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A Case with Resection of Primary Pulmonary Clear Cell Tumor
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A Case with Resection of Primary Pulmonary Clear Cell Tumor

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We experienced an extremely rare case of primary pulmonary clear cell tumor. The patient was a 57-year-old female who was suggested to have a nodular shadow in the right lower lung field. In chest CT, a well-defined 14-mm node was observed in the right median lobe. For diagnosis and treatment, thoracoscopic resection of the right pulmonary median lobe was performed. The tumor was white, solid tumor. The pathological findings showed an increase in solid, clear cells with clear and comparatively abundant cytoplasm. Immunohistochemical staining showed HMB45 (+), vimentin (+). The tumor was diagnosed as a primary pulmonary clear cell tumor.

Keywords: clear cell tumor, sugar tumor, PEComa, lung, lung cancer

Introduction

Primary pulmonary clear cell tumor (sugar tumor) is an extremely rare benign tumor that was first reported by Liebow and Castelman in 1963. Herein, we report our experience in a case with resection of this clear cell tumor, with a discussion of the relevant literature.

Case Report

A 57-year-old female visited a nearby hospital after falling. Since a nodular shadow in the right lower lung field was suggested, based on chest X-ray images, she was referred to our hospital.

Hematological values and biochemical examination findings showed no abnormalities. Tumor markers were within the normal range as indicated by CEA: 2.5 ng/ml, CYFRA: 0.5 ng/ml, and Pro-GRP: 29.7 pg/ml. Chest X-ray showed a shadow of a small nodule in the right lower lung field (Fig. 1). In chest CT, a well-defined 14-mm node with comparatively high contrast was observed in the right median lobe (S4) (Fig. 2). In abdominal CT, no abnormal findings were observed in both kidneys. In FDG-PET, no clear abnormal accumulations, including the shadow of node in the right median lobe, were observed. Based on chest CT findings, metastatic pulmonary tumor or benign tumor was suspected, and thus surgery was performed for diagnosis and treatment. Thoracoscopic resection of the middle lobe of the right lung was performed. In the intraoperative rapid diagnosis, no clear malignant findings were observed. It was determined to examine whether the tissue type was benign or malignant, based on fixed samples, and partial resection was subsequently performed. The tumor was visually observed to be a 19 × 13 × 10-mm white, uncoated, solid tumor. Histologically, sparse cellular atypia was observed, and necrosis and karyomitosis were not clear. Increased numbers of solid, clear cells with clear PAS-positive cytoplasm were observed (Fig. 3A). Immunohistochemical staining showed HMB45(+) (Fig. 3B), vimentin(+), TTF-1(−), SP-A(−), AE1/3(−), and CAM5.2(−). Based on the above-mentioned findings, the tumor was diagnosed as a primary pulmonary clear cell tumor.
Since then, follow-up observation has been performed for the patient on an outpatient basis, and no clear findings of redevelopment have been observed up to 6 months after the surgery.

**Discussion and Conclusion**

Primary pulmonary clear cell tumor is an extremely rare tumor, which was reported for the first time by Liebow and Castleman in 1963. To our knowledge, only 60 cases have been reported. Clear cell tumor is considered to be a benign epithelioid tumor. The tumor can develop at any age (8–73 years old), and tends to develop more often in females than males. The tumor develops as an isolated tumor in peripheral lung fields, in many cases. The diameter of the tumor is approximately 2 cm (1 mm–6.5 cm), and the tumor has no characteristic clinical symptoms and is often indicated in many cases by an abnormal
shadow in chest X-ray images. There has been a case of the tumor with a large diameter of $12 \times 10$ cm, and of tumor development in the trachea of a patient who had the chief complaint of blood-stained sputum. Preoperative definite diagnosis is difficult in many cases, and definite diagnosis in several cases has been made by percutaneous needle lung biopsy and transbronchial needle lung biopsy. For many of these cases, surgery must be performed for diagnosis and treatment, as was performed in our case, but, in many cases, diagnosis could not be made, even when intraoperative rapid diagnosis was performed. It has been reported that the change of the color of the tumor was useful for diagnosis. The nodule was adjacent to the visceral pleura and appeared blood-red. Its color was attenuated after the flow of blood was stopped using clamp forceps.

