



Case report

Primary adenoid cystic carcinoma of the lung: A case report and literature review

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ABSTRACT

Primary adenoid cystic carcinoma (ACC) of the lung is an unusual thoracic neoplasm with slow growing and low-grade malignancy. Usually, it is diagnosed at a higher clinical stage and is difficult to resect due to its central location. Herein, we report a 56-year-old man with hemoptysis associated with dyspnea and weight loss lasting for one month. Bronchial fibroscopy highlighted a budding nodular tumor in the left main bronchus. The patient underwent a left pneumonectomy with mediastinal lymphadenectomy. Microscopic examination showed tumor cells infiltrating the bronchial wall and the cartilage and concluded to an ACC of the left bronchus. Ear, nose, and throat examination as well as cervico-facial magnetic resonance imaging were performed to search a primary salivary gland tumor and were returned without abnormalities. The tumor was classified as a primary ACC of the left bronchus without lymph node metastasis. To avoid their misdiagnosis, ACCs of the lung should be well known by the pathologist and surgeons. Their pathological features may be misleading and referring to a benign lesion, however, the presence of cribriform foci and infiltrative pattern are very suggestive. Although, indolent and slow growing tumor, long-term recurrences are quite frequent, especially in case of unclear surgical margin.

1. Introduction

Malignant salivary gland type tumors, originating outside the head and neck, are rare. They are reported in the breast, skin, cervix, and lung [1]. In the pulmonary location, they account for less than 1% of all bronchopulmonary cancers and they are represented by adenoid cystic carcinoma (ACC) formerly known as cylindroma, mucoepidermoid carcinoma, epithelial-myoeplithelial carcinoma, and pleomorphic ex-adenoma. They originate from the peribronchial glands and they are usually proximally located [2]. Unlike other bronchopulmonary tumors, ACCs are not associated with smoking or other risk factors and they are considered as low-grade malignant neoplasms. Primary ACCs of the lung account only for 0.04–0.2% of all primary pulmonary tumors. Therefore, their clinicopathological behavior and management principles remain poorly understood.

2. Case presentation

A 56-year-old man, a tobacco smoker (66 pack years), with unremarkable family and personal history, was presented with hemoptysis with dyspnea and weight loss lasting for 1 month. On clinical examination, the patient had a severe shortness of breath with distended left chest and decreasing in thoracic amplification. On auscultation, breath sounds were reduced in the left pulmonary field with the presence of crepitation.

The chest radiography showed atelectasis with mediastinal enlargement. Then, a bronchial fibroscopy was performed and evidenced a budding tumor in the left main bronchus. Multiple directed biopsies had been realized for histological diagnosis. Microscopic examination with hematoxylin and eosin staining showed an invasive tumor proliferation (Figure 1A), with a mainly cribriform architecture associated with small clusters and tubes with eosinophilic content (Figure 1B). The tumor cells were small with a clear reduced cytoplasm and quit anisokaryosis. Mitoses were occasional. In view of this morphological feature, which combines a mainly cribriform architecture and no alarming cytology with

