

CASE REPORT: RARE CASE OF PNEUMOCYTOMA

Le Van Giao, Thieu Dinh Hung**

SUMMARY

Pulmonary sclerosing (Pneumocytoma) is a rare benign pulmonary tumor of primitive epithelial origin. Because of the unspecific radiological features mimicking malignancies and their histological heterogeneity, the differential diagnosis with adenocarcinoma and carcinoid tumors is still challenging. We report a case of sclerosing pneumocytoma, as well as a review of the literature. Immunohistochemical findings showed intense staining of the cuboidal epithelial cells for cytokeratin-pool and TTF-1, with focal positivity for progesterone receptors. Round and spindle cells expressed positivity for vimentin, TTF-1, and focally for the progesterone receptor. Since the pre- and intraoperative diagnosis should guide surgical decision-making, obtaining a sufficient specimen size to find representative material in the cell block is of paramount importance. This overview highlights what physicians need to know regarding clinical manifestations, radiological and histological features as well as recent advances in immunohistochemistry in the diagnosis of this disease.

Keywords: *Sclerosing pneumocytoma; histopathology; immunohistochemistry.*

I. INTRODUCTION

Pulmonary sclerosing pneumocytoma, formerly known as pulmonary sclerosing hemangioma, is a rare lung tumor. Without significant clinical symptoms, most cases have been found upon regular medical examination. In some patients it may be accompanied by chest pain, cough, and chest tightness, reflecting lung tissue compression caused by increased lesion size. One of the rare, benign tumors of the lung is sclerosing pneumocytoma, which represents a pulmonary neoplasm with a complicated and undefined histogenesis. This tumor was first described by Liebow and Hubbell over 60 years ago as an uncommon lesion with an uncertain origin. The original description by these two authors implied that this tumor originates from vascular endothelial cells; so, initially, this lesion was named sclerosing hemangioma, which is usually seen in adults over 50 years old, featuring a female-to-male ratio of 5:1 [1]. Although its name implicated a vascular neoplasm, further studies have reported the possible pulmonary epithelium (pneumocyte type II)

origin of this tumor. This conclusion has been strongly supported by immunohistochemical findings, and that is why alternative terms, such as pneumocytoma, sclerosing pneumocytoma, or papillary pneumocytoma, have been suggested [2], [3]. In the newest World Health Organization (WHO) classification of lung and pleural tumors from 2015, it has been classified under the more convenient name pneumocytoma [4], [3]. Although it is generally considered to be a benign tumor, it represents a diagnostic challenge due to its controversial etiology and biological behavior, as well as the diversity of pathophysiological findings.

We report the case with full diagnostic materials for doctors to refer to, thereby being able to have a better approach when diagnosing similar cases.

II. CASE REPORT

A female patient, 50 years old, was hospitalized on August 11, 2023, at the Oncology department of our 71 Central Hospital. Have a healthy history. A week before

* *Oncology Department, 71 Central Hospital*

admission, the patient had a mild, dry cough with no phlegm. Examination upon admission: The patient was alert, had good contact, average physical condition, normal skin and mucous membranes, no edema, no discharge. blood under the skin. Temperature 36.6 degrees Celsius; Blood pressure 130/80 mmHg; respiratory rate 18-minute cycles. Patients were treated with imaging diagnostic techniques: chest X-ray, chest computed tomography, pleural ultrasound, echocardiography, and abdominal ultrasound. Routine tests: hematology, blood biochemistry, lung cancer markers, Procalcitonin, urine

biochemistry, blood gas, electrocardiogram, respiratory function measurement, tuberculosis tests. All results were within normal limits and negative. Chest X-ray (Figure 1) shows a solid mass in the right lower lobe of the lung. Chest computed tomography (Figure 1) presents a tumor in the right lobe of the right lung, larger than 7 cm in size, with clear boundaries, non-invasive, no signs of metastasis, non-cavitated, and non-calcified. was removed by smoke excision of the right lower lung tumor. Then the tissue samples were taken for histopathology and immunohistochemical analysis.

