

Primary endobronchial paraganglioma with lymph node metastasis: a case report

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Abstract

A paraganglioma is an extra-adrenal tumor of the paraganglia often found in association with sympathetic and parasympathetic nerves. A primary pulmonary paraganglioma generally presents as multiple small tumors or a solitary mass; however, endobronchial involvement is extremely rare. A 49-year-old man was admitted to our hospital because of a chronic cough, intermittent dyspnea, and chest pain. Chest computed tomography revealed a rounded, high-density lesion in the left lower lung lobe. Fiberoptic bronchoscopy demonstrated an endobronchial mass characterized by smooth, hypervascularized mucosa. Transbronchial biopsy of the mass and immunohistochemistry results suggested a paraganglioma. The patient fully recovered after lobectomy and lymphadenectomy. Pulmonary paragangliomas are rarely reported. Complete surgical resection is considered the treatment of choice for pulmonary paragangliomas, and the long-term prognosis is generally good. However, life-long follow-up is mandatory because of the possibility of recurrence and metastasis. This case report adds valuable knowledge to the literature on pulmonary paragangliomas.

Keywords

Paraganglioma, lung, thoracic surgery, transbronchial biopsy, immunohistochemistry, case report

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Introduction

Approximately 90% of tumors originating from chromaffin cells are located in the adrenal gland and are termed pheochromocytomas, whereas the remaining 10% of cases have an extra-adrenal origin and are termed paragangliomas.¹ Paragangliomas are rare tumors that reportedly occur at a

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rate of two to eight cases per million people each year.² Paragangliomas mainly occur in body parts rich in paraganglia, such as the head, neck, mediastinum, posterior peritoneum, and even thyroid.³ To the best of our knowledge, fewer than 30 cases of paragangliomas with a pulmonary presentation have been documented, and endobronchial involvement is even more rare.

Primary pulmonary paragangliomas are often asymptomatic and discovered incidentally. Chest computed tomography (CT) studies help to confirm a clinical suspicion of a pulmonary paraganglioma. However, histopathological evaluation is necessary for a definitive diagnosis. A correct pathological diagnosis and radical surgical treatment are fundamental to achievement of clinical recovery.^{2,4}

We herein report a case of a primary pulmonary (endobronchial) paraganglioma to help clinicians consider paragangliomas as a differential diagnosis and to correctly manage these tumors.

Case presentation

A 49-year-old man was admitted to our department because of a cough, intermittent

chest pain, and dyspnea. His medical history was unremarkable. Physical examination revealed no abnormalities. Chest CT showed a rounded, high-density lesion of 1.5 cm in diameter in the left lower lobe, and the lesion was associated with distal atelectasis. The CT values within the lesion on the plain scan and enhanced scan were 54 and 160 HU, respectively (Figure 1(a)). Neither suspected adenopathies nor distant metastases were detected. Positron emission tomography/CT showed high-rate ¹⁸F-fluorodeoxyglucose uptake. The standardized uptake value was 9.8 within the lesion (Figure 1(b)). Cranial magnetic resonance imaging revealed no abnormalities.

The patient underwent fiberoptic bronchoscopy, which demonstrated an endobronchial mass that was occluding the entire bronchus of the dorsal segment of the left lower lobe and that was characterized by smooth, hypervascularized mucosa (Figure 2(a)). A biopsy of the mass suggested an atypical neuroendocrine tumor (Figure 2(b)). The immunohistochemistry test results were positive for synaptophysin (Syn), chromogranin A (CgA), CD56, and S-100 and negative for thyroid transcription

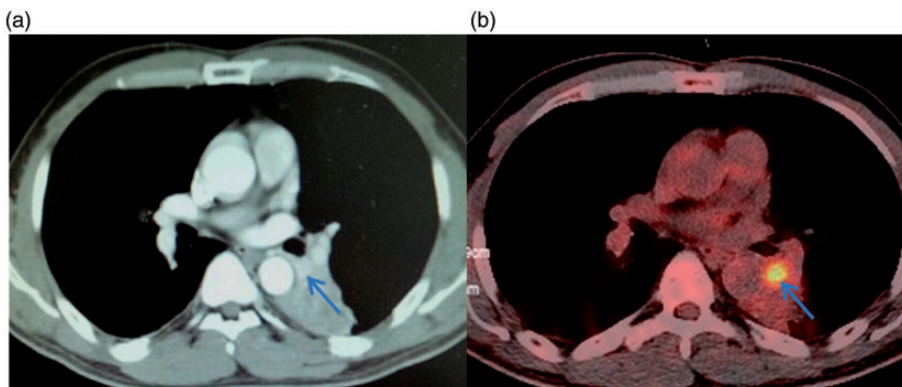


Figure 1. (a) Chest computed tomography scan showing a pulmonary paraganglioma (arrow) of about 1.5 cm in diameter. (b) Positron emission tomography/computed tomography imaging showing the same tumor (arrow).

