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CASE REPORT

A Rare Case of Benign Hamartoma and Malignant Primary Pulmonary Lymphoma Coexisting in a Patient Mimicking Invasive Pulmonary Mycosis: a Case Report and Literature Review

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SUMMARY

Background: **Pulmonary hamartomas are the most common benign tumors of the lungs and can occur anywhere in the lungs, normal hyperplasia, congenital malformation, inflammatory changes, and tumorigenesis are hypothesized to underlie the pathogeny, but the definite etiology remains to be elucidated. Primary pulmonary lymphoma (PPL) refers to clonal lymphoid hyperplasia of one or both lungs in patients who have no detectable extrapulmonary lymphoma or bone marrow involvement at the time of diagnosis and during the subsequent 3 months. It is rare for both diseases to occur in the lungs of the same patient.**

Methods: **Appropriate laboratory tests, Chest CT scan, bronchoscopy and CT-guided percutaneous lung biopsy.**

Results: **Laboratory tests showed (1-3)-β-D-glucan was 226.3 pg/mL and sputum culture of Aspergillus niger. Chest Computer Tomography (CT) scan showed multiple flaky high-density shadows in both lungs, proven to be right hamartoma with left lung pulmonary primary lymphoma by bronchoscopy biopsy and CT guided percutaneous needle lung biopsy.**

Conclusions: **When there are high density shadows or nodules in different parts of one patient's lung, these lesions may not be the same disease. Therefore, it is necessary to conduct biopsies of the lesions in different parts of the lung.**

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KEY WORDS

PPL, pulmonary hamartoma, invasive pulmonary fungal disease, bronchoscopy biopsy, CT guided percutaneous needle lung biopsy

CASE REPORT

Pulmonary hamartoma is the most common benign tumor of the lungs that accounts for about 75% of benign lung tumors [1], while primary pulmonary lymphoma (PPL) is the rarer malignant tumor of the lungs, accounting for 1% of malignant lymphoma and 3.6% of extranodal lymphoma [2,3]. The imaging manifestations of these two diseases are so variable and sometimes similar to those of invasive pneumomycosis that they are difficult to identify [4]. The presence of both benign and malignant tumors in the lungs of one patient is extremely rare, making the definitive diagnosis much more difficult.

We presented an elderly male patient whose chest CT showed multiple flaky high-density shadows in both lungs, positive serum (1-3)-β-D-glucan by G test and Aspergillus niger sputum culture, firstly diagnosed as invasive pulmonary fungal disease, which proved to be left lung hamartoma with right pulmonary primary lymphoma by bronchoscopy biopsy and CT guided percutaneous needle lung biopsy. A 65-year-old man came to hospital with cough and dyspnea. He developed transient fever 20 days ago with a temperature of 37.9°C, accompanied with cough, a small amount of sputum and dyspnea. At ordinary times he has a good constitution and can do general physical work, there was no history of chronic illness other than hypertension for him. The physical examination showed low respiratory tone in the upper right lung and no abnormalities in other organ tests. Then he received appropriate laboratory tests. Laboratory tests showed (1-3)-β-D-glucan was 226.3 pg/mL (the reference value was 0 pg/mL to 60 pg/mL), high-sensitivity C-reactive protein was 10.9 mg/L (the reference value was 0 mg/L to 8 mg/L), and erythrocyte sedimentation rate was 35 mm/hour (the reference value was 0 mm/hour to 15 mm/hour), white blood cell was normal, the tumor series was negative, there is a small amount of Aspergillus niger in the sputum culture. Chest CT scan showed multiple flaky high-density shadows in the right lung and flaky high-density shadows in the mediastinum of the upper lobe of the left lung, which were considered inflammatory lesions and multiple lymph nodes in the mediastinum (Figure 1A, 1B). At first, we are highly suspicious of fungal infection due to positive serum (1-3)-β-D-glucan by G test and Aspergillus niger sputum culture, so we applied oral voriconazole antifungal and atomized amphotericin B therapy. After one month of treatment, chest CT reexamination showed no significant change compared with the last time.

We arranged a bronchoscopy, which revealed that the neoplasm had completely blocked the bronchial opening in the anterior upper lobe of the right lung and that the remaining bronchi were normal (Figure 1C, 1D). The tumor was taken by forceps for pathological examination. Immunohistochemical results showed CK positive, LAC (lymphocyte positive), CD138 (plasma cell positive), κ: λ = 1:1. Necrosis and cartilage components were seen, but no malignant components were observed, so the pathology of the tumor is hamartoma (Figure 1E, 1F). So far, the diagnosis seems clear, but are the dense shadows in both lungs caused by the same source?