Among the characteristics of image diagnosis for this disease, an isolated round tumor is generally observed in the peripheral lung field in chest X-ray images and tends to increase gradually with a smooth margin. Chest CT shows a well-defined solid tumor with uniform absorption. Although no relationship is observed with the bronchi and blood vessel shadow, some cases have exhibited bleeding and necrosis with a cyst formed in the tumor center, and other cases have exhibited comparatively high imaging effects. Diseases with problematic differentiation, based on images, include benign tumor in the lung (pulmonary hamartoma, sclerosing hemangioma, fibroma, lipoma, polymorphic adenoma, etc.), inflammatory pseudotumor, and lung cancer.

Among the characteristics of the tumor, its gelatin-like divided surface is slightly yellow or slightly brown, the tumor is solid and non-elastic with a clear border with the pulmonary parenchyma and no covering, and calcification, hollowing, bleeding, and necrosis are rarely observed. Histologically, spindle-shaped or polygonal, solid tumor cells with clear cytoplasm are increasingly found between sinusoid-like blood vessels, and no atypia or karyomitosis are observed. The tumor cells contain PAS-positive cytoplasm including glycogen granules to be digested by diastase. Therefore, it is also known as a sugar tumor. In immunostaining, in many cases the tumor is negative for keratin, an epithelial marker, and positive for HMB-45 and Melan A, melanoma-associated antigens. However, a portion of the tumor cells may be positive in some cases, and thus it has been reported that diagnosis is difficult with a small amount of specimen. In our case, the tumor was positive for HMB-45, which was useful for diagnosis.

There were various hypotheses regarding the development of the tumor.

Recent data suggest melanocytes would undergo differentiation into the tumor based on the expression of factors, such as HMB45 positive, expression of S100, and melanosome, within the tumor. HMB45 is one of the melanoma-associated antigens. Mesenchymal tumors, which consist of epithelium-like or spindle-shaped perivascular epithelioid cells (PEC) that exhibit an
HMB45-positive clear acidophilic cytoplasm and tend to distribute around blood vessels, are referred to as PEComa.\(^3\) Benign clear cell tumors in the lung, pancreas, and uterus; angiomyolipoma (AML) in the kidney and liver; lymphangioleiomyomatosis in the lung (LAM); and clear cell myomelanocytic tumor in the falciform ligament in the liver are considered to be PEC-derived tumors and are collectively referred to as PEComas. It has been reported that LAM and clear cell tumors developed concomitantly in the lung in a patient with nodular sclerosis, and thus the potential correlation between individual diseases should be discussed in the future.\(^8\)

In the differential diagnosis of this tumor, lung metastasis of clear cell carcinoma from the kidney could be considered regarding the lack of karyomitosis, and the fact that argyrophil fibers encircle the individual tumor cells in renal cancer with silver impregnation staining.

The prognosis is considered to be generally favorable. There are no case of lymph node metastases but only one argued report of fatal recurrence and liver metastasis.\(^9\) Although the progress was slow, and thus surgical resection is considered necessary and must be resected enough margin. In particular, in cases of tumors with symptoms or necrosis, or those with a diameter of 2.5 cm or larger or mitotic index of 1 per 50 high-power fields, marked pleomorphism and nuclear atypia are considered to have malignant factors, and thus close follow-up observation should be performed in the future.\(^10\) However, according to WHO guidelines, excision is the treatment of choice, and no adjuvant therapy is recommended.\(^3\)

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**Disclosure Statement**

I declare that I have no conflict of interest in connection with this paper, other than any noted.

**References**