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Case Study

Primary Adenoid Cystic Carcinoma of The lung: A Case Report and Review of the Literature

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ABSTRACT

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Adenoid cystic carcinoma (ACC) is a malignant salivary gland-type tumour. Primary location in the lung is very rare. The tumor grows insidiously and infiltratively, sometimes extending to the lung parenchyma and mediastinum. The diagnosis is confirmed by histopathological examination. Its prognosis remains unpredictable, considering the risk of local recurrence and distant metastasis. The treatment of choice is based on a carcinological surgery resection followed by radiotherapy. To date, only a small number of cases and retrospective series have been described. We report a case of a 67-year-old Moroccan woman with a primary adenoid cystic carcinoma of lung.

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INTRODUCTION

Adenoid cystic carcinoma is a malignant salivary gland type tumour that consists of epithelial and myoepithelial cells. It shows variable morphological configurations including tubular, cribriform, and solid pattern, according to the fourth edition of the WHO classification of tumors of the lung, published in 2015 [1]. The common location of this variant is the salivary glands of the head and neck. Primary pulmonary location represents less than 0,2% of all lung malignancies [2]. This tumour remains a rare disease, and only a few cases have been reported in the literature. We report a new case of a primary ACC of the lung with emphasis on their behavior clinical, histological and immunostaining features, and compare them with literature data.

CASE REPORT

We report a case of a 67-year old female with diabetes mellitus and hyperlipidemia treated with oral medications for 10 years. She had no history of smoking. She consulted for a chronic cough complicated over two months by haemoptysis of average abundance. There were no other systemic complaints. The initial physical examination findings were normal. Chest radiography was normal. A chest-computed tomography (CT) demonstrated a mass at the expense of inferior lobar right bronchi measuring 51 by 36 that invaded the right atrium and the pulmonary veins (Fig 1). There was associating mediastinal and bilateral hilar lymphadenopathy. A bronchoscopy-

guided biopsy was performed. The histopathological examination showed a biphasic neoplasm composed of epithelial and myoepithelial cells. Architecturally, the tumor was arranged in glandular, tubules and cribriform patterns. It is composed of small-sized cells with homogeneous hyperchromatic nuclei and scant cytoplasm. Mitotic figures were absent. The tumor cells surrounding connective tissue cylinders with myxoid material. The stroma was fibrous with areas of hyalinization (Fig 2). There was no evidence of perineural or vascular invasion. In our case, the luminal cells were positive for Keratin, S-100 and CD117. The myoepithelial component was positive for keratin and SMA. The Ki-67 proliferation index was estimated to 5% (Fig 3). The conclusion of the pathology report was in favor of adenoid cystic carcinoma of the lung according to the WHO 2015 classification. For the clinical staging, a general physical examination and a thoracoabdominal pelvic computed tomographic scan was performed and did not show any tumors in other regions, including the salivary and thyroid glands, or distant metastasis. Thus, the diagnosis of primary adenoid cystic carcinoma of the lung was retained. The tumor was classified T4N2M0 according the American Joint Committee on Cancer Staging (AJCC 2017). The patient was inoperable and was referred for neoadjuvant chemotherapy then assessment for eventual surgery or radiotherapy. To date, the patient has received chemotherapy and is pending assessment.

