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# Clear Cell ‘’ Sugar ‘’ Tumor of The Lung

## Akciğerin Berrak Hücreli Şeker Tümörü

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### Abstract

Clear cell tumors of the lung are extremely rare neoplasms, and only a limited number of cases have been reported in literature to date. It is an atypical and mostly benign peripheral primary lung tumor belonging to the family of perivascular epithelioid cell tumors, and is referred to also as a “sugar tumor” since it consists of clear cells containing intracytoplasmic glycogen. The case presented here was diagnosed with a clear cell sugar tumor of the lung during the pandemic, but died due to COVID-19 pneumonia before surgery.


**Keywords:** *Sugar tumor, clear cell tumor of the lung, PEComa.*


### Öz

Akciğerin berrak hücreli tümörü, literatürde şimdiye kadar bildirilen sınırlı sayıda vaka ile son derece nadir bir neoplazmdır. Perivasküler epiteloid hücre tümörleri ailesinin atipik ve çoğunlukla iyi huylu periferik primer akciğer tümörüdür. İntrasitoplazmik glikojen içeren berrak hücrelerden oluştuğu için “şeker tümörü” olarak adlandırılır. Pandemi döneminde akciğerin berrak hücreli şeker tümörü tanısı alan olgumuz COVİD-19 pnömonisi nedeniyle operasyon şansını kullanamadan hayatını kaybetmiştir.


**Anahtar Kelimeler:** *Şeker tümör, berrak hücreli akciğer tümörü, PEComa.*

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The perivascular epithelioid cell tumor (PEComa) family is a group of rare mesenchymal tumors characterized by a perivascular distribution of epithelioid and spindle cells. Since first being identified in 1963, they have been found in many organs, including the kidneys and other genitourinary regions, retroperitoneum, uterus, liver and lungs (1). Angiomyolipomas, lymphangioleiomyomatosis and clear cell tumors of the lung (CCTL) are all PEC tumors (2). CCTLs are clear cells containing large amounts of intracytoplasmic periodic-acid-Schiff positive glycogen, leading them to be referred to as "sugar tumors" (3). Such tumors can be easily confused with renal clear cell tumor metastases and clear cell lung carcinoma (4). The only definitive means of distinguishing this benign tumor from other malignant tumors is through histologic examination supported by immunohistochemistry (5). The immunohistochemical staining pattern is unique, and is positive for HMB-45 and S-100 proteins and negative for cytokeratin. Unstable positivity for vimentin, CD68, CD34 and cathepsin-B positivity, neuron-specific enolase, synaptophysin as well as CD1a expression has also been identified (3). Although a few patients presenting with chest pain, shortness of breath, cough and hemoptysis have been reported, it is usually asymptomatic and detected incidentally (2). There are no significant findings from physical or laboratory examinations (6). It usually occurs in adults older than 40 years and more often affects women (1). It appears as a solitary, homogeneous, round, well-circumscribed and peripheral parenchymal nodule that does not exhibit cavitation or calcification radiographically (4). It can be seen in any lobe, but is mainly identified below the pleura, unrelated to the bronchi or vascular structure (6). On computed tomography (CT), it shows hyperintense characteristics due to its rich vascular stroma, and can show FDG uptake in positron emission tomography (PET) (3). It is usually benign, and complete resection of the affected lobe is the only treatment; adjuvant therapy is not recommended (4). Malignant cases have been reported in the literature, albeit rarely (1), and so post-surgery follow-up is vital (2). Tumors larger than 5cm with pure ground glass opacities, nuclear pleomorphism, high mitotic activity and coagulative necrosis are at risk of recurrence and/or metastasis (7,8).

This case presented here with this rare tumor seeks to raise awareness of the condition and to emphasize the importance of correct diagnosis to prevent unnecessary large lung resections.

