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Case Report

Primary carcinoma ex pleomorphic adenoma of the bronchus: report of two cases and review of the literature

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Abstract: Primary carcinoma ex pleomorphic adenoma in the tracheobronchial system is an exceedingly rare neoplasm arising from minor salivary glands. Two cases of this unusual entity were presented. All the lesions were associated with bronchial system, while neither of the patients had a history of a head and neck salivary gland neoplasm. Both cases were followed up for more than 3.5 years. Thus, further data concerning biological behavior and prognosis were made availably. In addition, we provided a review of all cases published to date and summarized the data presently known, for the first time, with the emphasis on the computed tomography (CT) findings. The diagnosis of carcinoma ex pleomorphic adenoma should be considered in elderly patients with slowly progressive symptoms of dyspnea and cough. The continued clinical evaluation and long-term follow-up seems to be of utmost importance for better diagnosis and treatment of primary carcinoma ex pleomorphic adenoma of the bronchus.

Keywords: Primary carcinoma ex pleomorphic adenoma, tracheobronchial system, primary salivary gland-type tumors, pleomorphic adenoma, computed tomography

Introduction

Primary salivary gland-type tumors are occasionally encountered in the tracheobronchial system, as minor salivary glands are evenly distributed throughout the trachea in the submucosal region. Carcinoma ex pleomorphic adenoma (CXPA), which is defined as an epithelial malignancy arising in association with a primary or recurrent benign pleomorphic adenoma (mixed tumor) [1], comprises the vast majority of malignant mixed tumors of the salivary glands. Albeit rare, primary CXPA should be expected in the respiratory tract. Up to now only 9 cases of this entity have been published.

On account of the rarity of primary bronchial CXPA, the diagnosis and prognosis are controversial. Radiology findings were seldom discussed. Herein, we reported 2 cases of primary bronchial CXPA with a follow-up of at least 3.5 years. All the lesions were associated with bronchial system, while neither of the patients had a history of a head and neck salivary gland neoplasm. We describe radiologic findings and complete clinical courses, and analyze the diagnosis and prognosis of this entity. Furthermore, a review of all cases published until now is provided. Permission for this submission was obtained by the Second Affiliated Hospital of Zhejiang University institutional review board.

Case reports

Case 1

A 61-year-old male patient presented with complaints of recurrent cough and expectoration for the last 2 months and fever for 10 days. Physical examination revealed moist crackles over the left lower lung field. A chest radiograph indicated the presence of patchy opacities in his left hilum and this warranted a CT scan for further characterization. A contrast-enhanced computed tomography (CECT) of the thorax was performed (**Figure 1A**, **1B**), which revealed an eccentric, well-defined homogenous soft tissue mass arising from the bronchial system of the

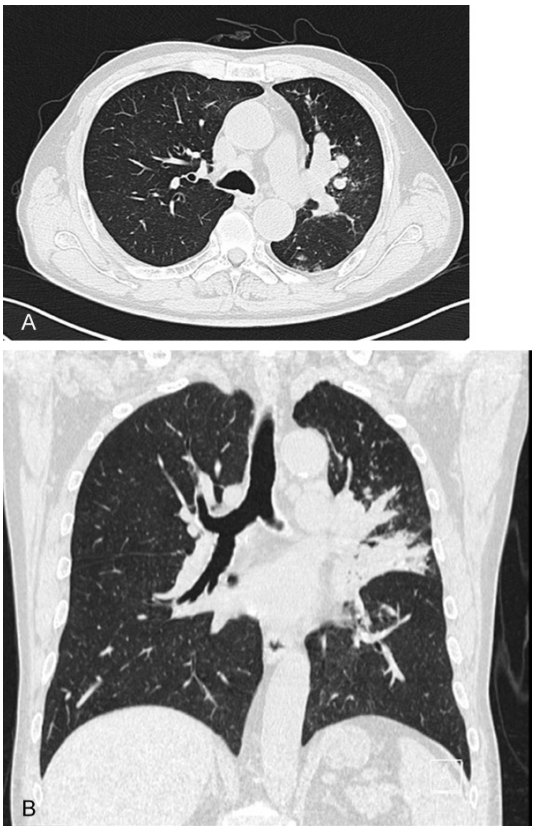

Figure 1. A. Axial image of contrast-enhanced computed tomography of the thorax showing the tumor in the bronchial system of the left upper lobe. B. Coronal image showing filled bronchiectasis with distal obstructive pneumonia.

