Pulmonary Multiple Nodules: Benign or Malignant?

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To the Editor: A case of primary thyroid fibrosarcoma with pulmonary metastasis is very rare. It is difficult to be diagnosed especially when pathological manifestation is atypical and early pulmonary metastasis coexists with some benign lesions. Here, we report that a case of thyroid fibrosarcoma with pulmonary and subcutaneous fat metastasis coexisting with solitary pulmonary sclerosing hemangioma (PSH) in lung. This report may improve better understanding of differential diagnosis of benign and malignant lesions primary thyroid fibrosarcoma in the lung.

A 55-year-old Chinese woman with a history of a dry cough lasting for 5 months and progressive dyspnea lasting for 3 months was admitted to hospital. Eight months ago, she had a surgery of thyroid neoplasma resection, and pathological diagnosis was thyroid aggressive fibromatosis (AF). Lung computed tomography (CT) scan showed one solitary nodule in the left lingular lobe at the same time [Figure 1a1 and 1a2], but because there was no respiratory symptom, further examination had not been performed. Five months ago, the patient complaint about dry cough and multiple small nodules in bilateral lung beside the previous nodule in left lingular lobe were detected on reexaminated lung CT scan [Figure 1b1 and 1b2]. Hence, percutaneous needle lung biopsy (PNLB) of one largest nodule in left lingular lobe was conducted, and the pathological diagnosis was PSH [Figure 1e1 and 1e2]. Because of benign feature of PSH, the patient did not undergo any treatment. Three months ago, the patient underwent lung CT again due to serious cough and dyspnea. Moreover, enlarged multiple nodules, whose characteristic was not in accordance with PSH, were detected in lung CT [Figure 1c1 and 1c2]. Hence, the repeated PNLB was performed in nodule in superior lobe of the right lung. Histopathologic examination showed hyperplasia of spindle cells with tendency toward the pulmonary inflammatory myofibroblastic tumor (IMT) [Figure 1f1 and 1f2]. In this admission, repeated lung CT showed further enlarged multiple nodules and partial fusion [Figure 1d1 and 1d2], and two nodules were also found in subcutaneous adipose tissue, located in armpit and abdomen. Biopsy of subcutaneous nodules was performed, and histopathologic examination showed hyperplasia of spindle cells with a lesser degree of nuclear atypicality and necrosis [Figure 1g1 and 1g2]. With multidisciplinary consultation, we found that the pathological findings in lung and subcutaneous adipose tissue were consistent with that in thyroid neoplasm [Figure 1h1 and 1h2]. The final diagnosis of the patient was thyroid fibrosarcoma with pulmonary and subcutaneous adipose metastasis accompanied with solitary PSH in the left lung. The patient gave up treatment and discharged herself from hospital after the diagnosis.

This case was characterized of two totally different kinds of rare pathological findings showed on the same lung, benign lesions, and malignant lesions, which increased the difficulty of diagnosis of this case. In this case, the pathological diagnosis of resected thyroid neoplasm was initially AF by medical history, which is one kind of rare benign soft-tissue tumor (<3% in all soft-tissue tumor), and thyroid AF is very less frequent.[1] Histopathologic examination of thyroid AF reveals that a spindle-cell proliferation with fibroblastic characteristics and with no atypia and thin capillary vessels, and thyroid cells do not display any features of papillary thyroid cancer. Because of rare hematogenous metastasis of AF, the pulmonary metastasis of thyroid neoplasm was not considered first especially when pathological manifestation had been confirmed as PSH in nodule in left lung. PSH is a relatively rare benign tumor with the characteristic of prominent sclerotization and vascularization of the lung tissue.[2] The epithelial origin of the tumor is also supported by thyroid transcription factor-1 and epithelial membrane antigen positivity in both the surface cells and round cells in the majority of the cases. Distinguishing from pulmonary metastases, PSH is often detected incidentally as a round, well-defined homogenous mass on routine chest radiograph without clinical symptom, and contralateral lung nodules and lymph node involvement are extremely rare in PSH.[2] The diagnosis is based on pathological examination of the biopsy material. Hence, facing the successively progressive multiple nodules in bilateral lung, PNLB was done on nodule in the right lung. A tendency of pulmonary IMT was considered by pathological examination without referring to pathological section of thyroid neoplasm.

IMT is one kind of uncommon and presumably benign (noncancerous) tumor made up of cells called myofibroblastic spindle cells, without nuclear atypia. Pathological features of IMT are necrosis, hemorrhage, focal calcification, and mitotic activity.[3] IMT is most commonly found in the lung, orbit, peritoneum, and mesentery. Signs and symptoms vary depending on the site of the tumor. Surgical