## CASE

A 69-year-old male patient was referred to our hospital from an external center with complaints of shortness of breath, cough, chills and stabbing chest pain. He had a history of kidney transplantation in 2014 for chronic kidney failure and was being treated for DM and HT comorbidities. He had a 40-pack/year smoking history but had quit 3 months earlier. A physical examination revealed the patient to be weak and pale. Laboratory examinations revealed mild leukocytosis and neutrophilia, deep anemia, and elevated urea, creatinine, CRP and procalcitonin. In a chest X-ray, an irregular limited and homogeneous increase in density was observed in the right paracardiac area (Figure 1). The patient was admitted to our hospital with a preliminary diagnosis of pneumonia and lung cancer. A COVID PCR test performed prior to hospitalization was negative. On thorax CT, a mass lesion measuring approximately 7x5.5cm was observed in the posterior of the lower lobe of the right lung with a broad base on the pleura (Figure 2). On bronchoscopy, a lobulated, necrotic lesion obstructing the right lower lobe entrance was observed. Forceps and brush biopsies were performed, and the findings first suggested benign cytology. In the endobronchial biopsy specimen, bronchial epithelial cells with minimal reactive changes on the surface and cells with clear-granular eosinophilic cytoplasm showing sporadic mild nuclear atypia under the epithelium were observed. These cells were S-100 (+), HMB-45(+), CD34 (-), cytokeratin (-), Chromogranin (-), Synaptophysin (-) and TTF-1 (-) applied by the Immunohistochemical method. The findings were initially found to be compatible with "Clear Cell Tumor (Sugar Tumor - PEComa)" (Figure 3). On PET CT, an increased 18FDG uptake at malignancy level associated with post-obstructive atelectasis, consolidative parenchymal changes and a pleural effusion reaching 2 cm thickness was observed in the areas adjacent to a paravertebral axial mass lesion at the center of the right lung lower lobe, which measured approximately 3.6x5.1 cm on the axial axis and 7.2 cm on the craniocaudal axis. Surgery was planned for the patient after consultation with thoracic surgery specialists, but upon testing positive in a preoperative COVID-19 PCR test, he was admitted to the COVID ward. On a repeated thorax CT, diffuse areas of ground-glass consolidation were observed in both lungs. The patient's general condition deteriorated despite the treatment, and metabolic acidosis and hypoxic respiratory failure developed, as a result of which the patient was transferred to the intensive care unit. The patient was intubated in the intensive care unit and connected to invasive mechanical ventilation, but died despite the interventions.

## DISCUSSION

CCTL, belonging to the PEComa family, is a very rare condition, with no more than 60 cases reported in literature to date (4). There has been no systematic report to date describing its radiological and clinicopathological

characteristics (6). Our case presented with characteristics that were similar and dissimilar to other cases reported in literature. Although the condition can be seen in all age groups, it is most common among older adults and women (1,4). Our reporting of a patient with hepatic angiomyolipoma and a sugar tumor of the lung suggests that PEComa may be multifocal.

Hepatic angiomyolipoma presenting alongside a sugar tumor in the lung suggests that these tumors may be multifocal (9). The patient presented in this study was a 69-year-old male patient. Patients are usually asymptomatic or present with such nonspecific symptoms as shortness of breath, chest pain and cough (1). A male patient presented with hemoptysis (10), while the complaints of a female patient with essential thrombocytosis were headache and fatigue (11). PEComa is usually detected on routine scans as a well-circumscribed, peripheral, "coin" lesion close to the pleura (1). An 18-year-old male patient exhibited highly different radiological characteristics, with a 12x10cm cystic mass involving the left lung lower lobe and lingula on thorax CT (12). Our case had the appearance of a centrally located, irregularly circumscribed and large-sized lesion and a mass detected on radiological imaging. The patient was admitted to the hospital with signs of infection due to atelectasis, consolidation and pleural effusion distal to the lesion. Sugar tumor of the lung has been reported in patients with such systemic diseases as hypertension, hyperlipidemia, COPD, hypothyroidism and anemia (2,13,14). Sugar tumors have been observed in female patients with a history of chemoradiotherapy for cervix squamous cell carcinoma (13) and a breast cancer diagnosis (15). In male patients, sugar tumors synchronous with primary lung adenocarcinoma (7) and synchronous with rectal adenocarcinoma (16) have been identified. Our case had DM and HT. No sugar tumor of the lung has been reported in literature to date in a kidney transplant patient.

