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CASE REPORT

PD-1/PD-L1 negative schwannoma mimicking obstructive bronchial malignancy: A case report

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Abstract

Schwannomas are homogeneous tumors of schwann cells and occur at peripheral and cranial nerves on the upper limbs, the head and neck area. Rarely, a bronchial schwannoma may appear in the lung and be misdiagnosed as lung neoplasms. Here, we report a 56-year old woman with a 5.8 × 7.0 × 2.8 cm lesion in her right upper lobe bronchus. The lesion had a maximum standardized uptake value (SUV_{max}) of 8.5 by 18-fluorodeoxyglucose positron emission tomography (FDG-PET). Bronchoscopy showed a mass obstructing the bronchus that bled easily. Despite repeated biopsies, a lung malignancy could not be excluded, and surgical resection was subsequently performed. Pathological examination demonstrated a primary bronchial schwannoma that was positive for molecular markers S-100 and SOX-10, negative for immune checkpoint marker PD-1/PD-L1 but also demonstrated certain uncommon pathological features. This case highlights the heterogeneity of bronchial masses and the diagnostic challenge for differentiating benign and malignant tumors in the thorax.

Key points

- Rare bronchial schwannoma mimics lung malignancy and poses a diagnostic challenge.
- This case of bronchial schwannoma, unlike peripheral schwannoma, lacks PD-L1. Pathological features indicate autonomic nerve origin for pulmonary schwannomas.

Introduction

Schwannomas are homogeneous tumors consisting only of schwann cells, the principal glia of the peripheral nervous system.[1] Although a schwannoma can occur at any site where peripheral and cranial nerves are present, schwannomas are more frequently found on the upper limbs, the head and neck area, and more rarely a bronchial schwannoma may appear in the lung and be misdiagnosed as lung neoplasm. In this report, we present a rare case of primary bronchial schwannoma with potentially malignant clinical features and uncommon pathological characters.

Case report

A 56-year-old female was referred to the Huashan Hospital with a history of an unexplained chronic dry cough on physical exertion. She was a non-smoker with no other notable medical history. Her scan with 18-fluorodeoxyglucose positron emission tomography

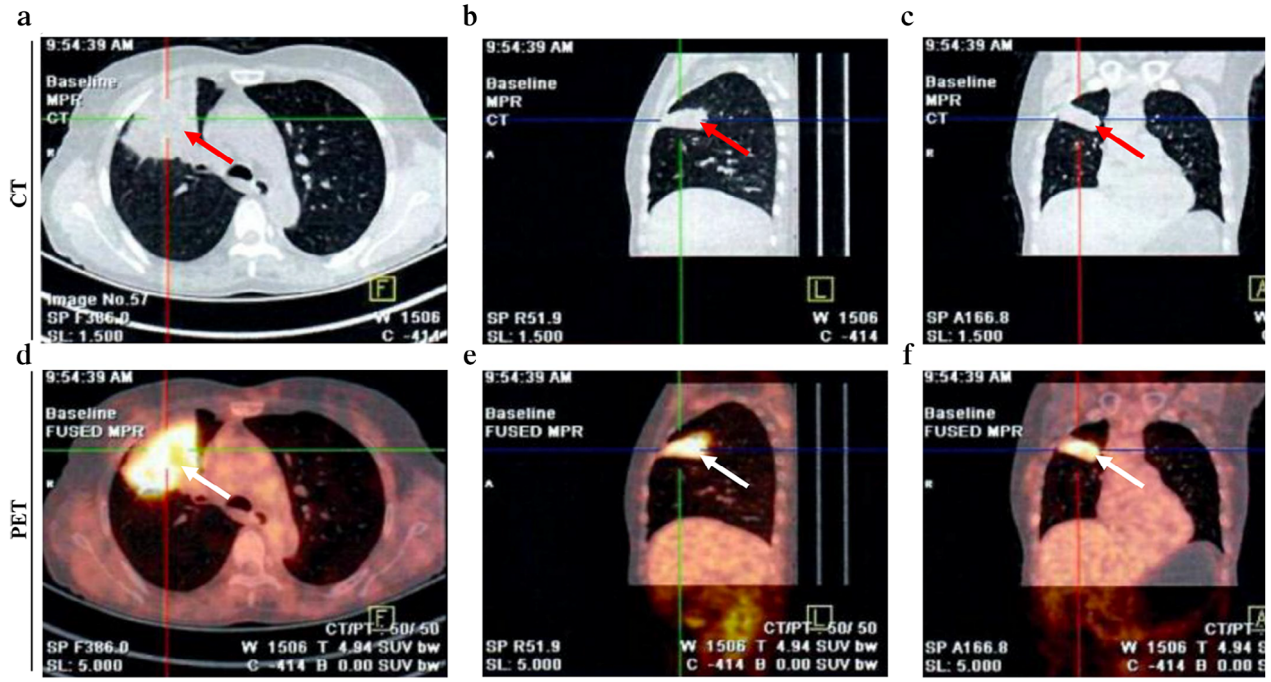

Figure 1 The bronchial schwannoma is highlighted with fluorodeoxyglucose-positron emission tomography (FDG-PET). Computed tomography (CT) scan (**a**) transverse; (**b**) sagittal; (**c**) coronal planes; (**d**) PET transverse; (**e**) sagittal; and (**f**) coronal planes highlight a mass of 5.8 × 7.0 × 2.8 cm in size in the right upper lobe close to the hilum (arrows).

