

Clear cell tumor of the lung

Two case reports and a review of the literature

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Abstract

Background: Clear cell tumor of the lung (CCTL) is a rare and mostly benign pulmonary tumor arising from perivascular epithelioid cells. We reported 2 cases of CCTL in a 24-year-old man with chest pain and a 59-year-old man with dyspnea.

Methods: Their chest CT images revealed a well-defined, homogeneous nodule located in the peripheral region of lung parenchyma. The solid nodule showed intense heterogeneous postcontrast enhancement in the arterial phase and a homogeneous appearance in the venous phase. The two patients underwent thoracotomy, and pathological examinations, including immunohistochemical studies revealed that both cases were benign clear cell tumors.

Results: Due to the fact that only a few cases about CCTL were reported, clinicopathological aspects and radiological characteristics of this type of tumor are not well established.

Conclusion: CCTL is a rare and benign primary tumor and majorly occurs in middle-aged and elder people. The finding of a small vessel extending along and partially wrapping up one side of the mass in the CT-enhanced images might be a helpful feature to differentiate CCTL from other lung neoplasms.

Abbreviations: CCTL = clear cell tumor of the lung, CK = cytokeratin, EMA = epithelial membrane antigen, HMB = human melanoma black, HU = hounsfield units, LAM = lymphangioleiomyomatosis, PEComa = perivascular epithelioid cell tumor, SFT = solitary fibrous tumor.

Keywords: case report, clear cell tumor of the lung, CT imaging, differential diagnosis, pathology

1. Introduction

Clear cell tumor of the lung (CCTL) is a mostly benign and rarely seen pulmonary neoplasm first described by Liebow and Castleman in 1963.^[1] It belongs to perivascular epithelioid cell tumor (PEComa), which is a new classification category defined in the World Health Organization Classification of Tumours in 2002.^[2] In the World Health Organization soft-tissue volume, PEComas are defined as “mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells.” PEComas include clear cell tumor, lymphangioleiomyomatosis, angiomyolipoma, and clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres.^[2–4] Previously, although several cases of CCTL have been reported, it still remains as a rare type of primary pulmonary tumor, and there are hardly any existing systematic reports to

describe the radiological and clinicopathological characteristics of CCTL. In this report, we present 2 cases of CCTL, summarizing to get the gist after making a thorough review of more than 20 peer-reviewed literatures to specifically address its radiological, clinical, and pathological features.

Our institutional review board did not require its approval or patient informed consent for this type of review.

2. Case presentation

2.1. Case 1

A 24-year-old male presented with right chest pain for 2 days. The mild pain was on the right side of the chest wall and had no association with breathing or position. The patient denied fever, cough, hemoptysis, or night sweats. Physical examination showed no abnormalities and he had no history of tobacco use. The preliminary blood test, liver, and kidney function tests were also normal. Chest radiographs revealed a round nodule in the lower lobe of the right lung. The chest computed tomography (CT) scan showed a defined, homogeneous nodule with the size of 3 cm × 2.5 cm located in the lateral basilar segment of the right lower lobe (Fig. 1). There was no calcification, necrosis, or cavitation within the lesion. After administration of the contrast agent, the mass showed intense, heterogeneous, and curvilinear enhancement in the arterial phase (35 seconds) with a CT value of 93 hounsfield units (HU) and a homogeneous nature in the venous phase (70 seconds) with a CT value of 90HU (Fig. 1). A small tiny vessel appeared to be extending along, partially wrapping up one side of the tumor and finally converging into the right inferior pulmonary vein (Fig. 1). No pathologically enlarged mediastinal or hilar lymph nodes were seen. Then, a right thoracotomy was conducted, revealing a well-encapsulated ovoid