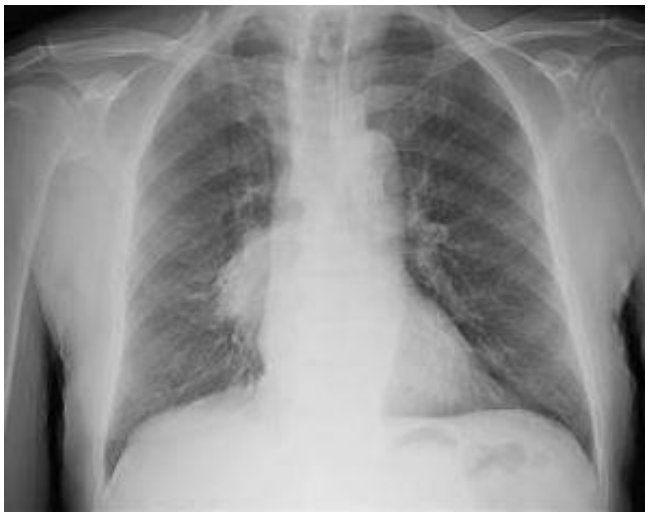

*Figure 1: An irregular limited, and homogeneous increase in density was observed in the right paracardiac area on chest X-ray*

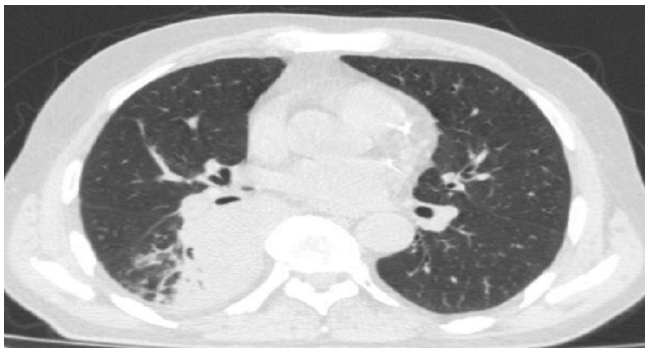

*Figure 2: A mass lesion measuring approximately 7x5.5cm was observed on thorax CT in the posterior of the lower lobe of the right lung, with a broad base on the pleura*

Given their nonspecific clinical and imaging characteristics, the pathological evaluation of these tumors is crucial for an accurate diagnosis (1). It is vital to distinguish CCTL from pulmonary adenocarcinoma and other malignancies, such as clear-cell variant and renal clear-cell tumor metastases (5) as CCTL can be treated only by surgical resection, with no need for adjuvant chemo or radiotherapy (3). In CCTL, clear cells containing large amounts of intracytoplasmic glycogen are mitotically inactive and supported by very little connective tissue. Blood is supplied to tumor cells in abundance by large, thin-walled sinusoidal vessels (6). Tumor cells are positive for the HMB-45 and S-100 proteins and negative for cytokeratin in Immunohistochemical staining, and these parameters are sufficient for a definitive diagnosis (3). Our case had all of these characteristics.

The clinical course is generally benign, but rare cases with malignant characteristics have been reported (1). A patient who underwent a right upper and middle lobectomy due to a large sugar tumor in the right upper lobe suffered a local recurrence in the thorax and chest wall after 6 months (17). Three months after the resection of duodenal and thoracic tumors that were compatible with sugar tumors, two metastatic tumors were detected in the brain (8). The metastasizing of malignant CCTLs from lung to lung has also been reported (18). Characteristics such as tumor size over 5 cm, high mitotic activity, nuclear pleomorphism and coagulation necrosis are considered among the criteria for malignancy (8). Although our case was at risk of malignancy due to the size of the lesion, its histopathological evaluation was benign. No metastases were detected on PET CT or brain MRI scans. A right lower lobectomy was planned for our patient, but he died of COVID pneumonia before surgery.

