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Clear cell "sugar" tumor of the lung - case report

Case report

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Abstract: Background: The clear cell "sugar" tumor of the lung is an extremely rare benign mesenchymal tumor. Aim: To report a case of the sugar tumor and discuss diagnostic differentiation of the tumor. Case report: A 53-year female presented with persisting cough. A CT scan revealed a round, 10 mm nodule located within the right lower lobe. The nodule was easily removed during thoracotomy. On the gross examination, the tumor was well circumscribed, and had a homogenous grayish-white appearance on the cut surface. The tumor consisted of round and oval cells with abundant clear cytoplasm, showing PAS pozitive abundant glycogen granules, which were removed by diastase pre-treatment before further staining with PAS. Immunohistochemical studies revealed the tumor cells were positive for HMB-45, vimentin, S-100 protein and very few cells for CD-117. The tumor cells were negative for αSMA, CK-7, AE1/AE3, CD-10, chromogranin and TTF-1. Conclusion: Based on the clinical, pathohistological and immunohistochemical data, the diagnosis of the primary clear cell sugar tumor of the lung was established.

Keywords: *Clear cell pulmonary tumor • Sugar tumor*

Cover letter

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Zdravko Kosjerina, MD, PhD, Prof.

1. Introduction

The clear cell "sugar" tumor of the lung is an extremely rare, benign, mesenchymal tumor; it was originally described in 1963 by Liebow and Castelman [1]. Since then, only about 50 cases of this tumor, mostly sporadic, have been reported in the English literature [2].

The tumor has usually presents as a solitary and asymptomatic pulmonary nodule on a chest radiogram. The sugar tumor may occur in any lobe and is mainly located under the pleura, with no communication with the bronchi [3]. It occurs in all age groups, but is most often seen in the elderly, and affects both sexes equally [4].

This tumor is composed of clear cells with large amounts of intracytoplasmic glycogen and is therefore called the clear cell or sugar cell tumor [5]. Because of their perivascular epithelioid cell differentiation, these

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tumors belong to the family of perivascular epithelioid cell tumors, or PEComas [6].

The tumor cells show immunoreactivity to human melanoma black HMB-45 and S-100 protein and no reactivity to Cytokeratin 7, which establishes the definitive diagnosis [7]. The immunohistochemical features of these tumors are most important for distinguishing them from metastatic renal carcinoma and primary clear cell carcinoma of the lung.

2. Case report

A 53-years old female patient, a 30 pack-year smoker, was admitted to hospital because of a cough that persisted over two months and an abnormal shadow on a chest X-ray. She was diagnosed as having chronic obstructive lung disease and took medications for that disorder.

The chest CT scan revealed a round 10x10 mm nodule located within the posterior basilar segment of the right lower lobe (Figure 1). No pathologically enlarged mediastinal lymph nodes or other nodes were seen. The patient's bronchoscopy results were essentially normal. A right anterolateral thoracotomy was performed, and the nodule from the right lower lobe was easily removed from the surrounding pulmonary parenchyma by enucleation. The diagnosis on the frozen-section study was clear cell tumor; therefore, a right lower lobectomy was performed.

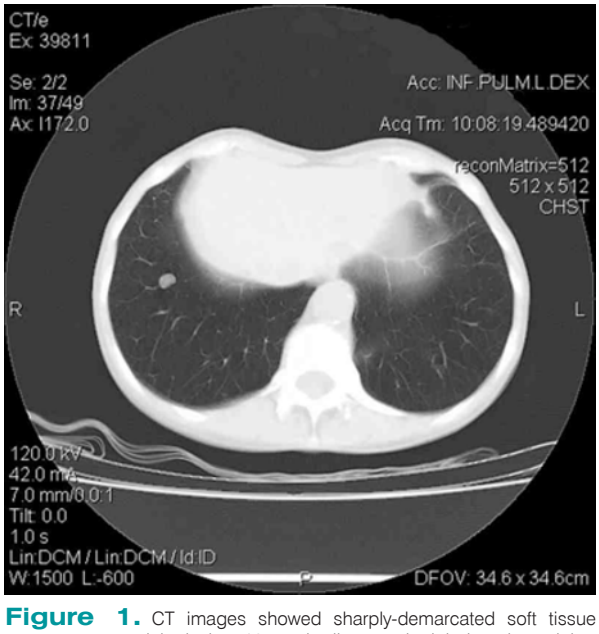

Figure 1. CT images showed sharply-demarcated soft tissue nodular lesion, 10 mm in diameter, in right lung lower lobe. No signs of perifocal reaction were noted in surounding lung parenchima.

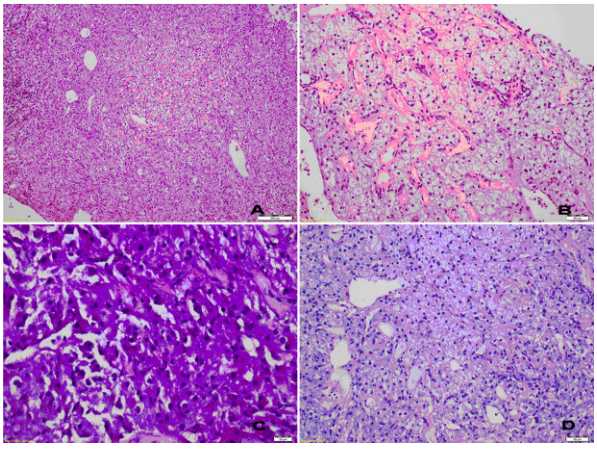

Figure 2. Photomicrograph showing round to oval cells with uniform nuclei and abundant clear cytoplasm (A and B); most neoplastic clear cells had intracytoplasmic PAS-positivity (C); these disappeared following diastase digestion (D).

