

Contrast-enhanced ultrasound angiography-guided punch biopsy of pulmonary sarcomatoid carcinoma: a case report

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► Case report

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ABSTRACT

Background: Pulmonary sarcomatoid carcinoma (PSC) is a rare, hidden-onset, rapidly progressive, poorly differentiated non-small cell lung cancer. Its accurate diagnosis is troublesome. Herein, we reported a case of pulmonary sarcomatoid carcinoma diagnosed by contrast-enhanced ultrasound angiography-guided lung biopsy and described the imaging features in this case. **Case presentations:** A 75-year-old female patient developed a productive cough and edema of both lower limbs, accompanied by post-exercise chest tightness and shortness of breath. **Diagnosis:** Neoplastic space-occupying lesion of the upper right lung. Interventions: The pathological diagnosis of the right lung mass was achieved through contrast-enhanced ultrasound (CEUS) and CEUS-guided core needle biopsy. **Outcomes:** The biopsy results supported the pathological diagnosis of pulmonary sarcomatoid carcinoma. The typical imaging features of CEUS angiography for such a lesion in this case differing from contrast-enhanced computed tomography have not been reported in previous literature. **Conclusion:** CEUS angiography-guided lung biopsy is a safe and effective diagnostic method for pulmonary sarcomatoid carcinoma, which is superior to enhanced computed tomography-guided biopsy as to the space-occupying lesion adjacent to the thoracic wall. CEUS has potential value in the diagnosis of PSC.

INTRODUCTION

PSC is a rare, highly invasive, biphasic type of poorly differentiated non-small cell lung cancer, with five subtypes ⁽¹⁾, and represents 0.3% - 3% of all malignant tumors of the lung ⁽²⁾. At least 10% of sarcomas or sarcoma-like (spindle or giant cell) differentiation typically consist of PSCs. Gloria *et al.* reported that the biphasic nature of PSC is associated with epithelial-mesenchymal transition (EMT), which leads to its increased invasiveness and treatment difficulty ⁽³⁾. PSC is resistant to conventional platinum-based chemotherapy and has a worse prognosis compared to other subtypes of non-small cell lung cancer ⁽⁴⁾ making definitive diagnosis through routine examinations challenging. The main diagnostic procedure used is computed tomography (CT)-guided percutaneous lung biopsy. Unlike contrast-enhanced CT, contrast-enhanced ultrasound angiography can in real time observe a tumor's blood supply, with high temporal resolution. In PSC cases, it can distinguish the blood supply of the pulmonary arteries from bronchial arteries, and find the discrepancy in early perfusion of the tumor arteries. This is largely beneficial for PSC diagnosis and can

provide real-time blood supply to guide the punch biopsy for improving the quality of sampling. Herein, we reported a PSC case, described the presentation of contrast-enhanced ultrasound angiography for PSC diagnosis, and discussed the advantages of transthoracic lung biopsy guided by such angiography. Especially these newly discovered contrast-enhanced ultrasound features have not been described in previous literature.

CASE PRESENTATION

History of present illness

A 75-year-old female was admitted to this hospital because of an undefined space-occupying lesion in the right upper lobe of the lung. Half a month ago, the patient began to have a productive cough and edema of both lower limbs, gradually accompanied by chest tightness and shortness of breath after exercise. The patients reported no fever, chills, hemoptysis, or night sweats. The outpatient plain CT scan of her chest revealed a soft-tissue mass located in the posterior segment of the right upper lobe, along with a significant area of blurred shadowing in the same lobe.

Relevant tests and imaging examinations

After admission, the patient received a contrast-enhanced chest CT scan and laboratory tests for her blood and sputum samples. The CT scan revealed a soft-tissue mass in the posterior segment of the right upper lobe that exhibited heterogeneous enhancement, measuring approximately 82 mm by 74 mm. The mass displayed inconsistent density and contained shadows from small blood vessels. It showed slight uneven enhancement with a prominent ring-like enhancement at the edges. Additionally, there was partial bronchial truncation in the right upper lobe, accompanied by patchy ground-glass opacities and cystic shadows in both the right upper and middle lobes, though no significant enhancement was noted. Enlarged mediastinal lymph nodes were also observed (figure 1a, b). This indicated the possible presence of a neoplastic lesion or pneumonia in the right upper lobe or metastasis to the mediastinal lymph nodes. On laboratory examination, carcinoembryonic antigen level was normal and the levels of squamous cell carcinoma-associated antigen, cytokeratin, and specific neurogenic enolase were slightly increased (table 1); no abnormality was found in acid-fast staining of sputum smear and fungal sputum culture. As suggested, the possibility of lung infection was small, and the tumor markers were not specific enough to confirm the presence of cancer. In light of the potential presence of a tumor, electronic bronchoscopy and transbronchial lung biopsy (TBLB) were conducted the following day. Bronchoscopy indicated that the bronchial mucosa in the posterior section of the right upper lobe was infiltrated. The pathological results of the TBLB biopsy indicated the absence of tumor lesions and the presence of inflammatory changes according to morphological features. The results of bronchoscopy and TBLB biopsy together did not support the diagnosis of a lung tumor. The next day's ultrasound examination of abdominal and superficial lymph nodes found no obvious abnormality in the liver, gallbladder, spleen, pancreas, kidney, and adrenal glands; the lymph nodes in the right supraclavicular fossa were abnormally enlarged, while no obvious abnormality was found in other superficial lymph nodes. Combined with ultrasonography, metastatic lymph nodes in the right supraclavicular fossa may be considered, but the primary focus was still unclear. Besides, the emission CT bone scan reported no obvious bone metastasis.