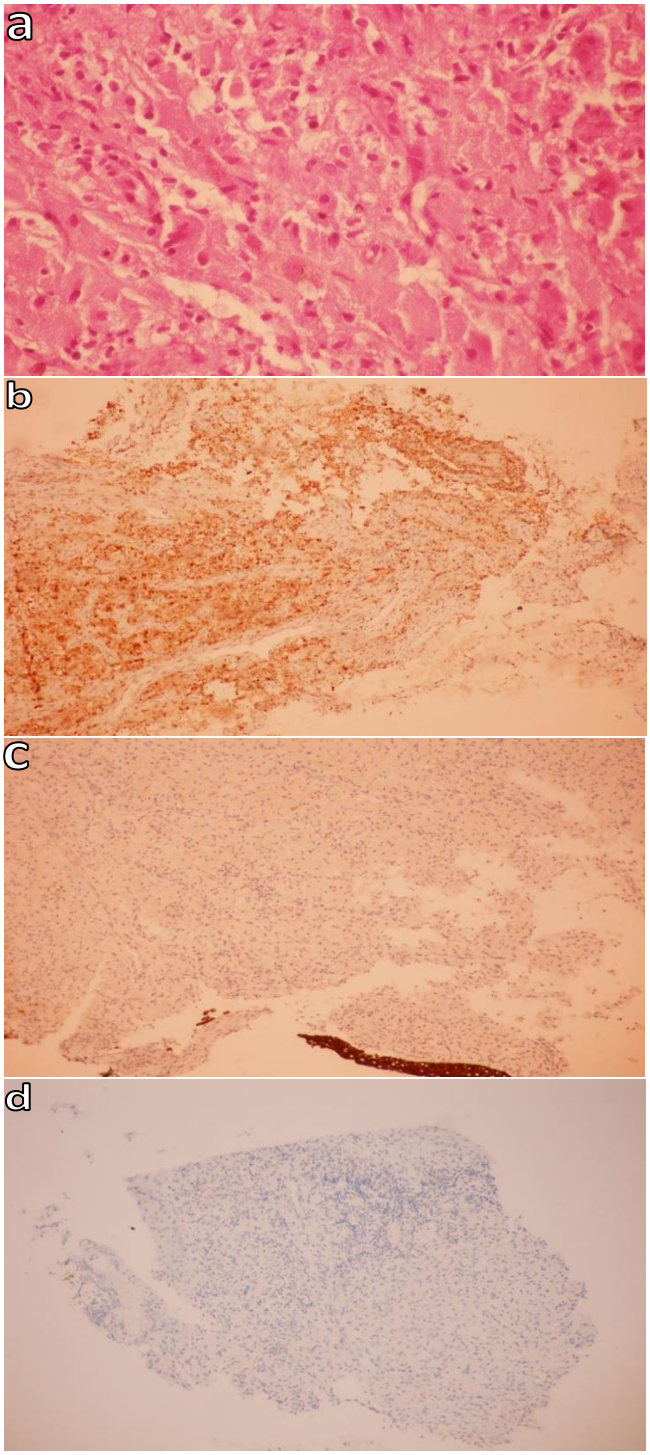


***Figure 3:*** *A sugar tumor consisting of clear associations stained with hematoxylin-eosin (x400)* ***(a)****; Immunohistochemical staining positive for the S-100 protein (x40)* ***(b)****; Cytokeratin immunohistochemical stain showing the negative tumor cells (x40)* ***(c)****; Immunohistochemical staining showing cytoplasmic positivity to HMB-45 (x40)* ***(d)***

## CONCLUSION

Clear cell sugar tumors of the lung are incidentally detected, very rare and benign tumors that usually present as a solitary pulmonary nodule in the periphery of the lung. Their unique Immunohistochemical characteristics are used for definitive diagnosis. Surgical resection is the only treatment, and no adjuvant therapy is required. Given the variety in the cases reported in literature, it should be understood that these tumors may exhibit very different radiological and clinical characteristics, carry a risk of malignancy, may accompany other malignancies and may be multifocal.

## CONFLICTS OF INTEREST

None declared.

## AUTHOR CONTRIBUTIONS

Concept - H.Ş., S.B.; Planning and Design - H.Ş., S.B.; Supervision - H.Ş., S.B.; Funding - S.B.; Materials - S.B.; Data Collection and/or Processing - H.Ş.; Analysis and/or Interpretation - H.Ş.; Literature Review - S.B.; Writing - H.Ş.; Critical Review - H.Ş.

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