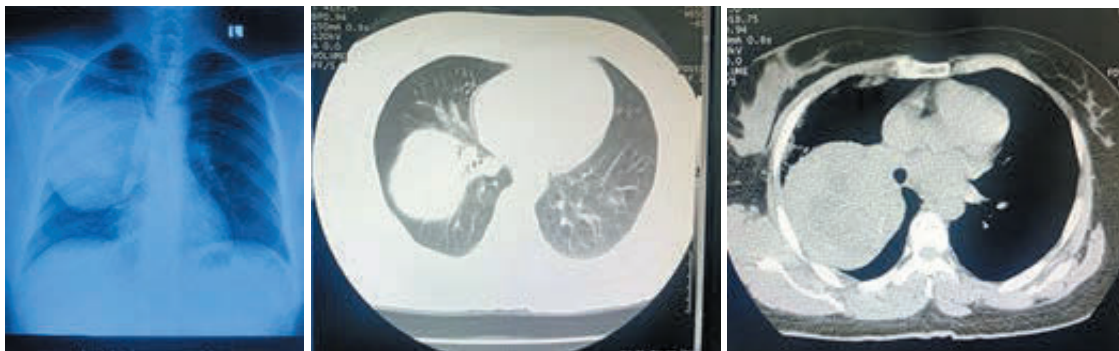


Figure 1. Chest X-ray and chest computed tomography

- Pathohistological examination (Figure 2) of the tissue revealed that this tumor was typically composed of two cellular components: surface epithelial cells that resemble type II alveolar pneumocytes, and round stromal cells. These cells were typically arranged in four major histological patterns: papillary, sclerosing, solid, and hemorrhagic. The papillary pattern was composed of complex papillae without a typical fibrovascular core. The papillae were lined with surface cells covering

the stroma with round cells. The sclerosing pattern was formed by hyalinized collagen on the periphery of hemorrhagic areas, in papillae, or solid areas. The solid pattern was characterized by sheets of uniform round cells or small tubules covered with surface cells, while large blood-filled spaces covered with epithelial cells that can contain hemosiderin deposits, foamy macrophages, or cholesterol fissures formed a hemorrhagic pattern.

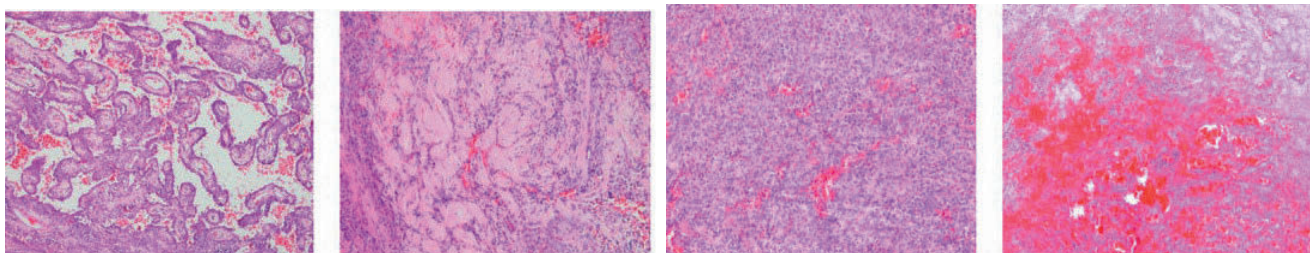


Figure 2. Histological patterns of sclerosing pneumocytoma. (A). Papillary pattern; (B). Sclerosing pattern; (C). Solid pattern; (D). Hemorrhagic pattern.

- Immunohistochemical analysis (Figure 3) showed positive expression of TTF-1 and panCK in surface epithelial cells, and TTF-1 positive and panCK negative expression in stromal cells. round. Additionally,

complementary staining for estrogen receptor and progesterone receptor: positive reaction of tumor cells on progesterone and estrogen receptors.