Table 1. Results of laboratory tests of the blood sample.

Item	Result	Normal range
D-dimer	1020 ng/mL	0~500 ng/mL
C-reactive protein	48.08 mg/L	0~6 mg/L
Squamous cell carcinoma antigen	1.79 ng/mL	<1.5 ng/mL
Cytokeratin fragments	10.76 ng/mL	0~7 ng/mL
Neuron-specific enolase	10.21 ng/mL	0~9 ng/mL
Carcinoembryonic antigen	3.18 ng/mL	0~5 ng/mL

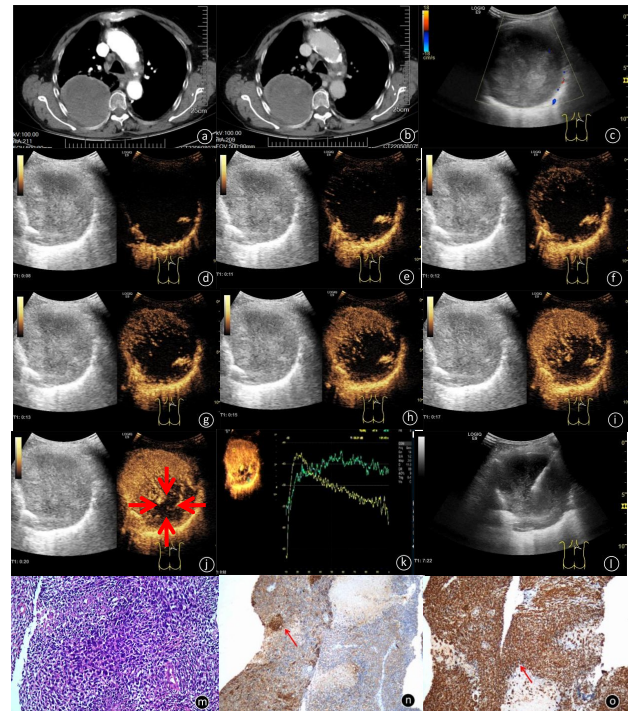


Figure 1. Images of various tests. (a) Arterial phase of contrast-enhanced CT. (b) Venous phase of contrast-enhanced CT. (c) The conventional color Doppler image showing only a few blood-flow signals in the space-occupying area of the right lung. (d) The blood supply of pulmonary arteries in the tumor was visualized at 8 seconds after injection of the contrast agent. (e–j) The blood supply of bronchial arteries was visualized at 11 seconds after the injection of the contrast agent; numerous orderly parallel line-like enhancements were presented in the same direction from the top inside to the bottom outside; a black non-enhancement area appeared in the lower part of the tumor indicates local necrosis (red arrow). (k) The time–intensity curve of contrast-enhanced ultrasound angiography showing fast presentation and fast disappearance of enhancement. (l) Contrast-enhanced ultrasound angiography guided the lung biopsy and helped avoid the necrotic area. (m) Hematoxylin-eosin staining of the sample (200-fold magnification). (n) Immunohistochemistry of PCK (100-fold magnification). (o) Immunohistochemistry staining of vimentin (100-fold magnification).

CEUS and ultrasound-guided biopsy

Given the abnormal manifestations of contrast-enhanced chest CT and superficial lymph node ultrasound, further investigation on the suspicious space-occupying lesion in the right lung and the possible metastasis to the right supraclavicular lymph nodes were warranted. As the suspicious space-occupying lesion may be the primary focus and was located close to the parietal pleura, contrast-enhanced ultrasound angiography was performed (Ultrasonic equipment: GE, logiq E9. Ultrasound contrast agent: Italy Bracco Imaging B.V., SonoVue®). The intravenous bolus injection of contrast agent was administered through the elbow vein, and the real-time dynamic changes of the undefined space-occupying lesion were observed (figure 1c). In detail, the pulmonary artery imaging was achieved at 8 s