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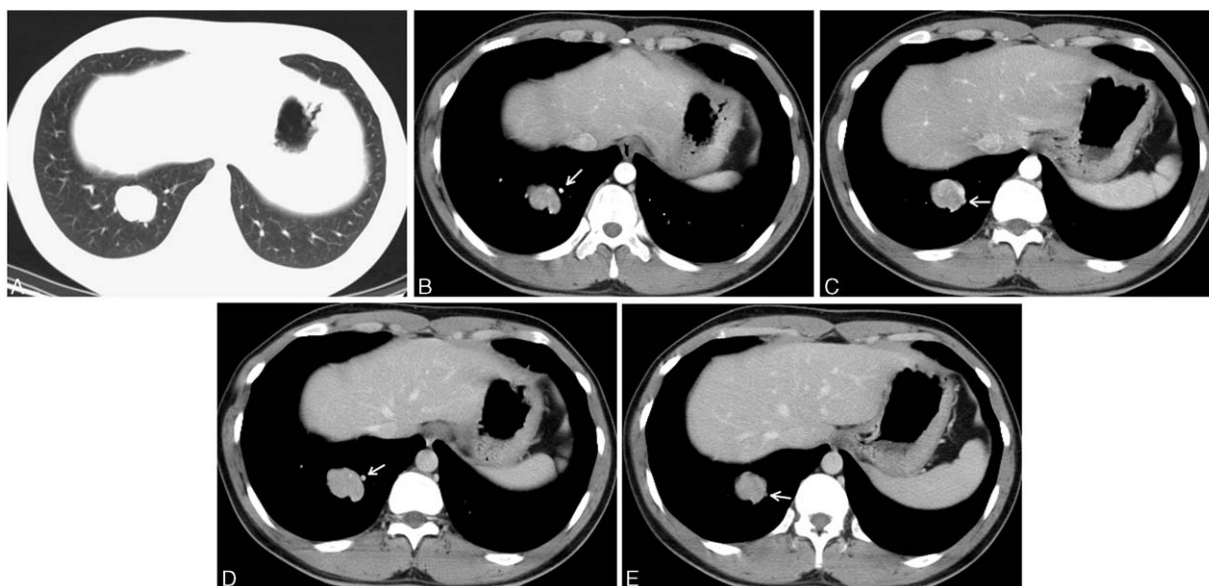


Figure 1. Chest computed tomography (CT) findings of a 24-year-old yang man. Chest CT scan discovered a solitary, rounded, and smooth-surfaced mass with the size of 3.0 cm × 2.5 cm located in the lateral basilar segment of the right lower lobe (A). The contrast-enhanced CT imaging showed heterogeneous curvilinear enhancement measuring 93HU in the arterial phase (B, C), and a homogeneous nature measuring 90 HU in the venous phase (D, E). A small vessel appeared to be extending along and partially wrapping up one side of the tumor (B–E).

intrapulmonary tumor. The frozen section biopsy showed the tumor was composed of round, pump cells arranged in nests and cords with abundant clear cytoplasm (Fig. 2). These findings provided us with strong evidence that this patient was bearing CCTL, thus only segmentectomy was performed instead of lobectomy. Immunohistochemical analysis showed the tumor had a positive reaction to human melanoma black (HMB)-45, Melan-A, Syn, CD56, PLAP, and periodic acid-Schiff protein but no reactivity to SMA, S-100, cytokeratin (CK), epithelial membrane antigen (EMA), CD10, CgA, or CD117. Based on these findings, diagnosis of benign CCTL on this patient was confirmed. No evidence of tumor recurrence or metastasis was found during the 12-month follow-up period after the surgery.