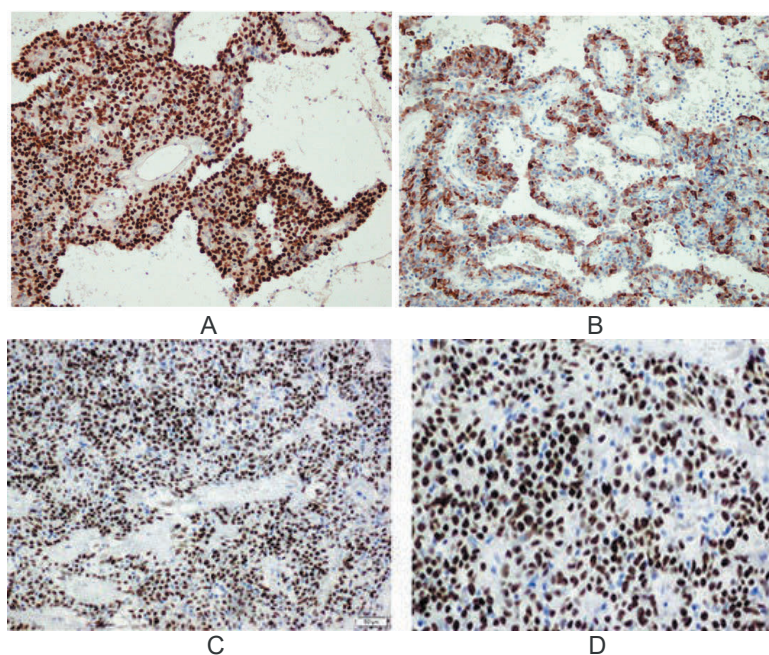


Figure 3. (A) Immunohistochemical analysis showing positive expression of TTF-1 in both surface and round cells. (B) Immunohistochemical analysis shows positive expression of panCK in surface cells, but negative expression in round cells. (C) Immunohistochemical analysis showing a positive reaction of the tumor cells on progesterone receptors. (D) Immunohistochemical analysis showing a positive reaction of the tumor cells on estrogen receptors.

III. DISCUSSION

In most cases, pulmonary sclerosing pneumocytoma has a benign behavior. Shibata and colleagues [12] reported a patient with pulmonary sclerosing pneumocytoma that progressed into severe exertional dyspnea 47 years after detection of abnormal shadow through X-ray. The tumor measured 20 × 16 × 15 cm, weighed 2.3 kg, and occupied the whole left thoracic cavity. This case indicated that pulmonary sclerosing pneumocytoma was not self-limiting despite its benign nature. Some pulmonary sclerosing pneumocytoma cases have been reported with multiple lung involvement

Pulmonary sclerosing pneumocytoma is considered to be a rare benign neoplasm originating from type II pneumocytes. Current studies have reported that the female population is affected more frequently, with the

tumor generally occurring in the middle-aged population, with peak age incidence between the 4th and 7th decade [5, 3]. This was in concordance with our study. Female patients are commonly diagnosed with this tumor in Asia, with low incidence in Western countries

The majority of patients are asymptomatic, with the tumor being incidentally revealed as a soft-tissue mass on routine chest radiographs [6, 3]. In our study, two-thirds of patients had no symptoms of the disease, while the most frequent symptom in clinically manifested disease was cough followed by fatigue, expectoration, and dyspnea. This history of unspecific symptoms can be explained by the fact that the most frequent location of the tumor is within the lung parenchyma, and, as the mass grows with variable speed, the compression of adjacent lung tissue is usually manifested through the symptoms