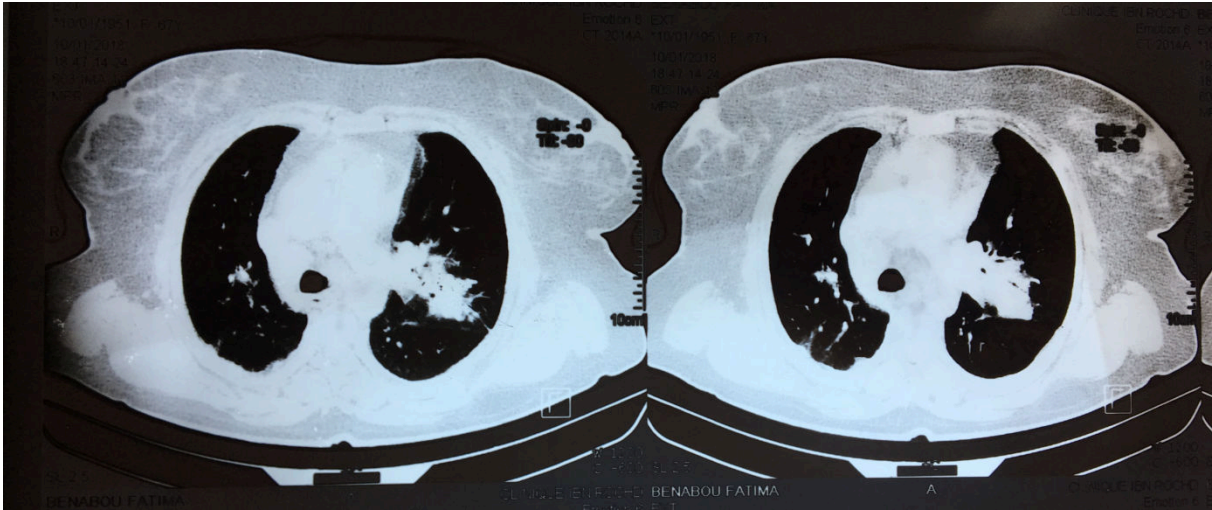


Fig 1 : A chest-computed tomography showing a mass at the expense of inferior lobar right bronchi measuring 51 by 36 that invaded the right atrium and the pulmonary veins.

