



Case report

Clear cell “sugar tumor” of the lung: Diagnostic features of a rare pulmonary tumor



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ABSTRACT

Clear cell tumor of the lung (CCTL) is an extremely rare neoplasm with about 50 cases reported in the literature so far. CCTL belongs to a family arising from putative perivascular epithelioid cells and is otherwise named as “sugar tumor” due to its high cellular glycogen concentration. Due to its rarity, diagnostic features of this entity are not widely known and this usually leads to misdiagnosis. Herein, we report a case of benign CCTL, which was primarily evaluated intraoperatively by FNA cytology and then by a pathological examination of the resected tumor. The cytologic preparations were moderately cellular and showed multiple large, irregular, cohesive clusters of ovoid or spindle tumor cells. Cells had clear cytoplasm, showing positivity with the periodic acid-Schiff (PAS) staining method owing to the glycogen (sugar) content. The rapid cytologic report excluded the possibility of malignancy and a middle lobectomy along with an anterior upper segmentectomy was performed. Immunohistochemistry revealed a diffuse positivity for HMB45, MART-1, SMA and focally for desmin, while specimen was negative for pancytokeratin cocktail AE1/AE3, cytokeratin7, cytokeratin20 and EMA. These findings confirmed the diagnosis of a benign CCTL. Due to its rarity and similarity with other clear cell tumors of the lung, awareness of this entity, recognition of the cytomorphologic features and familiarity with the associated clinical features can help clinicians avoid certain pitfalls in the diagnostic process. Considering its benign course, unnecessary extensive lung resections may also be avoided thus permitting conservative management of these patients.

1. Introduction

Clear cell tumor of the lung (CCTL) is a rare neoplasm that was first described by Liebow and Castleman in 1971 [1]. This type of tumor consists of clear cells that have large amounts of glycogen, thus showing extensive positivity for periodic acid-Schiff (PAS) staining. Therefore, CCTL is alternatively called “sugar tumor”. According to the 2015 World Health Organization (WHO) classification, CCTL belongs to a family arising from putative perivascular epithelioid cells, called “PE-Comatous tumors” of the lung. These include three distinct entities; a. lymphangioleiomyomatosis (LAM), b. PEComa, benign, including clear cell tumor, and c. PEComa, malignant [2].

To date, only few cases have been published in the literature and these have been mostly evaluated preoperatively by computed tomography (CT)-guided fine-needle aspiration (FNA) and core-needle biopsy [3]. Due to its rarity, diagnostic features of this entity are not widely known. Herein, we report a case of benign CCTL, which was primarily evaluated intraoperatively by FNA cytology and then by a pathological examination of the resected tumor. Timely high preoperative suspicion using intraoperative FNA helped avoid unnecessary extensive lung resection and thus permitted conservative management of the patient. To the best of our knowledge, no other case of BCCT describing a rapid cytologic examination has ever been documented in the literature.

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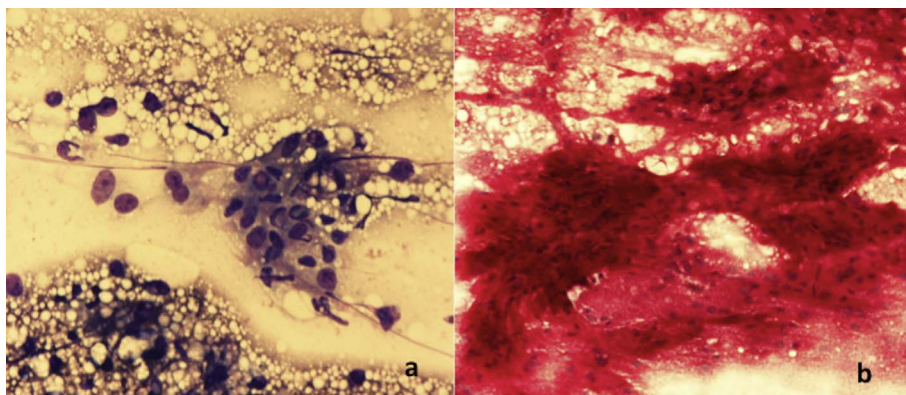


Fig. 1. a) May–Grunwald–Giemsa (MGG) stained preparations appearing moderately cellular and forming multiple large, irregular, cohesive clusters of ovoid or spindle tumor cells. b) Clusters consisting of oval or elongated, bland nuclei and thin semitransparent, vacuolated, clear cytoplasm and showing positivity with the periodic acid-Schiff (PAS) method owing to the glycogen (sugar) content.

