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Original Article

Imaging features, diagnosis and treatment of pulmonary sclerosing pneumocytoma complicated with lung cancer

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Abstract: Objective: Imaging features, diagnosis and treatment of pulmonary sclerosing pneumocytoma complicated with lung cancer were analyzed to improve the accuracy of diagnosis. Methods: The clinical data of 14 cases of pulmonary sclerosing pneumocytoma complicated with lung cancer treated in Chinese PLA General Hospital from January 2008 to August 2016 were collected. Their clinical characteristics, imaging, diagnosis and treatment features were analyzed. Results: Fourteen cases were confirmed pulmonary sclerosing pneumocytoma complicated with lung cancer pathologically. Twelve cases were considered as lung cancer in CT images, and two cases were considered as benign nodules. Four lesions were confirmed as pulmonary sclerosing pneumocytoma, which were considered as malignant tumor or metastatic cancer by CT diagnosis. Conclusion: The phenomenon of pulmonary sclerosing pneumocytoma complicated with lung cancer is rare. When multiple nodules are found in images with natures difficult to be determined, respective pathological basis should be obtained for definite diagnosis.

Keywords: Pulmonary sclerosing pneumocytoma, lung cancer, benign tumor, metastasis

Introduction

Pulmonary sclerosing pneumocytoma (PSP) is a rare benign tumor in lung. The term "sclerosing hemangioma" is changed to "pulmonary sclerosing pneumocytoma" in WHO Classification of Lung Tumors 2015. PSP was initially considered as vascular-derived; however, it is now considered as derived from primitive respiratory epithelium of pulmonary alveolus, especially type II alveolar cells [1, 2]. PSP has no significant clinical or imaging features, which is difficult to be differentiated from benign nodules such as hamartoma, tuberculoma and bronchial cysts etc, and from some lung cancer nodules [3]. The coexistence of PSP and lung cancer in the same lung is even less. Due to insufficient understanding of this disease, or limited to monism thinking, PSP complicated with lung cancer is easily misdiagnosed as primary lung cancer with metastasis, affecting tumor staging and treatment principle. This article reported clinical and imaging features as well as diagnosis and treatment of 14 cases PSP complicated with lung cancer, to improve the diagnosis level of PSP complicated with lung cancer.

Materials and methods

General clinical data

The clinical data of 14 patients pathologically confirmed as PSP complicated with lung cancer in Chinese PLA General Hospital were collected, of which there were 2 males and 12 females, with a ratio of 1:6, aged from 34 to 68, with the median age of 51. Eleven patients had no symptoms, 2 patients had chest tightness and shortness, and 1 patient had cough with blood in sputum. In one case, blood tumor marker CA15-3 increased, while in the remaining 13 cases, all blood tumor markers (CEA, NSE, CSS, CYFRA21-1, CA19-9, CA125, CA153, and CA724) showed normal.

Imaging analysis

The images were read separately by at least 2 radiologists to analyze, describe and judge the size, site and morphology of the lesions, and

then they were reviewed and commented by a physician with the qualification of deputy director of radiology department or higher.

Diagnostic methods

All 14 cases were pathologically and definitely diagnosed, of which, 7 cases underwent thoracoscopic surgical procedure, 5 underwent partial lobectomy with thoracotomy, 1 underwent da Vinci robot assisted thoracotomy, and 1 underwent twice CT-guided percutaneous lung puncture biopsy and once electronic bronchoscopy to obtain pathological basis.

Follow-up

The patients were followed up by telephone to investigate the therapeutic effect, condition change and survival status of patients, the cut-off date of follow-up was September 30, 2016.

Statistical analysis

In this study, the data were showed as rate, the comparison between groups was carried out using chi square test, $P<0.05$ was treated as statistically significant difference. The data were analyzed using SPSS17.0 software.

Results

Imaging features

All the 14 cases underwent lung CT examination prior to the surgery. Judgment from the lung CT images showed that, 6 cases with 1 malignant lesion and 1 benign lesion, 2 cases with 1 malignant lesion and multiple benign lesions, 4 cases with multiple malignant lesions, and 2 cases with 1 benign lesion. Compared to pathological results, 8 cases (8/14, 57.1%) had consistent CT imaging findings and pathological results, and 6 cases (6/14, 42.9%) had inconsistent CT imaging findings and pathological results.