2.2. Case 2

A 59-year-old male was admitted to our hospital because of dyspnea and tachypnea for 1 week after catching cold. He had a little bit weight loss of 2.5 kg in 1 month and his symptoms were aggravated after exercise. He had no history of fever, cough, expectoration, or hemoptysis. He had a history of systemic hypertension for more than 20 years, and was a current smoker with 20 pack-year history of smoking cigarettes. Physical examinations and laboratory studies showed no abnormalities. The chest CT plain scan disclosed a solitary, smooth-margined mass measuring 2.2 cm × 1.5 cm located in the anterior segment of the right upper lobe with a CT value of 45HU (Fig. 3). Contrast-enhanced CT scans revealed the mass had obvious ring-like enhancement measuring 85 HU with central low density area in the arterial phase and was persistently enhanced with a relatively homogenous appearance measuring 93HU in the venous phase (Fig. 3). A tiny vessel beneath the lesion was found to be closely attached to the mass and finally enter into the right superior pulmonary vein. No lymphadenopathy or pleural effusion was found. Owing to the localization and size of the tumor and the potential risk of malignancy, the patient was

subjected to an upper lobectomy. During the surgery, the mass was confined to the anterior basilar segment of the right upper lung and appeared grayish-white, well-circumscribed on cut surface. Neither necrosis nor hemorrhage was found in the tumor. Histological examinations revealed it was composed of round cells with typical round nuclei and abundant clear cytoplasm (Fig. 4). Immunohistological examination revealed the tumor was positive for Melan-A and S-100, but not for HMB-45, CK, EMA, SMA, Des, P63, and CK5/6. Finally, diagnosis of benign CCTL on this patient was established. The patient was followed for another 24 months after the surgery and is now living well without evidence of recurrent or metastatic disease.

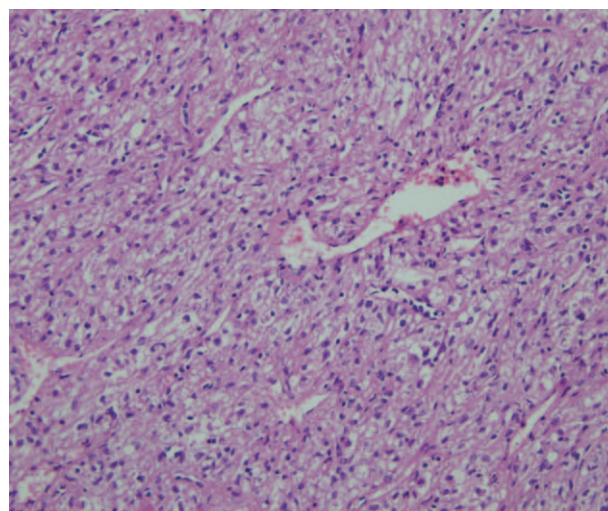


Figure 2. HE staining (×200) showed the tumor was composed of round cells arranged in nests and cords with abundant clear cytoplasm.