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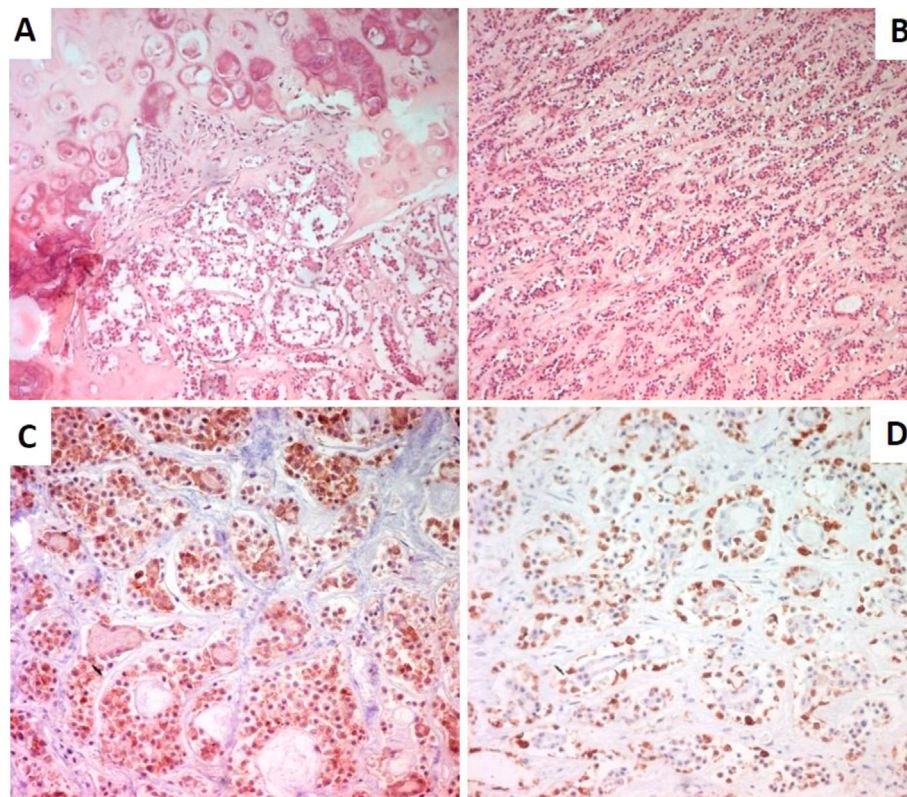


Figure 1. (A) Adenoid cystic carcinoma infiltrating the bronchial cartilage (Gx100). (B) Adenoid cystic carcinoma displaying tubular structures (Gx100). Membrane expression of c-Kit (C) and SMA (D) in adenoid cystic carcinoma of the lung (Gx200).

scant cytonuclear atypia, an ACC was suspected and an immunohistochemical study was performed. The tumor cells exhibited a positive expression of receptor tyrosine kinase inhibitors c-Kit (CD 117) (Figure 1C) and smooth muscle actin (SMA) (Figure 1D), confirming the epithelial and myoepithelial differentiation. While no synaptophysin and protein 63 (P63) staining was identified. The proliferation index, Ki-67, was estimated to be only 1%. Therefore, the pathology report confirmed an ACC of the left bronchus.

To identify a primary salivary gland tumor, an ear, nose, and throat examination (ENT) examination as well as cervicofacial magnetic resonance imaging (MRI) were performed and were displayed no abnormalities, confirming the pulmonary origin of the tumor. Furthermore, the staging process did not show any lymphatic or distant metastasis.

The patient underwent a left pneumonectomy with mediastinal lymphadenectomy. A left pneumonectomy of $19 \times 11 \times 3$ cm with a bronchial segment of 4 cm was received in our Pathology Department. The dissection of the specimen showed a brownish, soft polypoid bronchial tumor of 2.2 cm and located at 0.2 cm from the bronchial surgical section. Lymph node dissection has brought back 12 anthracotic lymph nodes.

On microscopic examination, the tumor had the same morphology seen in the biopsies. The tumor cells infiltrated the bronchial wall as well as the cartilage. Images of perinervous sheathing had been seen without evidence of vascular emboli. The bronchial surgical margin was unclear. Elsewhere, pulmonary parenchyma was the site of emphysematous lesions associated with hemorrhagic suffusions and inflammatory changes. The 12 nodes were devoid of metastases. Consequently, the tumor was classified as a primary ACC of the left bronchus without lymph node metastasis (pT1bN0Mx). The postoperative course was uneventful, and the patient was subsequently lost to the follow-up.

This case report was approved by the ethics committee of Farhet Hached University Hospital. Written informed consent was obtained

from the patient for publication of this case report and the use of accompanying images.