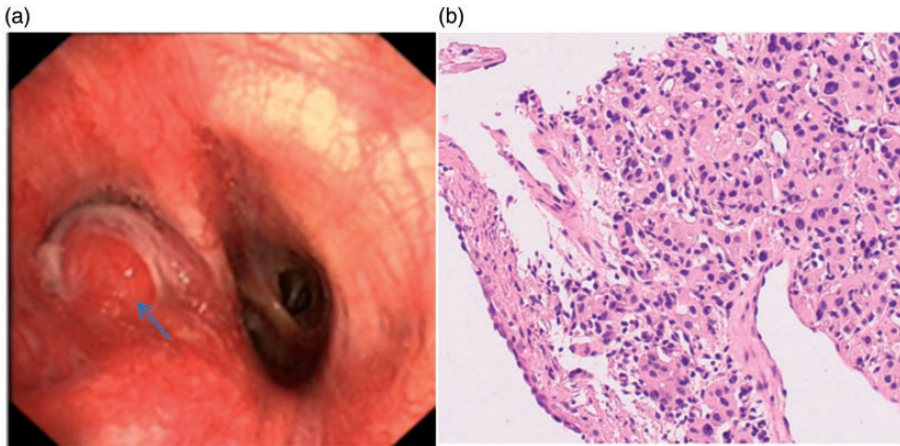


Figure 2. (a) The pulmonary paraganglioma was an endobronchial mass characterized by smooth, hyper-vascularized mucosa (arrow). (b) Hematoxylin–eosin staining (100 \times) showing the peripheral capsule and rich microvasculature.

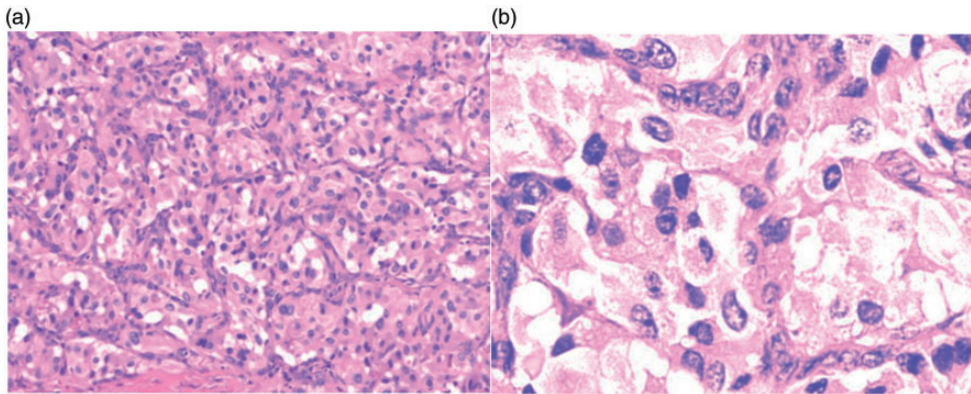


Figure 3. (a, b) Typical anastomosing cords of tumor cells arranged in a trabecular pattern or a nesting pattern, separated by rich microvasculature.

factor 1, p63, and cytokeratin; these results were consistent with a paraganglioma.

Preoperative biochemical tests were performed to determine the serum and urine levels of fractionated metanephrines, and the tumor was confirmed to be nonfunctional. Our patient was treated with video-assisted thoracoscopic surgery involving lobectomy of the left lower lobe and lymphadenectomy. Thoracoscopy showed that the mass was growing through the bronchus

but had not invaded surrounding structures. The margins of the frozen specimen were negative. Lymphadenectomy was performed, and lymph node metastasis was detected in station 10L.

Sections of the mass (1.5 \times 1.2 \times 1.0 cm) showed a cellular tumor surrounded by a thin band of fibrous tissue in a trabecular pattern (Figure 3(a), (b)). Immunohistochemical staining was positive for CD56, Sy, CgA, and S-100. Cytokeratin, epithelial membrane

antigen, and thyroid transcription factor 1 were negative. These findings were consistent with a paraganglioma. The lymph node from station 10L was consistent with a malignant neoplasm (Sy+, S-100+, CgA+).

At the subsequent 6- and 11-month follow-up visits, the patient had fully recovered from his resection without complications and remained active without airway symptoms. Chest CT 11 months postoperatively showed no evidence of recurrence.