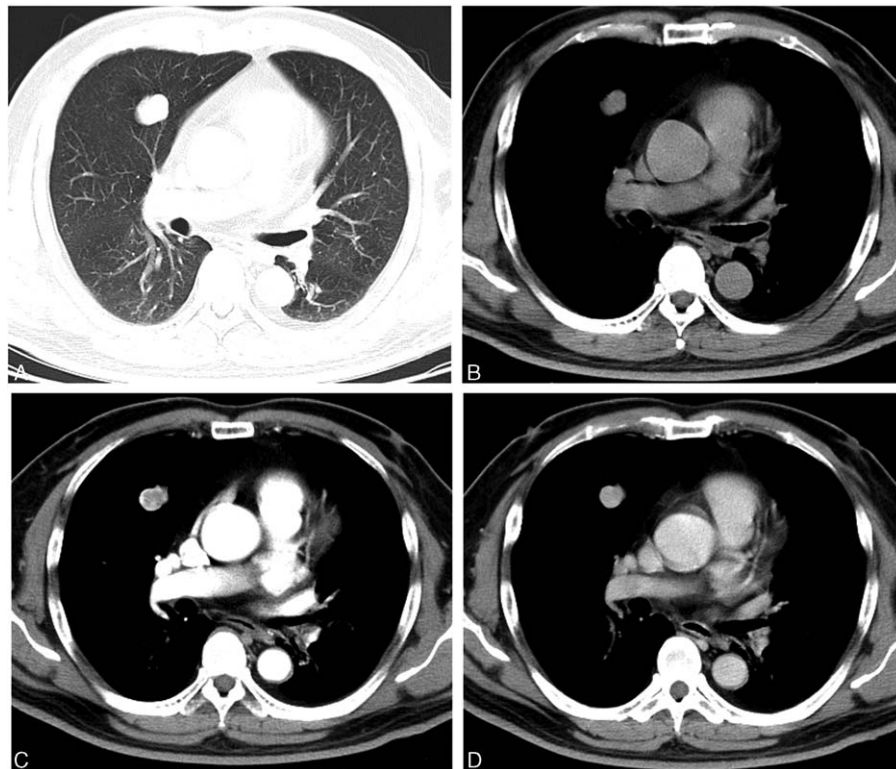


Figure 3. Chest computed tomography (CT) images of a 59-year-old male. CT plain scan revealed a defined, homogeneous mass measuring 2.2 cm × 1.5 cm located in the anterior segment of the right upper lobe with a CT value of 45HU (A, B). The contrast-enhanced image showed the mass had obvious ring-like enhancement with central low density in the arterial phase with a CT value of 85HU (C), and a relatively homogenous appearance with a CT value of 93HU in the venous phase (D).

3. Discussion

Clear cell tumor of the lung (CCTL) comprises of clear cells with large amounts of intracytoplasmic periodic acid-Schiff-positive glycogen. Therefore, it has been termed “clear cell tumor” or “sugar tumor.” The “clear cells” are pump, rounded, and mitotically inactive cells, with distinct cell borders. They are arranged in masses and cords, and supported by very little connective tissue. The blood is supplied by abundant large, thin-walled sinusoidal vessels intervened in the tumor cells. The tumor cells show immunoreactivity for HMB-45 and S-100 protein but not for CK or EMA, and these can collectively establish the definitive diagnosis.^[5] In the present case, immunohistochemical analysis of the 2 cases is typical for CCTL: positive for HMB-45 and S-100 protein respectively and negative for CK and EMA.

The typical clinical manifestation is an isolated and asymptomatic incidentaloma on routine chest radiograph or CT scan. A few people may present with chest pain, breathlessness, cough, blood sputum, or hemoptysis,^[6] and there are no significant findings upon physical or laboratory examination. Patients usually range in age from 8 to 73 years with equal sex prevalence, especially in middle-aged and elder people.^[7,8] The biological behavior of this neoplasm is traditionally considered benign; however, malignant CCTL has also been discovered and reported in several other literatures.^[9–12] Certain clinicopathologic features such as a diameter >2.5 cm, the presence of symptoms, and extensive necrosis or abundant mitoses visible under an optical microscope are correlated with more aggressive behavior.^[13–15] Surgical resection is an acceptable curative

approach for CCTL, as the tumor’s benign behavior is not invariable, and chemotherapy or radiotherapy has not demonstrated significant benefits for malignant CCTL.^[16]

Characterized CT imaging of CCTL is a rounded or ovoid peripheral parenchymal nodule with smooth margins measuring

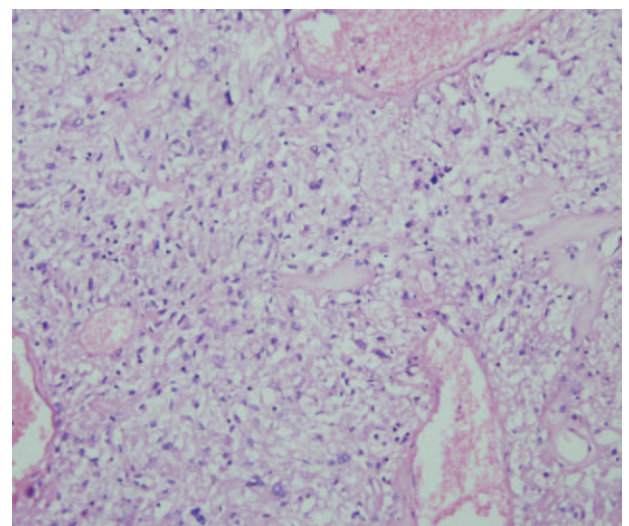


Figure 4. HE staining (×200) showed the tumor was composed of round cells with typical round nuclei and abundant clear cytoplasm.