It is entirely possible that the dense shadows in both lungs are from different sources. To resolve this doubt, we continued with a CT guided percutaneous biopsy of the left lung (Figure 2A, 2B). Rapid On-Site Evaluation (ROSE) staining showed a large number of lymphocytes under 100 x magnification (Figure 2C, 2D). Immunohistochemical results showed CK negative, TTF-1 negative, CD20 strongly positive, PAX-5 strongly positive, CD15 negative, CD30 individual positive, EBER negative, EMA negative, CD3 negative, CD5 negative, CD21 positive, CD23 positive, CyclinD1 negative, Bcl-2 strongly positive, CD10 negative, ki-67 index 15%. A large number of lymphocyte infiltrates were observed in the lung tissues, mainly B lymphocytes, and pathologically it was low grade B cell malignant lymphoma (Figure 2E, 2F). Subsequently, in order to evaluate the disease, an iliac bone marrow puncture was performed. The result of gene rearrangement was negative, and the bone marrow image was normal, indicating that there was no lesion in the bone marrow. The patient underwent Positron Emission Tomography-Computed Tomography (PET-CT) at another hospital, and the result was a nodular change near the mediastinum of both lungs. The PET-CT showed a concentration of radioactivity, indicating increased metabolism. In addition, no evidence of malignancy was found in other parts of the body. Finally, the diagnosis of the patient was confirmed as right pulmonary hamartoma combined with primary lymphoma of the left lung. The patient agreed to be transferred to the hematology department for chemotherapy treatment, chest CT is periodically reviewed, and he is still in follow-up.

DISCUSSION

PPL is an extremely rare disease, accounting for less than 1% of both lung malignancies and non-Hodgkin's lymphoma (NHL) [5,6]. The rarity of PPL may be due to the relatively low level of lymphoid tissue in the lung compared to other sites [7]. Pulmonary hamartoma is the most common benign tumor of the lungs. Rarely have these two diseases been reported in the same patient [8, 9]. We report a new case of a patient with both PPL and pulmonary hamartoma and highlight the clinical and diagnostic challenges of these treatable diseases. The clinical and imaging manifestations of both diseases are nonspecific, and sometimes overlap with fungal infections in imaging findings, so they are highly misdiagnosed in clinic [10]. The initial CT examination and laboratory ex-