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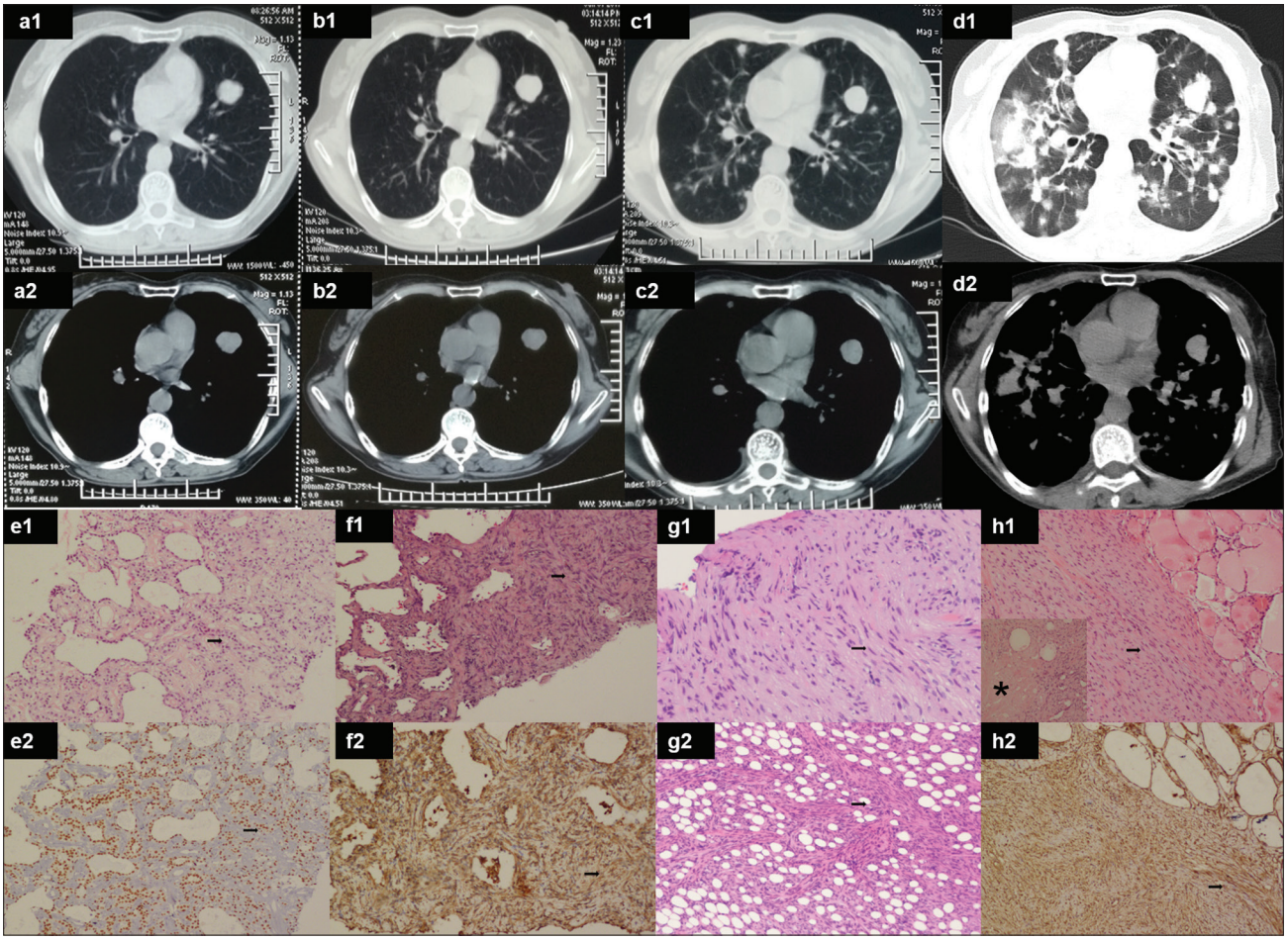

Figure 1: Lung computed tomography scan images: March 2017 (a1 and a2); June 2017 (b1 and b2); August 2017 (c1 and c2); November 2017 (d1 and d2). Microscopic (hematoxylin and eosin staining, ×200) and immunohistochemical results of the nodule of the lung, thyroid, and subcutaneous tissue: round cells hyperplasia (e1) and thyroid transcription factor-1 positivity (e2) in nodule in the left lung; spindle cells hyperplasia with a lesser degree of nuclear atypicality (f1) and vimentin positivity (f2) in nodule in the right lung; spindle cells hyperplasia in subcutaneous tissue in armpit (g1) and abdomen (g2); spindle cells hyperplasia with a lesser degree of nuclear atypicality and necrosis (signed with*; h1) and vimentin positivity (h2) in thyroid neoplasm.

removal should be considered when possible, and oral steroids or radiation therapy was chosen in some reports.[3] In this case, after consideration of pulmonary IMT, the patient took systemic steroids for one month. However, rapid progressive metastatic nodules in lung and new subcutaneous adipose tissue indicated high-grade malignant biological behavior of the disease, which was not in accordance with biological characteristic of IMT. At last, thyroid fibrosarcoma with pulmonary and subcutaneous fat metastasis was diagnosed after multidisciplinary consultation, especially pathological consultation with all the sections in multiple-sites (thyroid, right lung, subcutaneous nodules, and left lung).

Primary thyroid fibrosarcoma is very rare because thyroid sarcomas constitute <1% of all thyroid tumors and thyroid fibrosarcoma constituted 9.2% of all thyroid sarcomas.[4] Fibrosarcoma is composed of relatively monomorphic spindled cells, showing no more than a moderate degree of pleomorphism. Cells with variable atypia and view of spindle cell neoplasm containing lots of collagen fibers are remarkable in H and E staining. In immunohistochemical staining, these spindle cell areas are stained positively with vimentin, which is accordance with the results in our case.[4,5] Sometimes, it is difficult to differ fibrosarcoma from well-differentiated cells from fibroma or fibromatosis, but poorly differentiated cells express obvious atypia. Due to a small number of reported cases, the prognosis of thyroid fibrosarcoma is difficult to be predicted; however, the multiple sites metastasis of fibrosarcoma generally indicate poor prognosis.

Malignant tumor should be considered, when rapid progressive biologic behavior happens in clinical, even if thyroid fibrosarcoma is a rare disease. Because of early hematogenous metastasis of fibrosarcoma, its distant metastasis should been evaluated before surgery. In addition, multiple-site biopsy for multiple pulmonary nodules is necessary and important, when pathological findings are not accordant with clinical manifestations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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