3. Discussion

ACC is a rare but distinct salivary gland-type malignant neoplasm arising uncommonly as a primary tumor in the lung. ACC represents 0.04–0.2% of all lung cancers. ACC of the lung has a slow growing and prolonged clinical course and hence, it is regarded as a low-grade malignancy. The site of origin is the trachea-bronchial glands in the airway submucosa, with a morphology similar to ACC arising in the salivary glands [3, 4].

Although our patient was an elderly smoking man, ACC of the lung was reported mainly in young patients, with a slight female predominance [4, 5]. Unlike other lung carcinomas, smoking is not thought to be a definite risk factor for the development of primary ACC [1, 6]. Clinically, coughing was the most common symptom, followed by hemoptysis and shortness of breath. Symptoms were not specific and misleading, explaining the delay in diagnosis. As a results, several patients are wrongly treated for asthma and bronchitis [3, 6].

The correlation between the histological patterns and clinical behavior of ACC of the lung has been suggested. Indeed, this tumor exhibits three predominant histological growth patterns. The most frequent and predominant pattern is the cribriform followed by the tubular pattern and then the least frequent and the most aggressive is the solid pattern. In contrast to the cribriform type, which shows a more benign behavior, solid ACC has been associated with a more destructive clinical course and early distant metastases. Vascular emboli and lymph node metastases are uncommon, while perineural invasion has been frequently reported, which was consistent with our findings [6, 7].

The morphologic features of ACC of the lung are not very distinctive to give a confirmed diagnosis in routine hematoxylin and eosin stains. To

improve the diagnosis of these tumors, some pathologists had stressed the importance of identification of focal areas bearing the more conventional cribriform morphology [2].

In order to eliminate the diagnosis of conventional adenocarcinoma and small cell carcinoma of lung in areas showing a predominant solid or tubular pattern, the immunohistochemistry study is highly recommended [1]. In fact, the expression of myoepithelial markers, such as P63, SMA, C-kit, and S-100 protein, is a strong argument for ACC of the lung. Interestingly, Huang et al. [8] reported a rare case of lung ACC exhibiting immunoexpression of CK, SMA, Calponin, C-kit, P63, and S-100 protein. Cytogenetically, a loss of heterozygosity of chromosome 3p14 and 9p was described [9]. However, EGFR and KRAS mutations have not been reported yet. The MYB rearrangement is specific for ACC and may be useful in case of diagnosis ambiguity [9, 10].

Despite their generally slow and indolent growth, ACC of the lung may be more aggressive in some cases [2]. Indeed, due to the extensive spread along the major axis of the trachea or the stump bronchus at the time of diagnosis, residual tumors at the resection margin were common as described in our case [1, 6, 11]. Prognosis depends on the histological subtype, tumor staging as well as surgical margin status [1, 4]. Interestingly, in the recent study of Han et al. [12], most of primary pulmonary ACC cases were diagnosed at an early clinical stage and showed a favorable prognosis. Furthermore, the tumor size and the patient age were considered independent prognostic markers [12]. However, Junejo et al. [13] reported a rare case of histologically confirmed renal metastasis from ACC of the right lung after three years of primary presentation.

Surgical resection is the optimal management of ACC of the lung. To control residual disease and recurrences, radiotherapy is indicated for unresectable tumors and incomplete resection. ACC of the lung may show a partial response to targeted therapies. The place of Imatinib has been demonstrated in strongly c-Kit expressing tumors [3, 14].

4. Conclusion

Although its scarcity, primary ACC of the lung should be well recognized by the pathologist and surgeons to avoid misdiagnosis. The microscopic features may be misleading to a benign lesion and showing only cribriform clusters. Therefore, the immunohistochemistry study remains indispensable to confirm the myoepithelial differentiation. Although, ACC of the lung is indolent and slow growing tumor, long-term recurrences are quite frequent. The prognostic parameters depend on predominant histological pattern, tumor staging and surgical margin status.

Declarations

Author contribution statement

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Data availability statement

Data will be made available on request.

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The authors declare no conflict of interest.

Additional information

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