There were 12 cases with pathologically confirmed lung cancer and CT imaging judged malignant lesions, which imaging features included: Lesion number: 9 cases with a single lesion, and 3 cases with multiple malignant lesions or metastases; Lesion size: the maximum diameters of 1.0 cm-4.1 cm; Site: for multiple malignant lesions, the lesion with maximum diameter was dominant, and there were 5 cases with malignant lesion in upper lobe of left lung, 1 case in lower lobe of left lung, 4 cases in upper lobe of right lung, 1 case in lower lobe of right lung, and 1 case in middle lobe of right lung; Density: 9 cases with solid density, 2 cases with ground glass density, and 1 case with mixed density; Signs of malignant tumor: irregular edges, lobulation, spicule, pleural indentation, and vacuoles.

There were 8 cases pathologically confirmed PSP and CT imaging judged benign nodules, and the imaging features of pulmonary sclerosing nodules included: Lesion number: 6 cases with a single pulmonary nodule, 2 cases with multiple pulmonary nodule lesions, of which there was 1 pathologically confirmed PSP in each case, and the remaining nodules were chronic inflammation; Lesion size: the maximum diameter of 0.7 cm-1.6 cm. Site: 2 cases with single nodule in upper lobe of left lung, 2 cases in lower lobe of left lung, 2 cases in upper lobe of right lung, 1 case in lower lobe of right lung, and 1 case in middle lobe of right lung; 5 cases in the same lung lobe with lung cancer lesion, and 3 cases in the same side but different lobe; Density: 7 case with solid and uniform density, and 1 case with partial ground glass density; Edge: 1 case with short spicule and vessel convergence sign observed, and the remaining 7 case with smooth and intact edges.

There were 4 cases pathologically diagnosed as PSP, while judged malignant lesions by CT imaging, of which 3 cases were considered as lung metastases, and 1 as bronchioloalveolar carcinoma. The imaging features included: Number: 2 lung nodule lesions in each case; Lesion size of lung cancer: maximum diameter of 1.0 cm-4.1 cm; lesion size of PSP: maximum diameter of 0.7-1.5 cm; in 1 case, maximum diameter of PSP lesion was larger than that of lung cancer lesion; Site of lung cancer: 2 cases in upper lobe of left lung, 1 case in lower lobe of right lung, and 1 case in middle lobe of right lung; site of PSP: 2 cases in upper lobe of left lung, 1 case in lower lobe of left lung, and 1 case in middle lobe of right lung; 1 case in the same lung lobe with lung cancer lesion, 2 cases in the same side but different lobe, and 1 in the contralateral lobe with malignant lesion; Lesion density of lung cancer: 3 cases with soft tissue density, 1 case with ground glass density; lesion density of PSP: 3 cases with solid densi-

Table 1. Imaging features of lesions

	Lung Cancer	Pulmonary Sclerosing Hemangioma
Number	1 (13 cases, 92.9%)	1 (14 cases)
	2 (1 case, 7.1%)	Multiple (0 case)
Maximum Diameter	1.0 cm-4.1 cm	0.7 cm-1.6 cm
Site		
Upper lobe of left lung	5 (35.7%)	4 (28.6%)
Lower lobe of left lung	2 (14.3%)	4 (28.6%)
Upper lobe of right lung	4 (28.6%)	2 (14.3%)
Lower lobe of right lung	1 (7.1%)	1 (7.1%)
Middle lobe of right lung	2 (14.3%)	3 (21.4%)
Density		
Solid	11 (78.6%)	12 (85.7%)
Ground glass	2 (14.3%)	1 (7.1%)
Mixed	1 (7.1%)	0
Cystic	0	1 (7.1%)
Edge		
Lobulation	12 (85.7%)	0
No lobulation	2 (14.3%)	12 (85.7%)
Spicule		
Long spicule	3 (21.4%)	0
Short spicule	0	1 (7.1%)
Pleural stretching	2 (14.3%)	1 (7.1%)
Calcification	1 (7.1%)	1 (7.1%)
Ground glass shadow in lesion periphery	0	2 (14.3%)