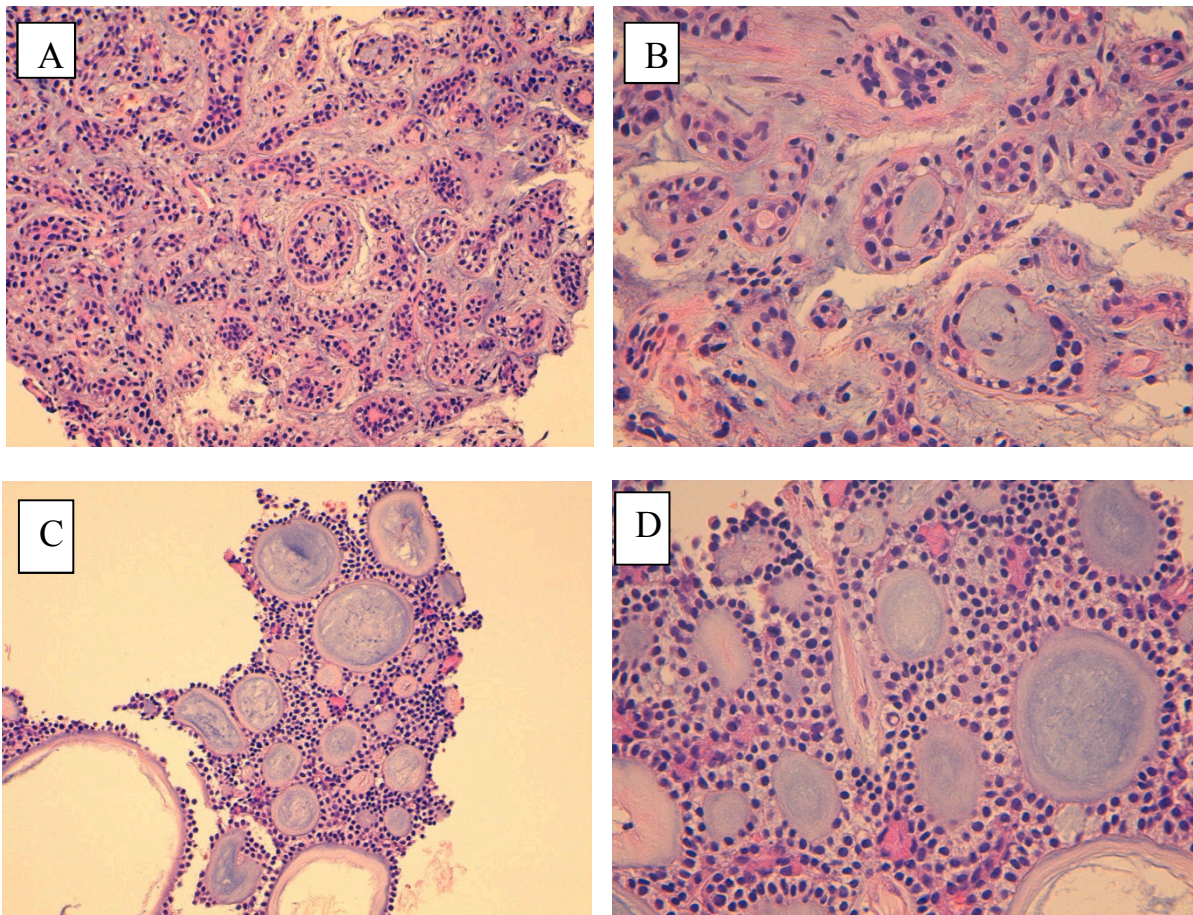


Fig 2 : Adenoid cystic carcinoma. A: Biphasic tumour composed of epithelial and myoepithelial cells. B: Showing predominantly tubular growth of small hyperchromatic epithelial cells. C: Tumour cells containing numerous sharply outlined luminal spaces and sometimes containing mucinous secretion within their lumens. D: homogeneous eosinophilic material deposited in the connective tissue.