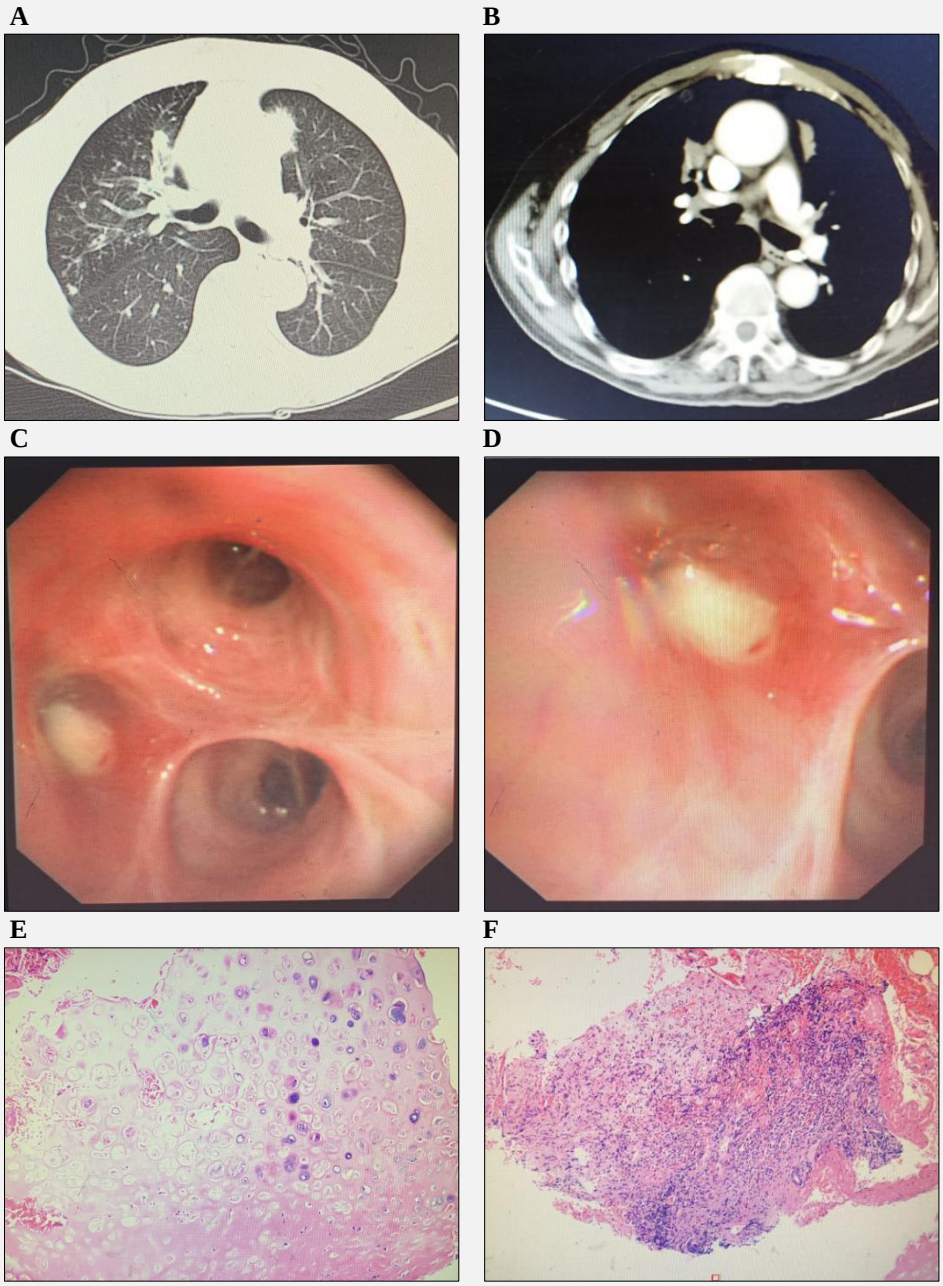

Figure 1. Chest CT scan showed multiple flaky, high-density shadows in the right lung and flaky high-density shadows in the mediastinum of the upper lobe of the left lung and multiple lymph nodes in the mediastinum (A, B). Bronchoscopy revealed that the neoplasm had completely blocked the bronchial opening in the upper frontal lobe of the right lung (C, D). The pathology of the tumor was pulmonary hamartoma.

amination of this patient confused us: chest CT showed multiple patchy high-density shadows in both lungs, G test showed positive serum (1-3)-β-D-glucan, and sputum culture showed Aspergillus niger. We, therefore, first diagnosed invasive pulmonary aspergillosis. But after one month of antifungal therapy, chest CT reexamination showed no significant change compared with the previous one. We began to question the diagnosis of "invasive pneumomycosis" and considered other diagnostic methods, such as bronchoscopy and CT-guided percutaneous lung biopsy. The pathology of a biopsy is the gold standard for the diagnosis of a tumor [11]. First, we found the