Discussion

Primary pulmonary paragangliomas are extremely rare (<1% of all paragangliomas) and can present as multiple small tumors or a solitary mass;^{1,5} endobronchial involvement is very rarely reported.⁶

Paragangliomas can arise from both the sympathetic and parasympathetic systems. In particular, those associated with the parasympathetic system do not produce catecholamines and are not associated with hypertension, headache, palpitations, sweats, or tremor. Generally, most pulmonary paragangliomas are nonfunctional and result in no evident clinical symptoms. Some patients develop respiratory symptoms, such as a cough, chest pain, or dyspnea, as in our case.¹

Pulmonary nonfunctional paragangliomas are usually incidentally detected by CT as nodules presenting typical features:^{1,4} isodensity or slightly low density as well as homogeneous and intense enhancement, except for necrotic areas with scarce enhancement. Mediastinal forms are usually located in the bifurcation of great vessels. Pulmonary paragangliomas shown by CT as a hypervascular mass can resemble endobronchial carcinoid or bronchogenic carcinoma, making differential diagnosis difficult.⁶ Positron emission tomography/CT can also be used to assess lymph node involvement and distant metastasis and to detect occult paragangliomas.

Preoperative diagnosis of pulmonary nonfunctional paragangliomas is difficult, and accurate diagnosis requires pathological examination. Fibrobronchoscopy can be used in the diagnostic protocol. However, biopsies and transbronchial needle aspiration can be challenging because these procedures may cause massive bleeding.^{4,6,7} Diagnosis based on bronchoscopic biopsies and fine-needle aspiration is difficult to achieve because a complete pathological examination of the tumor morphology and structure is necessary,⁴ especially when differentiating these tumors from neuroendocrine tumors.^{7,8}

Macroscopically, paragangliomas are usually well-circumscribed, yellow-reddish in color, and hard in consistency, and they can be completely or incompletely capsulated. Microscopically, they exhibit typical anastomosing cords of tumor cells arranged in a trabecular pattern or a nesting pattern separated by a rich microvasculature. Paragangliomas are typically composed of two types of cells: chief cells and sustentacular cells. The chief cells are characteristically assembled in compact nests surrounded by sustentacular cells, which stain positively for S-100 protein.⁸ Immunohistochemical testing is particularly important. Paragangliomas typically show positivity for CgA and Sy, while their negativity for cytokeratin and epithelial membrane antigen is an important differentiating factor from carcinoid tumors.⁸

Unlike most tumors, there are no histological characteristics, molecular features, or genetic markers that can clearly distinguish between benign and malignant paragangliomas. At the time of this writing, nonfunctional paragangliomas of extra-adrenal origin were not included in the American Joint Committee on Cancer TNM staging system. However, invasive biological behaviors of paragangliomas have been reported, including local infiltration of surrounding tissues and adjacent lymph node and distant metastases.^{6,7,9,10}

According to the 2017 recommendation by the World Health Organization, paragangliomas should be classified as metastatic or non-metastatic instead of malignant or benign.¹¹ Complete resection is the first-choice treatment for a solitary paraganglioma.^{4,7–10,12–14} In the present case, our patient underwent lobectomy of the left lower lobe and lymphadenectomy. After a discussion among a multidisciplinary team including oncologists, chemotherapy was not administered because the role of adjuvant treatment for these tumors has not yet been established. In fact, these tumors are relatively resistant to chemotherapy and radiotherapy.^{4,13,14}

After complete surgical resection, the prognosis of pulmonary paragangliomas is favorable.^{4,8} Annual follow-up with imaging studies and urinary catecholamine testing, especially for functional tumors, is recommended to potentially detect recurrence and metastases.¹ Van Slycke et al.¹⁵ reported that the mean incidence of recurrence of extra-adrenal paragangliomas was $15\% \pm 7\%$ at 5 years and $23\% \pm 9\%$ at 10 years after surgery. However, there are reports of recurrence and metastases even after a long time; therefore, life-long follow-up after surgical resection is mandatory.^{4,12}

Conclusions

In this case report, we have highlighted the presentation of a rare tumor as a primary endobronchial paraganglioma, which is difficult to diagnose. A complete pathological examination and immunohistochemical testing are often necessary. Even if most of such tumors have a low grade of malignancy, aggressive behavior has been reported. After complete excision, close, periodic, and life-long follow-up is mandatory.

Ethics statement

The patient provided consent for treatment. Ethical approval was not required because this

manuscript only reports a case; nevertheless, the patient provided written informed consent for the use of his data for scientific purposes.

Author contributions

Xi-yuan CHEN designed the study, Chengxiang WU and Xiao-jun HUANG performed the research and analyzed the data, and Xiao-jun HUANG wrote the paper.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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