mentioned [5]. Although pneumocytoma almost always involves the pulmonary parenchyma, rare cases of endobronchial presentation have been reported. The tumor in its endobronchial growth is usually presented as a polypoid mass with possible necrotic and hemorrhagic areas and edematous or ulcerative surrounding mucosa. Due to the growth, the tumor obstructs the lumen, which can lead to severe respiratory arrest. To reveal this rare location, a bronchoscopy is required. If not diagnosed properly, this tumor can lead to post-obstructive pneumonia. Furthermore, bronchial cytology may be insufficient for the definitive diagnosis; therefore, a biopsy should be performed whenever possible. Asymptomatic presentation can be related to extremely rare cases of pneumocytoma with pleural dissemination. There has been only one report of this tumor with this kind of transfer described in the literature; however, the transfer mechanism remains unclear [5,6]. Patients in our research were smokers. In other available reports, the incidence of smokers and nonsmokers with diagnosed pulmonary pneumocytoma was variable; however, none of these studies defined smoking as a risk factor or its influence on the development of this neoplasm [7].

The peripheral location of the tumor favors CT-guided biopsy rather than bronchoscopy-guided biopsy. There are only a few reports of cytological findings, and the epithelial cells by themselves are difficult to differentiate from the adenocarcinoma in situ (Bronchoalveolar carcinoma). Surgical resection is currently widely used for treating pneumocytoma. Xu and colleagues have suggested that surgical resection is curative for this tumor and that no additional treatment after the surgery and no evidence of recurrence define the excellent prognosis of the disease. Among the surgical techniques, video-assisted thoracoscopic surgery is the most common surgical procedure. Chen and colleagues have reported that 61.54% of all patients underwent this procedure [7]. In the present study, video-assisted thoracoscopic surgery, video-assisted mini-thoracotomy, and thoracotomy were equally performed.

Sclerosing pneumocytoma has no predilection for a particular lobe of the lung, but usually on the right lung, which was confirmed by a study analyzing 28 cases with a definitive diagnosis. Among the peripheral lesions,

five were located in the right upper lobe, four in the right middle lobe, six in the right lower lobe, nine in the left lower lobe, and three in the left upper lobe of the lung [8]. Our results are consistent with reports of unknown tumor location, but the tumor was also in the right lung.

The maximum diameter of the pneumocytoma in our patient was >7 cm. According to other studies, lesions range from 0.3 to 7 cm in greatest dimension [2, 12, 5, 6]. Some authors have assumed that clinical symptoms can be evident due to enlargement and consequent pressure on adjacent lung parenchyma. However, other authors have disagreed with this assumption. Furthermore, one of the studies reported no relationship between tumor size and clinical appearance of the tumor [5, 12, 6]. In patients in our study, tumors >7 cm presented with fatigue and mild cough. A tumor >7 cm should have shown signs of difficulty breathing, coughing, and sputum production.

Cytological findings of pneumocytoma have not been helpful in the diagnosis of this tumor [6]. In our research, we did not perform a cytological analysis since all of the lesions were small in size and accessible for a surgical procedure. Also, all of the patients were in good general condition without an increased risk for surgery. In three of the six patients included in this study, a diagnosis of pneumocytoma was made on a frozen section; in one case, a diagnosis of clear cell tumor was set; and in the other two cases, pathologists could not say with certainty what the nature of the lesion was, so they left the definitive diagnosis to be set on for formalin-fixed, paraffin-embedded tissue. Based on our experience, a diagnosis of this tumor can be a great challenge on frozen section specimens, taking into account the low technical quality of the frozen sections, the diversity of the histological image, and the fact that, for a frozen section analysis, usually one section from tumor tissue is taken. Within that particular section, all four patterns might not be found. For example, the presence of a hemorrhagic and a sclerotic component may lead to a misdiagnosis of pulmonary infarction at the organizing stage, while a finding of a papillary pattern can be interpreted as well-differentiated adenocarcinoma or a carcinoid tumor. The presence of a solid pattern is even more challenging and can result in a wide range of primary lung tumors,

including clear cell tumors (so-called “sugar tumor” due to intracytoplasmic glycogen or perivascular epithelioid cell tumors), poorly differentiated adenocarcinoma and squamous cell carcinoma or large cell carcinoma, as well as undifferentiated metastatic carcinomas, metastatic melanoma, or even some types of lymphoma [7,5].