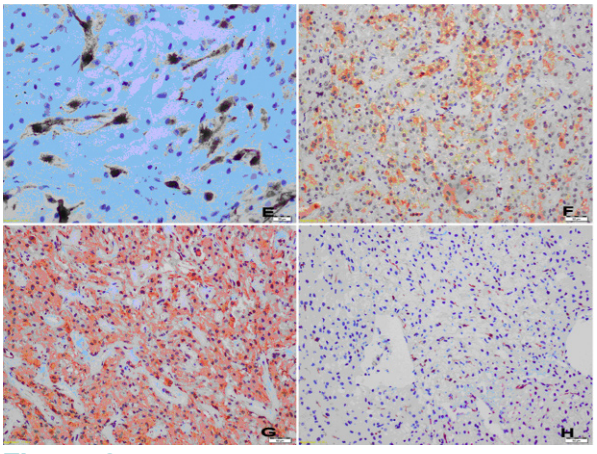

Figure 3. Many tumor cells showed cytoplasmic staining for HMB-45 (E); S-100 protein (F); Vimentin (G); rare cells are CD-117 positive (H).

On the gross examination, the tumor measured 10 mm in its largest dimension, was well circumscribed, and had a homogenous grayish-white appearance on the cut surface. The tumor was not surrounded by a fibrous capsule.

The light microscopy examination showed a proliferation of round and oval cells with typical round nuclei, indistinct nucleoli and abundant clear cytoplasm. Stromal vascularity was prominent, with vascular channels coursing through the tumour cells. There was no necrosis, haemorrhage, mitoses or cytological atypia of the tumour cells. PAS staining reaction revealed abundant glycogen granules in the cellular cytoplasm; these were removed by diastase pretreatment before further staining with PAS (Figure 2).

Immunohistochemical studies revealed that the tumor cells were positive for HMB-45, vimentin, S-100 protein and very few cells for CD-117 (Figure 3). The

tumor cells were negative for αSMA, CK-7, AE1/AE3, CD-10, chromogranin and TTF-1.

Her postoperative course was uneventful, and a subsequent diagnostic procedure (abdominal ultrasonography) excluded the presence of renal cell carcinoma. The patient was discharged nine days after surgery; eight months later, there was no evidence of a relapse or metastatic disease.

3. Discussion

The primary clear cell tumor of the lung is an extremely rare benign tumor, usually called the "sugar tumor" because of its large content of intracytoplasmic glycogen. It can occur in any age group (8–73 years), and affects both sexes equally [8]. Most patients are asymptomatic, except for a few cases with symptoms of hemoptysis [9] or thrombocytosis [6]. These tumors are rarely associated with tuberous sclerosis and lymphangioleiomyomatosis [10].

Radiographically, these tumors present as rounded, smooth-walled, peripheral parenchymal nodules with no evidence of cavitation or calcification. There is no specific lobar distribution [9]. One of the characteristics of sugar cell tumors on contrast-enhanced CT scans is the intense post-contrast enhancement that appears to be related to its rich vascular stroma [11].

Benign clear cell sugar tumor is often misdiagnosed as a pulmonary metastasis of the clear cell renal carcinoma or a primary clear cell carcinoma of the lung [12].

While the histogenesis of the clear cell sugar tumor is unclear, it seems to originate from perivascular epithelioid cells. The World Health Organization defines neoplasms with perivascular epithelioid cell differentiation (PEComas) as "mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells". Bonetti suggested a cellular link between clear cell "sugar" tumors, angiomyolipomas and lymphangiomyomatosis [13,14].

These tumors show HMB-45 reactivity, antibodies to perivascular myoid cell proliferation, and melanosomes, all of which suggest pericyte origin [15]; as shown in Table 1, the characteristic immunohistochemical features of most clear cell lung tumors include tumor cell positivity for HMB-45, vimentin and S-100 protein.

Table 1. Rates of immunohistochemical positivity for clear cell tumor in previous studies [2-6,8,10,13,15,19,21]

	Marker	Number of positive cases/ Total number of cases	%
1.	HMB-45 [2-6,8,13,15,19,21]	21/25	84.0
2.	HMB-50 [21]	6/9	66.6
3.	S-100 protein [3-6,8,13,19,21]	21/23	91.3
4.	Vimentin [2,4,5,13,19,21]	15/19	78.9
5.	Keratin (AE1/AE3) [2,5,6,8,15,19]	0/20	0.0
6.	NSE [4,5,19]	7/15	46.7
7.	CD1a [5]	1/1	100.0
8.	CD34 [5,8,19,21]	2/4	50.0
9.	TTF-1 [4,10,21]	0/3	0.0

The sugar tumor is generally benign; however, in rare instances, sugar tumors behave in a malignant fashion [19], leading to local invasion and multiple metastases [20].

The differential diagnosis of this tumor includes metastatic renal cell carcinoma, carcinoid tumor, granular cell tumor, acinic cell carcinoma, lung clear cell adenocarcinoma and metastatic malignant melanoma. These neoplasms can be separated from the sugar tumor by a combination of clinical presentation, physical examination, light microscopy, and histochemical and immunohistochemical stains. On histological examination, only the sugar tumor demonstrates abundant intracytoplasmic glycogen, HMB-45 positivity, and negative staining for cytokeratin and chromogranin.

The treatment for sugar tumor of the lung is limited to a surgical procedure: lobectomy, segmentectomy, partial resection and enucleation [21].

Given that one patient had hepatic metastases 10 years after the primary pulmonary resection [20], a long follow-up period is necessary.

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