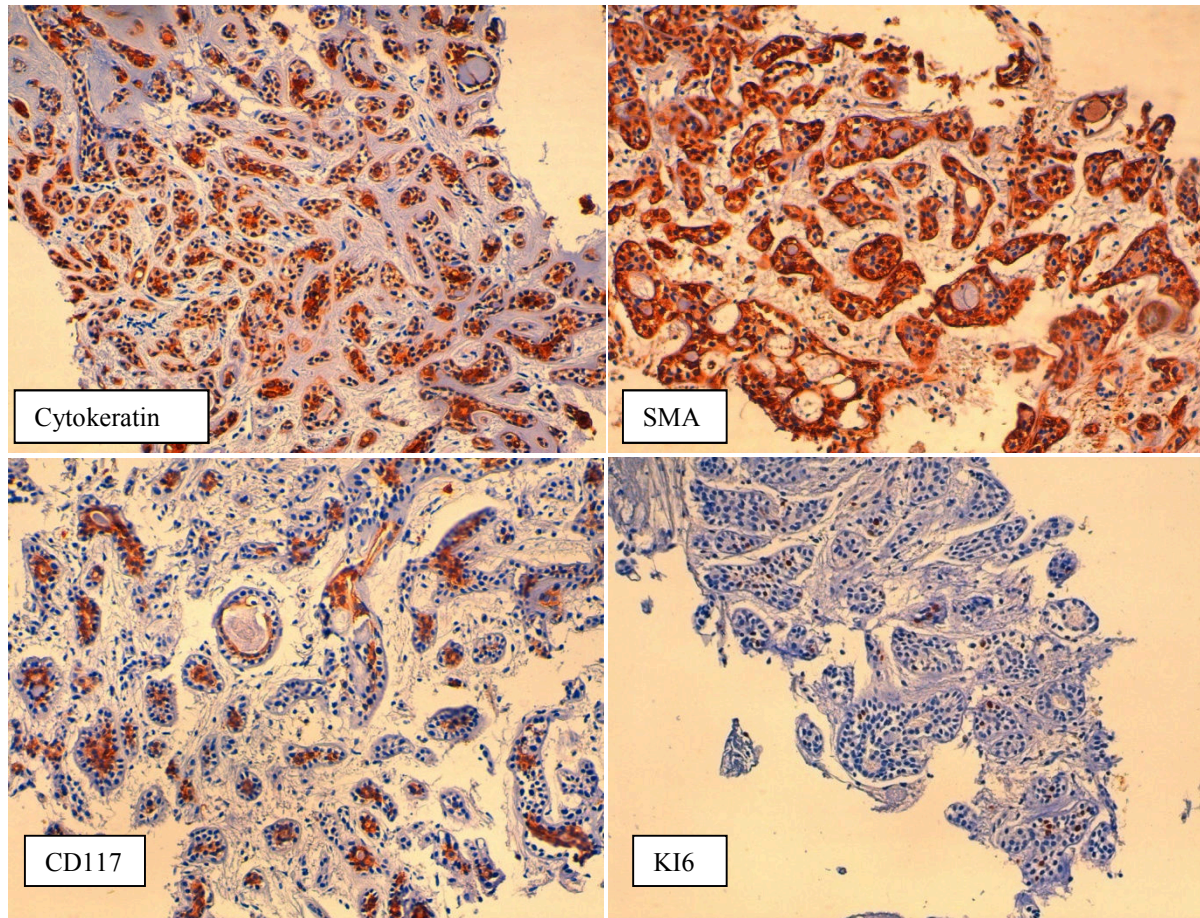


Fig 3 : The luminal cells were positive for Keratin and CD117. The myoepithelial component was positive for keratin and SMA. The Ki-67 prolifer

DISCUSSION

Primary adenoid cystic carcinoma of the lung is very rare malignant tumor. Typically, it can be observed mainly in salivary glands of the head and neck but it can occur in other tissues such as the skin, lachrymal glands, breast, vulva, upper digestive tract [3,4]. It arises from a dual cell population, associating ductal cells and myoepithelial cells with variable morphological configuration. It was initially described as a non-malignant glandular neoplasm; currently, however, it is referred to as a low-grade bronchial carcinoma [5]. Primary ACC of the lung remains a rare disease, and only a small number of cases have been dealt with in the literature. The tumor was first described by Bilroth under the name cylindroma of the nasal cavity, in 1856 [6]. The nomination ACC was introduced in 1953 by Foote and Frazel [7] and has been used to date. ACC of the lung typically arises as an endobronchial tumour [1] and originates from

the submucosal glands. Sometimes, it can extend to the lung parenchyma, infiltrating the cartilage and mediastinum [1]. In the literature, there is no evidence of an association with smoking [8,9]. In Ming-Ming et al's study, in which they reviewed all cases of the primary ACC published from 1993 to 2014 (34 cases), 67.6% were found to be never smoking [10]. However, Molina et al. reported in one series that smoking may be related to the incidence of ACC of the lung [11]. The average age at presentation is 50 years with no gender predominance [8, 11]. Clinically, the common symptoms include shortness of breath, cough, dyspnoea, wheezing, and hemoptysis due to airway obstruction [12]. Most patients had two or more clinical symptoms depending on the location of the tumor. It is a tumor which grows slowly with a potential to invade into the surrounding tissues. Imaging typically shows a centrally located polypoid mass that may have an endobronchial component. Compared with