(figure 1d) and the bronchial arteries imaging was initiated at 11 s; the blood supply of pulmonary arteries peaked at 12 s and the blood supply of bronchial arteries peaked at 17 s; their contrast enhancement was slightly increased and the distribution was uneven; the blood flow of pulmonary arteries was enlarged or obstructed in several sites, while the blood flow of bronchial arteries showed an orderly and parallel enhancement from inside to outside; the central area without enhancement was 3.0 cm × 2.7 cm (figure 1e-j); the space-occupying area gradually showed even and low enhancement at 32 s and then reduced and no enhancement (figure 1k). Collectively, ultrasound angiography suggested the presence of the space-occupying lesion with central necrosis. With the guidance of the angiography, a punch biopsy of the space-occupying lesion in the posterior segment of the right upper lobe was carried out for histopathological investigation (figure 1l).

Pathology examination

The hematoxylin-eosin staining and immunohistochemistry staining of the sample showed that PCK (for the focus), vimentin, EMA (for the focus), CK5/6 (for the focus), P40 (for the focus), Ki-67 (for the focus; 80%), CD34 (for the vessels) were found to be positive, while S-100 and STAT6 were negative (figure 1m-o). These results supported the pathological diagnosis of PSC (cT4N3M0, stage III) in the right upper lobe.

DISCUSSION

The gold standard for the diagnosis of PSC is to use the microscope for histopathological examination. Most PSC cases are first diagnosed at their middle or late disease stage, leaving less opportunity for surgical treatment⁽⁵⁾. Given no surgical specimens are obtained under such conditions, punch biopsy for histological or cytological analyses, in combination with imaging and immunohistochemical technique, can significantly improve the diagnostic accuracy of PSC⁽⁶⁾. Because of the biphasic differentiation of PSC, immunohistochemistry analysis frequently utilizes epithelial markers such as CK, EMA, CAM5.2, P40, P63, TTF-1, and napsin A, as well as mesenchymal markers like vimentin and desmin. The markers vimentin, EMA, CK5/6, and P40 tested positive via immunohistochemistry in our case, consistent with the literature reports.

The patient in our case had no obvious specificity in imaging examination and laboratory examination and no obvious positive results from bronchoscopy and biopsy under fiberoptic bronchoscopy. Therefore, a percutaneous biopsy of the space-occupying lesion in the lung was administrated. Percutaneous lung biopsy for previous cases was

mostly done under the guidance of CT, with high accuracy and few complications^(7, 8). Because the space-occupying lesion was located in the peripheral part adjacent to the chest wall and could be observed in real time under ultrasound, a CEUS-guided biopsy was performed for a definite pathological diagnosis.

The blood supply of the tumor can be observed by conventional contrast-enhanced ultrasound angiography before punch biopsy. Contrast-enhanced ultrasound angiography found that the tumor contains two sets of blood supply of pulmonary arteries and bronchial arteries, consistent with the composition of PSC tissues. The initial imaging of pulmonary arteries and bronchial arteries can be observed in sequence with only 3 to 6 seconds apart. Contrast-enhanced ultrasound angiography can capture the details of perfusion of these arteries due to its real-time presentation and high temporal resolution, superior to contrast-enhanced CT. With contrast-enhanced ultrasound angiography, the non-enhanced area within the tumor can indicate the necrotic area inside the tumor, which is typical in PSC cases. This is beneficial for PSC diagnosis and can guide punch biopsy and help avoid the necrotic area. It is worth noting that such angiography showed in this case the enlarged or obstructed/discontinuous blood supply of pulmonary arteries, and rare, characteristic enhancement of blood supply of bronchial arteries in an orderly and parallel manner from inside to outside. There have previously been less reports of these contrast-enhanced characteristics in the literature. Whether these arterial enhancement features in PSC are linked to spindle cells or fibrous cells and the growth arrangement of tumor cells and nutrient vessels merits further verification in more PSC cases.

As a rare, highly invasive non-small cell lung cancer, PSC is routinely diagnosed via chest imaging test and pathohistological analysis of a biopsy sample. Most PSC patients lose the possibility for surgical treatment when first diagnosed with the condition. An efficient diagnostic technique is the use of lung biopsy that was performed using CEUS⁽⁹⁾. Such biopsy, because of its safety, convenience, no radiation damage, real-time display of blood vessels, high diagnostic rate, and few complications, may be superior to enhanced CT-guided biopsy as to the space-occupying lesion adjacent to the thoracic wall⁽¹⁰⁾. Contrast-enhanced ultrasound angiography had certain characteristics in this case, and its guided transthoracic or even transbronchial lung biopsy may provide a powerful reference for PSC diagnosis, which requires further verification in future PSC cases.

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Conflict of interest: The authors declare that they have no conflict of interest. The patient has provided informed consent for publication of the case.

Ethical statements: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from the patient for being included in the study.

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