Table 2. Sites of PSP and lung cancer

Site	PSP (case)	Lung Cancer (case)
Upper lobe of left lung	5	4
Lower lobe of left lung	3	3
Upper lobe of right lung	2	4
Middle lobe of right lung	3	2
Lower lobe of right lung	1	1
In the same lung lobe with lung cancer	8 (8/14, 57.1%)	
In the same side but different lobe with lung cancer	5 (5/14, 35.7%)	
In a lobe at different side with lung cancer	1 (1/14, 7.1%)	

ty, 1 case with cystic density and thin and non-uniform peripheral wall; Lesion edge of lung cancer: 4 cases with lobulation sign; lesion edge of PSP: 4 cases without lobulation; Lung cancer had no calcification in lesions, PSP had calcification in 1 case; Lesion periphery of lung cancer: no ground glass shadow; lesion periphery of PSP: 2 cases with ground glass shadow.

There was 2 cases pathologically confirmed as PSP complicated with lung cancer and CT imaging judged single benign lesion, which imaging features included: Number: 1 lung nodule lesions in each case; Lesion size of lung cancer: the maximum diameters are 1.7 cm and 1.9 cm, respectively; Site: 1 case in middle lobe of right lung, and 1 case in lower lobe of left lung; Morphology: all in nearly round; Edge: smooth, and no lobulation; Density: soft tissue density; Calcification: 1 case with punctate calcification lesion at edge; CT enhancement: 1 case without any obvious enhancement, and 1 with obvious enhancement; Mediastinal lymph nodes: 1 case with multiple enlarged lymph

Table 3. Pathological types of PSP complicated with lung cancer

Pathological Type	Number of Cases	Percentage
Adenocarcinoma	11	78.6%
In situ adenocarcinoma	3	21.4%
Adenocarcinoma with *in situ* adenocarcinoma	2	14.3%
Tubular adenocarcinoma with micropapillary adenocarcinoma	1	7.1%
Carcinoid	3	14.3%
Small cell carcinoma	1	7.1%

nodes, and 1 case without any obviously enlarged lymph nodes (shown in **Table 1**).

Pathological results

All the 14 cases were pathologically diagnosed as PSP complicated with lung cancer. Sites: occurrence site of PSP: 5 cases in upper lobe of left lung, 3 cases in lower lobe of left lung, 2 cases in upper lobe of right lung, 3 cases in middle lobe of right lung, and 1 case in lower lobe of right lung. Occurrence site of tumor: 4 cases in upper lobe of left lung, 3 cases in lower lobe of left lung, 4 cases in upper lobe of right lung, 2 cases in middle lobe of right lung, and 1 case in lower lobe of right lung. There were 8 cases (8/14, 57.1%) with PSP and lung cancer in the same lobe, 5 cases (5/14, 35.7%) in the same side but different lobes, and 1 case (1/14, 7.1%) in different sides (shown in **Table 2**). Cytological type of malignant tumor: 11 cases (11/14, 78.6%) of adenocarcinoma, 2 cases (2/14, 14.3%) of carcinoid, and 1 case (1/14, 7.1%) of small cell carcinoma. For adenocarcinoma, there were 3 cases (3/14, 21.4%) of *in situ* adenocarcinoma, 2 cases (2/14, 14.3%) of adenocarcinoma with a little *in situ* adenocarcinoma, and 1 case (1/14, 7.1%) of tubular adenocarcinoma with micropapillary adenocarcinoma (shown in **Table 3**). The pathological staging of lung cancer performed according to TNM Classification for Lung Cancer, Version 8: 5 cases of Stage Ia1, 5 cases of Stage Ia2, 3 cases of Stage Ia3, and 1 case of Stage IIIa. The maximum diameter of PSP varied from 0.5 to 2.2 cm; comparison of pathological sizes of lesions: 9 lesions with size of PSP less than lung cancer, and 5 lesions with size of PSP larger than lung cancer (**Figure 1**).

Discussion

The coexistence of the 2 tumors with different natures, PSP and lung cancer, is extremely rare in lung(s) of the same patient. In early stage of lung cancer, the patient may show no obvious clinical symptoms and uneasy to find out the disease, most of which are screened out by health examinations. When multiple lesions are observed on CT images, considering the primary tumor with intrapulmonary metastases and limited to the monism thesis, the difficulty of diagnosis will be significantly increased and may lead to misdiagnosis, disturbing the staging and treatment for malignant tumors, if there is no pathologically diagnostic basis. Thus, the pathological diagnosis is particularly important for multiple lesions in lungs.