1.1. Case presentation

A 46-year-old man was referred to our hospital due to a right pulmonary nodule, accidentally found on chest roentgenogram during routine examination. His medical history was unremarkable and he also denied any tobacco use in the past. On physical examination, no signs of cough, hemoptysis, shortness of breath or evidence of voice hoarseness were noted. Chest CT revealed a 5.5 cm mass in the right upper and middle lobe while fiberoptic bronchoscopy showed no stenosis of bronchi, neither any endobronchial lesion. Therefore, video-assisted thoracoscopic surgery (VATS) was suggested and the lesion located between the right upper and mainly the middle lobe of lung was visualized. At that point, an intraoperative fine needle aspiration (FNA) was carried out and a rapid assessment revealed the benign nature of the lesion. The cytologic preparations were moderately cellular and showed multiple large, irregular, cohesive clusters of ovoid or spindle tumor cells (Fig. 1a). These clusters consisted of oval or elongated, bland nuclei and thin semitransparent, vacuolated, clear cytoplasm, which showed positive staining by the periodic acid-Schiff (PAS) method owing to the glycogen (sugar) content (Fig. 1b). Smear background contained blood cells, scattered lymphocytes as well as many single benign epithelial-like cells with ill-defined or no preserved cytoplasm. Furthermore, sinusoid-like vessels surrounded by neoplastic cells were observed. Overall, rapid cytologic report described the lesion as “negative for malignancy, probably lesion of mesenchymal origin”. Due to the large size and the involvement of both right middle and upper lobes, a right middle lobectomy and anterior upper segmentectomy was decided following surgical team consensus in order to eliminate any chance of occult malignant disease in the rapid cytologic examination.

Microscopy of the tumor revealed neoplastic cells arranged in insular patterns and separated by a rich delicate capillary network and sinusoid-like vessels (Fig. 2a). On higher magnification, cells were epithelioid-like with round or ovoid, polymorphic nuclei, apparent nucleoli and pale, vacuolated or clear cytoplasm (Fig. 2b). Finally,

mucin or fat were absent. Finally, immunohistochemistry (IHC) revealed a diffuse positivity for HMB45, MART-1, SMA and focally for desmin, mainly in areas where cells appeared oval or ovoid. Tumor reactivity was negative for pancytokeratin cocktail AE1/AE3, cytokeratin7, cytokeratin20 and EMA. These findings confirmed the diagnosis of a benign clear cell tumor of the lung (CCCL).

2. Discussion

Benign clear cell tumor (BCCT) or otherwise defined as “sugar tumor” of the lung constitutes an extremely rare entity, since only about 50 cases have been reported in the literature to date [3]. The neoplasm seems to present with a higher incidence in the elderly, although cases between the age range of 8–73 years have been reported. Between the two genders, it shows a slight female predominance and it also affects extrapulmonary tissues including the rectum and vulva [4]. The typical presentation is an asymptomatic patient with an isolated coin lesion detected accidentally on chest X-ray [3], although hemoptysis or high fever may present as initial manifestations [5].

Macroscopically, BCCL usually appears as a peripheral, small, rounded or ovoid lesion, with a diameter generally ranging from 1 mm “micro-sugar tumor” [6]– to 12cm [7]. The latter, described by Kavunkal et al., presented as a surprisingly large lesion (12 × 10cm) and in combination with its dense adhesions and increased vascularity, raised suspicion for an occult malignant potential, thus requiring pneumonectomy [7]. Of note, a recent review showed that tumor size is closely related to the patient's clinical presentation, since lesions > 2.2cm tend to produce symptoms more frequently when compared with smaller tumors [3].

