole, the symptom was not significantly improved, and she got low-grade fever. Thoracic CT showed further progression of disease especially in the upper lobe. By bronchoscopy biopsy, she was diagnosed as lung adenocarcinoma. This suggests that in patients with pulmonary carvitary tuberculosis or CCPA in whom a growing nodule is present or who show little improvement of symptoms despite standard therapy, additional diagnosis work-up should be performed in order to exclude malignancy.

Conclusion

The uniqueness of our case report is that the co-existence of lung adenocarcinoma, active pulmonary tuberculosis and pulmonary aspergillosis has -to the best of our knowledge- not been reported in the literature before. Repeated bronchoscopy and CT-guide needle biopsy are essential tools for the accurate diagnosis. However, PET/CT is helpful in the early differential diagnosis if malignancy is suspected.

Disclosure of conflict of interest

None.

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