The incidence of PSP accounts for approximately 11% of primary lung tumors [4]. Patients are usually women with a mean age of 46 years [5]. This series of cases has the male to female ratio of 1:6, and 85.7% of females, which is consistent with literatures. The most common symptoms of PSP are chest pain and cough [6], seldom hemoptysis [7], the early stage of lung cancer may also show no clinical symptoms, or only symptoms of chest pain, cough or hemoptysis, etc. In this series, 11 cases were identified by health examination, and 3 cases developed clinical symptoms of chest tightness, shortness, and cough with hemoptysis. Therefore, when the PSP and lung cancer coexist, it is difficult to judge which disease induced the symptoms.

Most CT imaging features of lung cancer are well-known. For example, the lesions show irregular nodule with soft tissue density or mass shadow, often occur in upper lobes with rough edges. Spicule sign, lobulation, pleural indentation sign, and vessel convergence sign can be observed, and a few cases have cavities or vacuoles, with or without enlargement of mediastinal lymph nodes. This series has 12 cases considered as lesions of early lung cancer by CT imaging, and small nodules in the

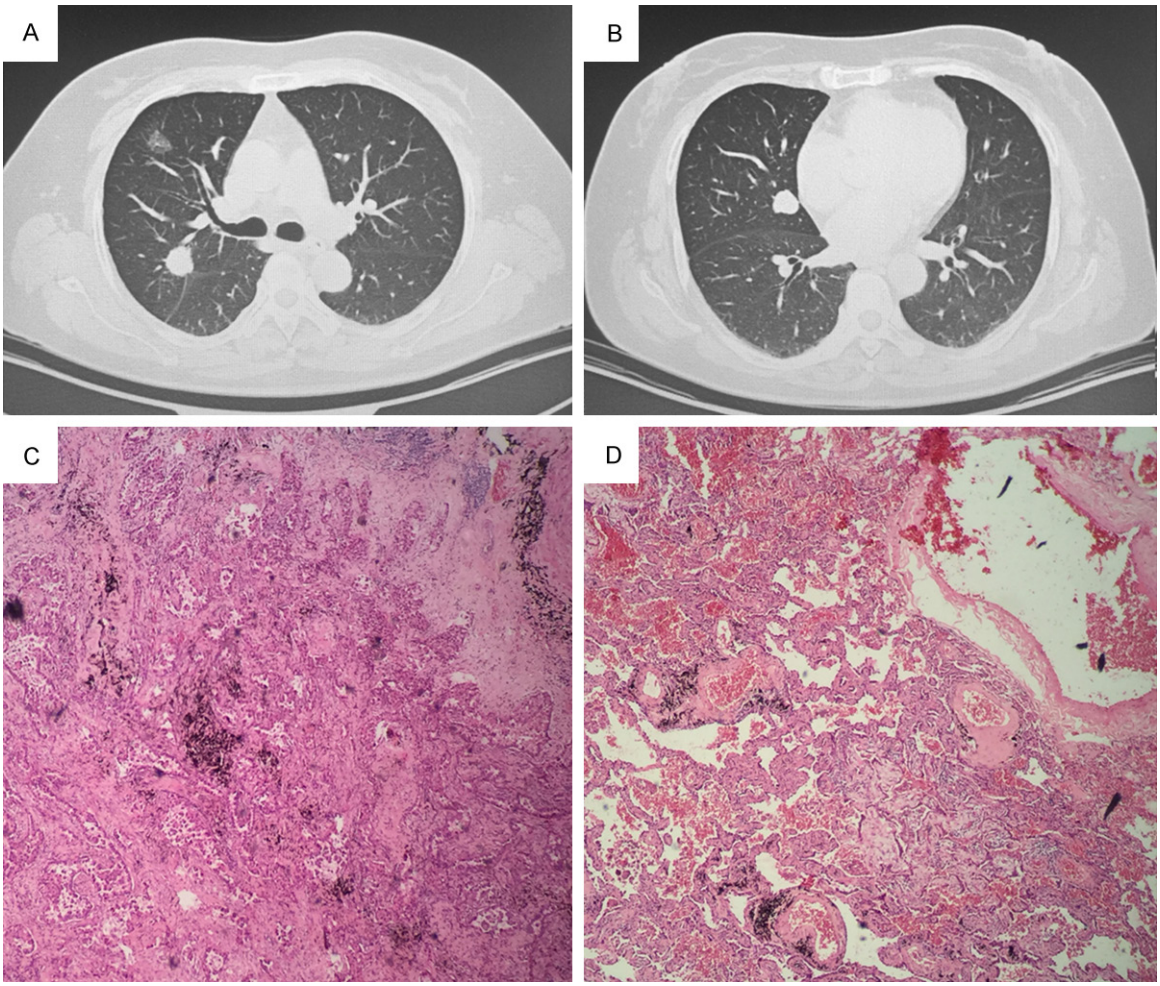

Figure 1. Imaging and pathology of pulmonary sclerosing pneumocytoma complicated with lung cancer. A: Adenocarcinoma in upper lobe of right lung; B: PSP in middle lobe of right lung; C: Pathology of adenocarcinoma in upper lobe of right lung; D: Pathology of PSP in middle lobe of right lung.

same lung are considered as benign nodules or metastases, no nodule identified as PSP from images. The CT images of PSP reported in literatures have some features: the lesions are usually separate nodules, and multiple nodules or those involved bilateral lung lobes are rarely seen [8, 9]; the diameter is 0.3-11 cm [1], showing slowly growth, in round or nearly round, with clear and smooth edges; lobulation and spicule can be seen in lesion periphery, with rare calcification, and uniform or nonuniform enhancement can be observed with enhanced CT. The other relatively characteristic signs include welt vessel sign [10], air crescent sign [11], and halo sign [1]. The images of these patients of PSP shows nodular lesions with regular edges and no lobulation, mostly single lesion, of which there is 1 case of short spicule sign, 1 case of pleural indentation sign, and 2 cases of halo sign (ground glass shadow in lesion periphery). It is difficult to judge PSP directly from images. In images with coexistence of PSP and lung cancer, it is easy to misdiagnose PSP as metastasis or other benign nodules. In another case, the image shows as cystic density, thin and nonuniform peripheral wall. This character was not mentioned in literatures, and pathology showed nodular mass in dark red, without any cystic change, which is considered to be related with CT scanning plane.