3 cm or less in diameter.^[6–8] One recent study indicates that tumors ≥ 2.2 cm in diameter are more likely to have lobulated appearance and more aggressive symptoms^[8]. Its density is generally homogenous without obvious evidence of hemorrhage, necrosis, cavitation, or calcification. It may occur in any lobe and is mainly located under the pleura without communication with bronchi or blood vessels.^[17] There are seldom specific lobar distributions; however, 1 case of malignant CCTL shows lung to lung metastases.^[12] After administration of contrast medium, the key characteristic of CCTL is the intense heterogenous enhancement in the arterial phase and an early washout pattern in delay phases.^[8,14] In our report, these 2 patients' tumors are located in the peripheral portion of pulmonary parenchyma measuring less than 3 cm in diameter. The typical curvilinear or circular patterns of enhancement in the arterial phase are presumably caused by the thin-walled vessels within the tumor. Histologically, the sinusoidal vessels without muscular coat composed of endothelial layer with continuity into small capillaries penetrate among the tumor cells.^[18] Thus, in the venous phase, the tumor has persistent enhancement and a homogenous appearance as a result of the gradual penetration of the contrast agent into the capillaries. In both patients, we can appreciate a small vessel extending along and partially wrapping up one side of the mass. This sign, to our knowledge, has not been reported in previous studies, which may be related to a shift on distal pulmonary venous branches by locally accumulated sinusoidal vessels.

Differential diagnosis of CCTL should include primary peripheral carcinoma, pulmonary metastasis, pulmonary sclerosing hemangioma, solitary fibrous tumor (SFT), paraganglioma, and tuberculoma. Pulmonary carcinoma shows invasive growth characteristics along the inside and outside of the bronchial wall. It may present as spiculated and lobulated outline with violations of bronchus, blood vessels, and surrounding tissue space.^[19] The vessel convergence sign, pleural indentation, and central necrosis are commonly seen at CT assessment. Pulmonary sclerosing hemangioma predominantly occurs in young or middle-aged women, and is characterized by a well-defined and heterogeneous enhancing soft-tissue mass. The air-trapping sign, tail sign, prominent pulmonary artery sign, and intratumoural cystic areas are helpful for differential diagnosis.^[20] Intrathoracic SFT originates from the pleura and can project into the pleural cavity in a pedunculated manner from the visceral pleura.^[21] In contrast CT imaging, SFT demonstrates heterogeneous, moderate enhancement as the tumor contains cystoid spaces filled with mucoid material.^[21,22] Paraganglioma mainly occurs in middle-aged female with or without hypertension. Functional paraganglioma generally has a rich blood supply and is significantly enhanced after contrast medium administration. Nonfunctional paraganglioma may show moderate enhancement due to the low density of blood vessels inside the tumor.^[23] Radiological manifestation of tuberculosis classically involves central necrotic tissue with disseminated foci, fiber proliferation, and calcification around the lesion.

4. Conclusions

We report 2 cases of CCTL and analyze its clinicopathological aspects and radiological characteristics. We conclude that, in most cases, CCTL is a rare and benign primary tumor and majorly occurs in middle-aged and elder people. Prominent characteristics of CT imaging of CCTL include a round, well-defined and homogeneous nodule located in peripheral lung zones. Moreover, it tends to show circular enhancement in the

arterial phase and persistent homogenous enhancement in the venous phase. To our knowledge, this is the 1st description of a small vessel extending along and partially wrapping up one side of the mass. This might consist in a helpful feature to differentiate CCTL from other lung neoplasms.

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