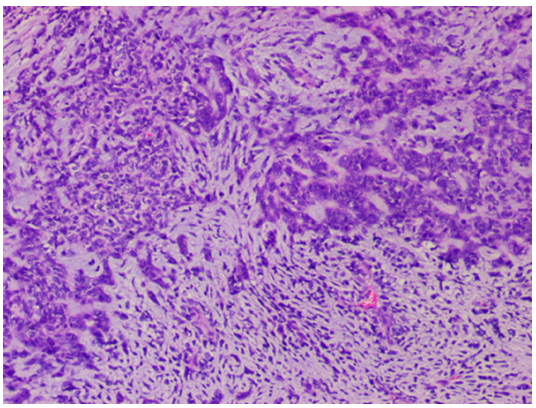

Figure 2. Medium power view disclosing areas resembling a low differentiative carcinoma associated with stromal mucoid degeneration (H&E, original magnification ×200).

left upper lobe, affecting the left main bronchus. There was filled bronchiectasis with distal obstructive pneumonia which might cause the fever. The mass showed strong enhancement after intravenous contrast medium. No mediastinal lymphadenopathy was noticed.

Primary tracheal malignant neoplasms such as squamous cell carcinomas and adenoid cystic carcinomas were supposed and a lobectomy was undertaken. Histopathological examination showed a partially well-demarcated tumor with a benign component resembling a pleomorphic adenoma. Merging imperceptibly with the pleomorphic adenoma area was the malignant component mimicking carcinomatous cells (**Figure 2**), suggestive of CXPA. Immunohistochemical studies showed focally positive for CK7 and p63, which was compatible with CXPA. Postoperatively, no chemotherapy was administered. Today, 3.5 years after operation, the patient is alive and well.

Case 2

A 65-year-old male patient presented with an 8-month history of paroxysmal cough and recurrent hemoptysis. His physical examination was unremarkable. On CECT of the chest, an endo- and extra-bronchial lesion was discovered in the left lower lobe, showing strong enhancement after intravenous contrast medium (**Figure 3**). The mass almost obstructed the left lower lobe bronchi, causing distal atelectasis and obstructive pneumonia. The enlarged and filled bronchus reflected the growth of the mass. The patient was supposed to have mucoepidermoid carcinoma and underwent a lobectomy. Histologically the tumor resembled a pleomorphic adenoma with malignant component (**Figure 4A**, **4B**). There was a positive immunostaining reaction for CK5/6, CK7, S-100, p63, CD10, CD117, SMA, and EMA. In view of this, CXPA was diagnosed.

Postoperatively, chemotherapy (docetaxel injection and nedaplatin) was applied. He was now alive 4 years after operation without further therapy.

Discussion

Primary salivary gland-type tumors of the lung account for 1% or less of all pulmonary neoplasms [2]. Primary carcinoma ex pleomorphic adenomas are even less common in the tracheobronchial system. Review of the literature disclosed 9 previously reported cases of pri-

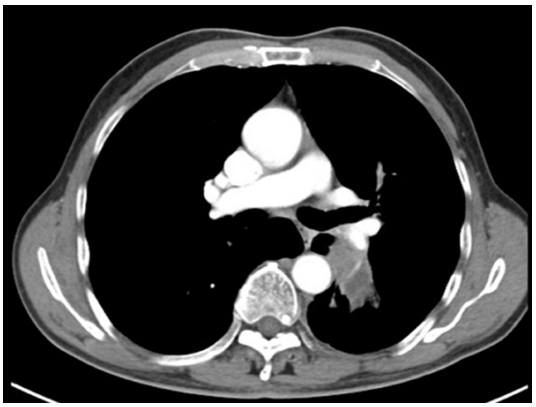

Figure 3. Axial image of contrast-enhanced computed tomography of the thorax (mediastinal window) revealing strong enhancement of the tracheal tumor after intravenous contrast medium.