For the multiple PSP or PSP with lymph node metastasis, it is unknown whether they are multicentric occurrence of PSP, or belong to intrapulmonary metastases [12, 13]. There is

also reported case of the third lumbar vertebra (L3) metastasis of PSP [14], therefore, not all PSP are benign as they have potential risk of metastasis [15, 16], and surgical treatment is recommended. The preferred treatment of early lung cancer is surgery, so in cases of PSP complicated with lung cancer, surgery is also recommended. And if allowed by the surgery method, benign and malignant lesions can be removed together. The prognosis of surgery for PSP is good, and currently only 1 case recurrence occurred in the original site with wedge resection of lung 10 years after PSP procedure, reported by Wei, *et al*. [17]. In these patients, all the 14 cases underwent surgical treatment, with good treatment effects, of which 1 case performed post-operation adjuvant chemotherapy.

In this series of cases, the cytological types of PSP complicated with lung cancer are mainly lung adenocarcinoma, with the incidence of 78.6%, and the incidence of 2 tumor occurred in unilateral lung lobes is 92.8%, suggesting PSP may have the same molecular genetic changes with lung adenocarcinoma, between which there may have a relationship [18]. Dacic *et al*. compare tumor suppressor genes in 2 tumors of PSP and bronchioloalveolar carcinoma by microdissection genotyping, and found similar allelic loss in some individual cases of two tumors, suggesting tumor suppressor genes on chromosome 5p may play a role in tumorigenic mechanism of sclerosing pneumocytoma. It also supported that PSP and bronchioloalveolar carcinoma have common origin, i.e., similar to non-mucinous bronchioloalveolar carcinoma, PSP also derives from cells of terminal lobular unit [19].

The incidence of PSP complicated with lung cancer is very low, and when complicated with lung cancer by images, the PSP is difficult to be identified; in addition, misdiagnosis easily occurs due to lack of recognition for co-occurrence of two diseases. The imaging and clinical features of PSP should be fully understood, and surgical pathology should be obtained as far as possible to get accurate diagnosis.

Disclosure of conflict of interest

None.

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