The diversity of pathohistological findings results in a wide range of differential diagnoses, which include various benign conditions and benign and malignant tumors [9]. Among the benign conditions, besides the already mentioned pulmonary infarction, scar tissue, reactive or reparative changes in inflammation, post-radiation changes, or changes as a result of a drug reaction can be misinterpreted as pneumocytoma. While the sclerotic pattern in pneumocytoma mimics scar tissue, reactive and reparative changes in response to inflammation or radiation or reaction to a drug result in hyperplasia of type II pneumocytes with a moderate degree of atypia and the formation of papillary structures, which imitate the papillary pattern of pneumocytoma. Benign tumors of the lung in the differential diagnosis of pneumocytoma are clear cell tumors, hamartoma, and hemangioma, with a variety of microscopic appearances [11, 3]. Positive endothelial cells are present. Among the malignant neoplasms, lepidic and papillary lung adenocarcinoma can imitate pneumocytoma; however, it does not exhibit the two-cell pattern of surface and round stromal cells, and a higher degree of cytologic atypia along with high mitotic activity is present. Carcinoid tumor can also be a diagnostic pitfall; however, a neuroendocrine appearance with rosette formation, “salt and pepper” chromatin, and positivity on CD56, Synaptophysin, and Chromogranin should lead to a proper diagnosis [9, 6].

A pathohistological examination is usually combined with an immunohistochemical analysis for the definitive diagnosis of pneumocytoma. Previous studies have reported that both surface and round cells show a positive immunohistochemical reaction on certain antibodies, which facilitates the diagnosis of the tumor. A positive nuclear reaction on TTF-1 has been observed in both cellular components, while panCK has been expressed only in the cytoplasm of surface epithelial cells [9, 3]. The fact that TTF-1 has been considered to be the characteristic antigen of alveolar epithelial cells strongly

suggests the primitive respiratory epithelium origin of pneumocytoma. Based on the findings of higher incidence in females, the immunohistochemical analysis included both estrogen receptors and progesterone receptors. According to one study, most patients were positive for both estrogen receptors and progesterone receptors, suggesting a relationship between this tumor and female sex hormones [6, 3]. Our study provided similar results, the patient was positive for TTF-1 in both cell types and panCK in facial surface epithelial cells, positive for both estrogen receptor and progesterone receptor.

Patients with pneumocytoma have an excellent prognosis with no need for additional treatment after surgical resection. This tumor is generally considered to be a benign lesion, although potential malignant behavior is expressed through lymph node metastasis which was first reported in 1986 by Tanaka and colleagues [10]. Adachi and colleagues have demonstrated 18 cases of lymph node metastases, with a higher incidence in younger patients. In another study, four cases of pneumocytoma with metastases in hilar lymph nodes were reported; however, after surgery, all patients were uneventful with no evidence of recurrence in five years. In the largest series of published cases, which included 100 patients, only one patient had lymph node metastasis [11], [9]. According to other studies, lymph node metastasis is more likely to occur in younger patients, with no influence on a patient’s prognosis. The mechanism of the metastasizing of pneumocytoma is still unclear. In our study, all patients showed no evidence of lymph node metastases.

IV. CONCLUSION

In this case report, we explored, in-depth, the diagnostic efficiency of Computerized tomography of the chest and immunohistochemistry, combined with pathological analysis, in the diagnosis of PSP. We highlighted the importance of immunohistochemistry in the acquisition of pathological specimens, especially for young to middle-aged females with amiable imaging changes and no clinical symptoms. The differential diagnosis of progesterone from adenocarcinoma and carcinoid through characteristic round and surface cells as well as specific immunohistochemistry staining plays a critical role in optimizing treatment strategy.

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Correspondent: Le Van Giao. Email: levangiaobv71tw@gmail.com

Received: 30/08/2023. Assessed: 30/08/2023. Accepted: 08/12/2023