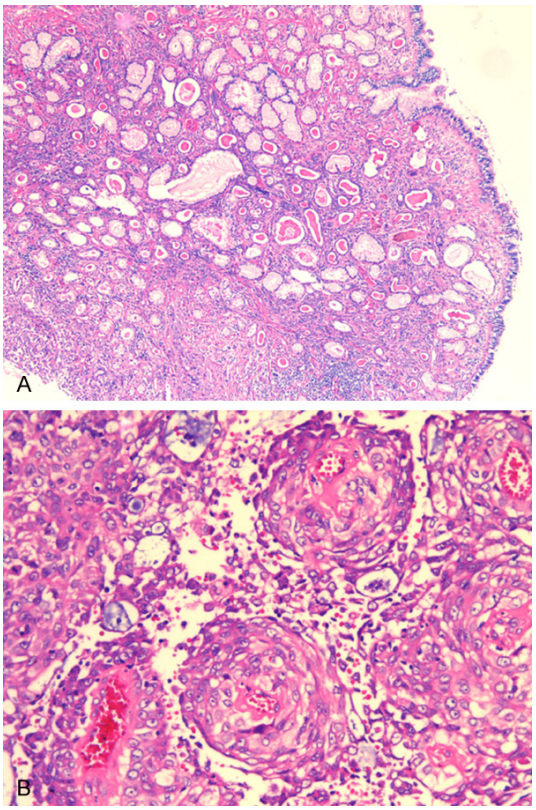

Figure 4. A. Low power view revealing gland-like architecture with islands and nests of atypical epithelial cells proliferation (H&E, original magnification ×40). B. High power view showing areas resembling a mucoepidermoid carcinoma associated with keratin pearl (H&E, original magnification ×400).

mary CXPA of the trachea and bronchi [3-7]. The largest series of own cases has been reported by Weissferdt *et al.* (5 cases) [3].

Comparing the data of our cases with those published, following findings were corresponded:

1. Our patients were in their seventh decade of life, when the mass was resected, while the highest incidences found in literature are in the sixth decades of life (average age: 58.2 years at first operation, varying from 44 years to 71 years).

2. Although the patients in both of our cases were man, women could also have this entity according to the literature. In the literature, the disease affected 3 women and 6 men.

3. In our first case, the patient had cough, expectoration and fever. In case 2, there were cough and hemoptysis. Symptoms may not distinct for this disease, but dyspnea and cough seems to be common. Hemoptysis, chest pain, or pleural effusion could also be present. However, most patients had chronic courses with slowly progressive symptoms.

4. The masses in both of our cases were localized in the bronchi of the left lung, but there seems to be no preferred location. In the literatures, 4 cases happened in trachea [4-7], 3 cases in the right upper lobe [3], one case in the right lower lobe and one in the left hilum [3].

5. In the literature, the size of the tumors varies from 1.3 [4] to 5 cm [3], while the tumors described in this report were comparatively big (7 and 5 cm). For the case described by Mori *et al.* [5], the size was not mentioned.

6. Both of our lesions were completely resected and the second patient received chemotherapy. In the reported cases, conservative but complete excision was the preferred treatment. Only in one case, pneumonectomy was applied [3]. Postoperatively 3 patients received radiotherapy [5-7]; 2 patients had chemoradiation [3] and one patient had chemotherapy [3].

7. Our patients lived well with a follow-up of at least 3.5 years after surgical removal of the tumors, while 2 fatal cases were reported [3]. Four patients in the literature were alive with disease during a 3-month [7], 16-month [4], 20-month [3], and 29-month [6] follow-up, respectively. The behaviour of tumor appeared to parallel that of the salivary gland counterpart

[8], which may explain the good prognosis in our cases. In our cases, both of the tumors had a low-grade malignant component.

Reports that discuss about the radiologic finding of CXPA, however, is lacking, not only because of the rarity of such tumors primarily occurring in the lower respiratory tract but also because there are no distinctive features found to diagnose the tumors when they occur in this site. Herein, we report 2 such cases in which the CT findings were reminiscent of a malignant salivary gland-type neoplasm, and we propose that CXPA should be expected.

There has been only one previous report of primary CXPA of the tracheobronchial system described the CT findings. Demirag *et al.* [6] reported a CXPA in the trachea of a 56-year-old man. CT scan showed a non-defined homogeneous mass in the trachea. The intraluminal tumor, arising from the lateral and posterior wall of the trachea, showed a relatively smooth surface.

In our present cases, on CT, the tumors appeared differently as a soft-tissue mass, usually having an endo-and extra-luminal growth pattern. The tracheobronchial wall was affected, which was not clearly displayed. The mass was sessile and eccentric, mostly intraluminal, resulting in asymmetric luminal narrowing. The margin of the tumor was irregular and the enhancement was relatively strong and heterogeneous. Filled bronchiectasis was characteristic, with distal atelectasis and obstructive pneumonia. No calcification or mediastinal lymphadenopathy was noticed.

Such radiologic appearance, though not specific, has been described with few tumors, are most commonly associated with malignant salivary gland-type tumors includes neoplasms such as adenoid cystic carcinoma, mucoepidermoid carcinoma and metastasis. However the diagnosis of CXPA should be considered in elderly patients with slowly progressive symptoms of dyspnea and cough.

Due to the fact that not enough cases with sufficient long term follow-up have been described until now, distinctive clinical features and CT findings cannot be concluded. Therefore, continued clinical evaluation and long-term follow-up seems to be of utmost importance for better diagnosis and treatment of primary CXPA of the bronchus.

Disclosure of conflict of interest

None.

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