mucoepidermoid carcinoma, ACC are larger, more frequently involve the central airways, and have a higher median FDG uptake [13]. Primary ACC in the peripheral lung must therefore be distinguished from metastatic lung tumor [14]. Histologically, three main growth patterns were observed in various proportions. The most predominant pattern was the cribriform (cylindromatous) characterised by nests of tumour cells containing numerous sharply outlined luminal spaces and sometimes containing mucinous secretion within their lumens. Also, we can see a homogeneous eosinophilic material deposited in the connective tissue surrounding the periphery of the cribriform component [8]. It is composed of small-sized cells characterised by a round hyperchromatic nuclei and scant cytoplasm. Mitotic figures were infrequent [1]. The second frequent pattern is a tubular which is constituted by two to three layers of small cuboidal cells, containing amorphous secretion within the lumen. The least frequent and most aggressive is a solid pattern included sheets of cells lacking luminal structures with vesicular nuclei and periodic mitotic activity. Immunohistochemistry demonstrates both ductal and myoepithelial phenotypes, including cytokeratin, vimentin, actin, S-100 protein and KIT. In a study of 49 patients with ACCL, Aubry et al. demonstrated that 33 patients showed KIT positivity [15]. In another immunohistochemical study on 17 out of a total of 34 patients, Hu et al. described other antibodies and the cells show positive staining for Keratin in 17/17 patients, P63 in 11/12 patients, Smooth muscle actin (SMA) in 6/9 patients, S-100 in 7/8 patients, vimentin in 10/12 patients, CK7 in 11/11 patients, GFAP in 1/3 patients and CEA in 2/9 patients. Staining was absent for Synaptophysin in 7 patients, CD56 in 7 patients, CK20 in 4 patients, Chromogranin A in 4 patients, CDX-2 in one patient, Thyroid transcription factor-1 in 14 patients [10]. Collagen type IV and laminin can be detected in basement membrane material around some of the epithelial cribriform and tubular structures [8]. In our case, the luminal cells

were positive for S-100, CD117 and TTF1. The myoepithelial component was positive for keratin and SMA. The Ki-67 proliferation index was estimated to 5%. The differential diagnoses include carcinoid tumours, basaloid squamous cell carcinoma. All of which can be typically distinguished by immunohistochemical staining. Pleomorphic adenoma with a focal cribriform component can simulate ACC. Metastasis from other organs should be carefully ruled out [12]. The majority of ACC contain alterations of the MYB gene, usually resulting in a fusion gene product with the NFIB gene by a t (6;9) translocation event. This fusion of MYB oncogene and NFIB transcription factor has been reported in 30-100% of adenoid cystic carcinoma of the head, neck and breast [16, 17]. However, ACC of the lung has not been thoroughly studied for rearrangements of the MYB gene. In a recent study, Roden et al. identified MYB rearrangement in 41% of 29 cases of pulmonary ACC [18]. Another finding is that ACC tumors frequently produce high levels of the receptor tyrosine kinase c-KIT and variably overexpress other growth factor receptors, including fibroblast growth factor receptor 1 (FGFR1), epidermal growth factor receptor (EGFR), and/or human epidermal receptor-2 (HER-2) [15-19]. Several other frequent mutations are recently published that may be relevant for drug development. Further data of pulmonary carcinoma of lung needs to be collected to establish molecular mechanisms. The treatment of Primary ACCL usually involves a radical surgery followed by radiation therapy. If the tumor is unresectable or metastasized, chemotherapy may be employed. After resection of the primary tumor, local and distant recurrences are quite common, and may occur over a 10 to 15 year later. Distant metastasis may eventually occur, hence careful follow-up observation is mandatory. The prognosis of primary ACC of lung remains unclear because of the paucity of reported cases for long-term follow-up. It depends on clinical staging of the tumor at the diagnosis, histological pattern (solid growth pattern is the most aggressive) and complete resection [8, 11,20].

CONCLUSION

We describe the case of a patient with primary adenoid cystic carcinoma of the lung, which is a rare tumor entity. Positive diagnosis is based on histopathological approach with three different subtypes of this tumor. Immunohistochemical staining confirm the diagnosis and can distinguish other differential diagnoses. The prognosis remains unpredictable and the treatment is based on surgery followed by radiation therapy. Our patient had an unresectable tumor, the reason why she received a neoadjuvant chemotherapy and we will continue to follow her to obtain long-term survival data.

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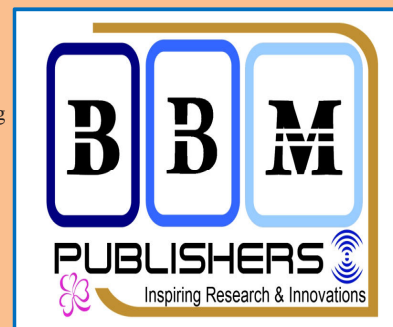
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