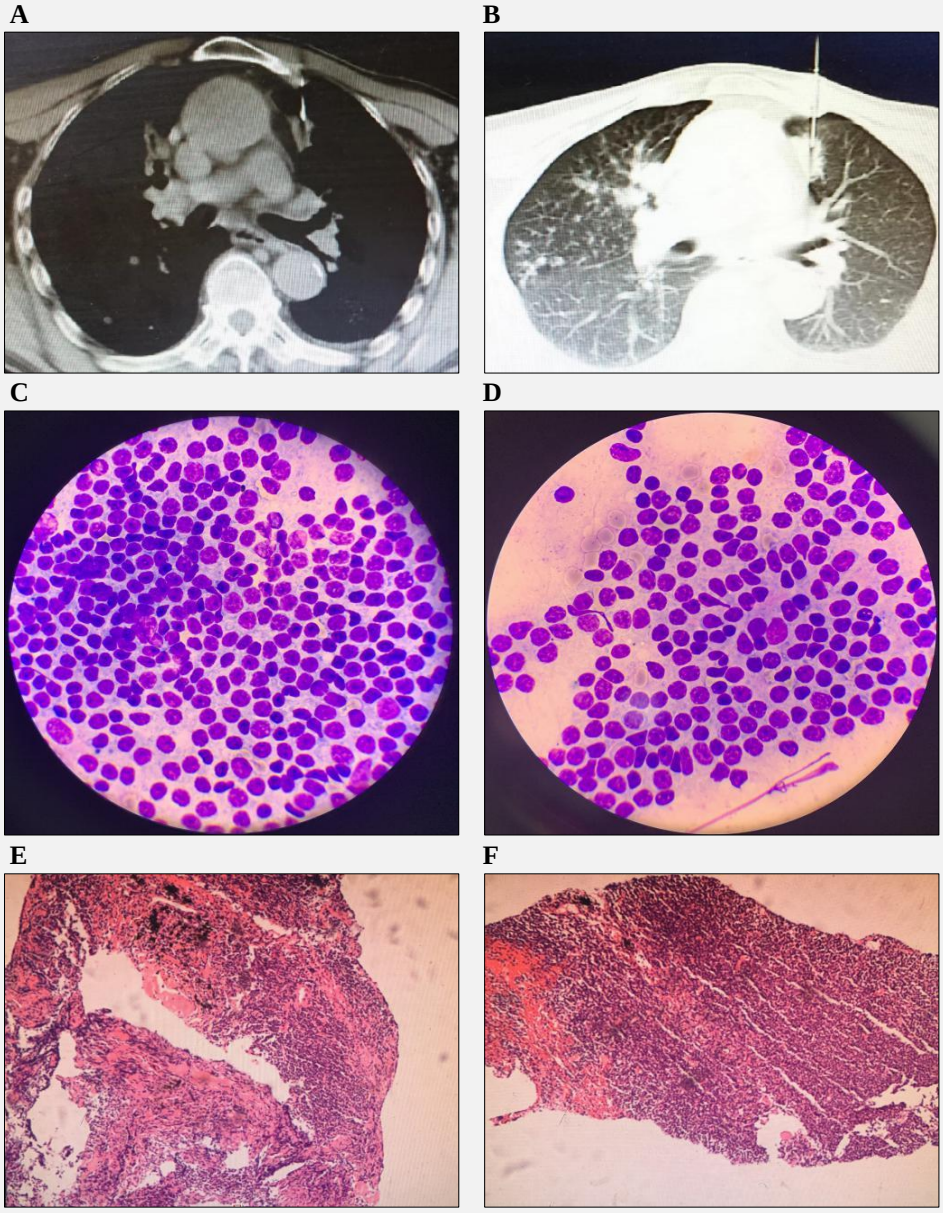

Figure 2. CT guided percutaneous biopsy of the left lung (A, B). Rapid ROSE staining showed a large number of lymphocytes (C, D). A large number of lymphocyte infiltrates were observed in the lung tissues, mainly B lymphocytes, and pathologically it was low grade B cell malignant lymphoma (E, F).

neoplasm of the patient's right lung through bronchoscopy, and the pathology of the tissue biopsy confirmed the pulmonary hamartoma. Pulmonary hamartoma is a tumor-like malformation of normal lung tissue caused by abnormal combination of normal lung tissue due to abnormal embryonic development. There are three types: intrapulmonary type, endobronchial type, and diffuse type [1]. In order to determine whether the patient had diffused pulmonary hamartoma, we performed CT-guided percutaneous lung biopsy on the high-density shadow of the left lung, and obtained a new discovery of primary lymphoma of the left lung. PPL is a malignant lymphoid hyperplasia that occurs in the lungs and is not found in other parts of the body. It can appear as a high-density shadow on CT images [12,13]. Mucosal associated lymphoid tissue (MALT) lymphoma is the most common type accounting for 70 - 90% [14]. The therapy of PPL relies on histology. Surgery, radiotherapy, chemo-

therapy or follow-up are commonly used. PPL has a better prognosis than secondary pulmonary lymphoma [15].

CONCLUSION

In conclusion, we report a new case of a patient with both PPL and pulmonary hamartoma and highlight the clinical and diagnostic challenges of these treatable diseases. When there are high density shadows or nodules in different parts of one patient's lung, these lesions may not be the same disease. Therefore, it is necessary to conduct biopsies of the lesions in different parts of the lung. This case illustrates the importance of bronchoscopy and percutaneous pulmonary puncture biopsy in differential diagnosis. If imaging findings are inconsistent with symptoms or anti-infection treatment is ineffective, a biopsy should be performed proactively.

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Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in the study were in accordance with ethical standards. Informed consent was obtained from all individual participants included in this study.

Declaration of Interest:
No conflicts of interest.

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