Radiographically, BCCL presents as a peripheral, rounded and well-demarcated nodule with no evidence of cavitation or calcification [3,8]. Although it may occur in any lobe, it tends to affect both lower lungs [3]. It is of great importance that it is not always possible to diagnose a BCCL preoperatively when relying solely on the radiographic findings.

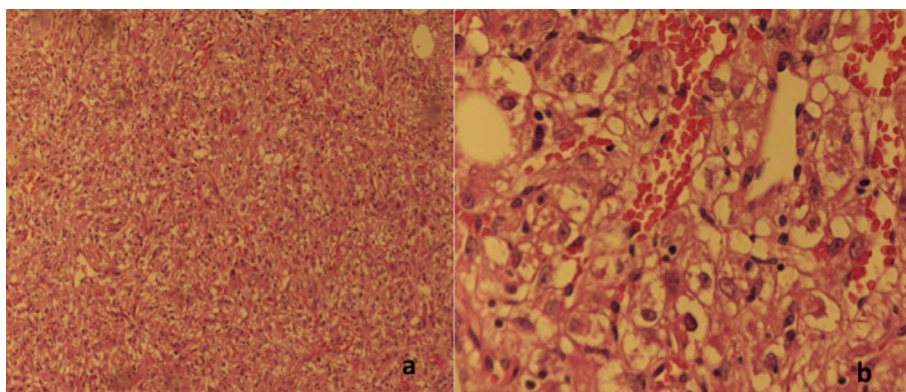


Fig. 2. a) Microscopy of the tumor revealing neoplastic cells arranged in insular patterns and separated by a rich delicate capillary network and sinusoid-like vessels (magnification × 10). b) On higher magnification, cells appearing epithelioid-like with round or ovoid, polymorphic nuclei, apparent nucleoli and pale, vacuolated or clear cytoplasm (magnification × 40).

Its intense post-contrast enhancement on CT scans, owing to its rich vascular stroma, may resemble a malignant neoplasm, such as primary or metastatic lung cancer [8] and thus lead to misdiagnosis.

Histologically, clear cell “sugar tumor” consists of round or oval clear cells containing abundant membrane-bound glycogen. Some tumor cells may have a “spidery” appearance [1]. There is a mild variation in nuclear size and nuclear membranes, nucleoli may be prominent, but mitoses are usually absent. Due to the glycogen rich cytoplasm, there is usually strong diastase-sensitive PAS positivity [3]. Scanty intervening stroma with prominent thin-walled sinusoidal vessels is characteristic. The presence of necrosis is extremely rare and should lead to consideration of malignancy as should significant mitotic activity and an infiltrative growth pattern [9].

The immunohistochemical staining pattern of BCCT is unique, positive for HMB-45 and S-100 protein and negative for cytokeratin7 [3]. Positivity for vimentin, CD68, CD34 and cathepsin-B inconstant positivity for neuron-specific enolase (NSE), synaptophysin as well as CD1a expression has been also described [5]. In our case, IHC revealed a diffuse positivity for HMB45 while negative for pancytokeratin cocktail AE1/AE3, cytokeratin7 and cytokeratin20.

Differentiating BCCT from other primary tumors of the lung such as a clear cell variant of bronchogenic carcinoma or acinic cell carcinoma of the lung as well as metastatic clear cell tumors is of great importance [10]. Cytological features of these tumor types may display similarities with BCCT; however, immunoreactivity with cytokeratin, CD10 and EMA definitively helps differentiate them from BCCT [9,10]. This is of great importance since literature suggests that virtually all CCTL can be treated solely by surgical resection with no need for adjuvant chemo- or radiotherapy [3]. However, the better understanding of the natural history of the disease would provide a strong basis for the formulation of relevant clinical practice guidelines.

In conclusion, BCCT of the lung is a very uncommon tumor that has characteristic but not specific morphologic features. Because of its rarity and similarity with other clear cell tumors of lung awareness of this entity, recognition of its cytomorphologic features and familiarity with the associated clinical features can help clinicians avoid certain pitfalls in the diagnostic process, thus permitting conservative management of these patients.

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Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.rmcr.2017.12.001>.

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