(FDG-PET) revealed a 5.8 × 7.0 × 2.8 cm mass close to the hilum (Fig 1a-c) with a maximum standardized uptake value (SUV_{max}) of 8.5 (average SUV 4.3) (Fig 1d-f), suggesting a pulmonary malignancy. Bronchoscopy showed that the right upper lobe bronchus was almost completely blocked by this mass whose smooth surface bled easily (Fig 2a). An irregular low echo lesion was revealed by visualization using endobronchial ultrasound (Fig 2b). However, repeated bronchoscopic biopsies revealed inflammatory infiltration but no malignant changes. Similarly, a chest computed tomography (CT)-guided fine needle aspiration found no sign of malignancy.

Given the potential risk of a malignancy based on the patient's age, her high SUV_{max} and the bronchoscopic appearance of the lesion, a right upper lobectomy via lateral thoracotomy and locoregional lymph node

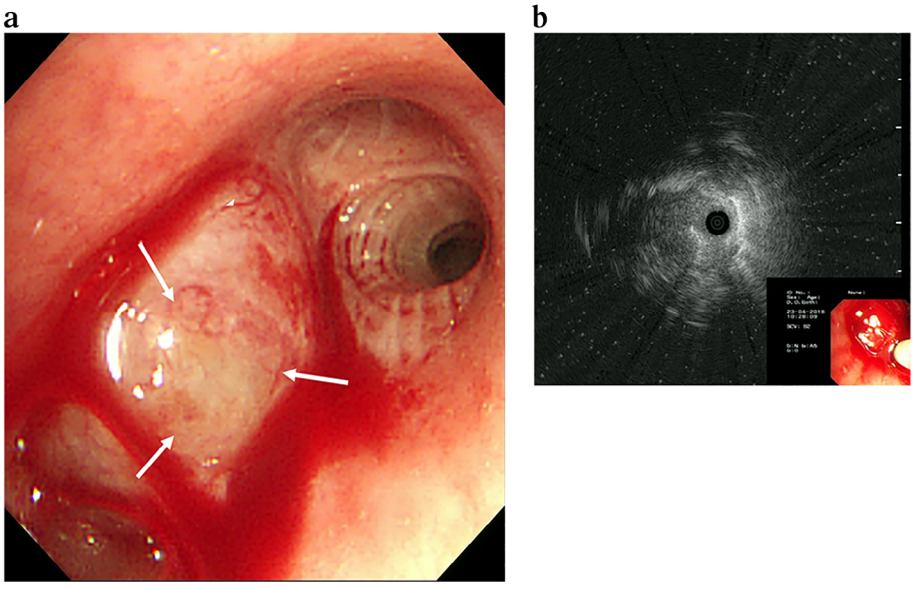

Figure 2 Visualization of the mass using bronchoscopy. (**a**) Bronchoscopy demonstrated that the right upper lobe bronchus was completely blocked by a mass with a smooth surface, wide base and propensity to hemorrhage (white arrows). (**b**) Endobronchial ultrasound identified an irregular hypoechoic soft tissue mass.

dissection was performed. The subsequent pathological examination revealed that all lymph nodes were non-malignant. Hemotoxylin & eosin (H&E) stain of the lesion showed proliferation of typical spindle cells arranged in fascicles and embedded in shredded collagen, forming Verocay bodies in some areas (Fig 3a). Most of the mass showed compact hypercellular Antoni A areas (Fig 3b) with nuclear pleomorphism. Irregularly spaced hypocellular Antoni B areas were also observed. The tumor did not display blood vessel congestion nor an outer fibrous capsule; instead, it was covered with ciliated airway epithelium (Fig 3b) (red arrow). Additional immunostaining showed positive staining for neural marker S-100 (Fig 3c) and SOX10, another marker with increased specificity for tumors of neural crest origin (Fig 3d). The spindle cells within the mass showed low proliferation activity, with only 2% of cells immunopositive for the proliferation marker Ki67. The cells also lacked expression of the receptor-tyrosine kinase marker, CD117 and smooth muscle actin (SMA). Lastly, the tumor was negative for the immune checkpoint pathway molecules, programmed cell death 1 (PD-1) (Fig 3e) and its ligand (PD-L1) (Fig 3f). Based on these histopathological findings, a diagnosis of primary bronchial schwannoma was made. The patient made an uneventful recovery from surgery and was discharged without complication or medication.

Discussion

A schwannoma is a benign nerve sheath tumor that is composed entirely of well-differentiated schwann cells and is typically encapsulated with fibrous tissue.[1] In a 10 year study of approximately 40 000 cases, schwannomas accounted for 5% of all soft tissue tumors.[2] Although they can arise from any peripheral or cranial nerve site, schwannomas are more frequently found on the head, neck and limbs, with a preponderance for females over males (~3:1).[3,4] Bronchial schwannomas are rare. A study on 62 confirmed cases of intrapulmonary or bronchial schwannoma suggesting that they account for 0.2% of all pulmonary neoplasms.[4,5] However, they are of clinical importance as a differential diagnosis of other potentially malignant lung neoplasms.

On radiological imaging, bronchial schwannomas mostly present as a round mass with a well-defined margin. Their morphological features can mimic malignant lung tumors particularly with their high FDG uptake on PET scan. FDG-PET is commonly used to differentiate benign and malignant lung tumors and has been shown to do so with greater than 90% sensitivity and specificity.[6] High SUV in lung neoplasm is associated with high tumor aggressiveness (eg, size, invasion) and a high SUV confers poor prognosis.[6,7] While schwannomas are benign tumors, their SUVs have been shown to range from negative or benign (below 2.5) to

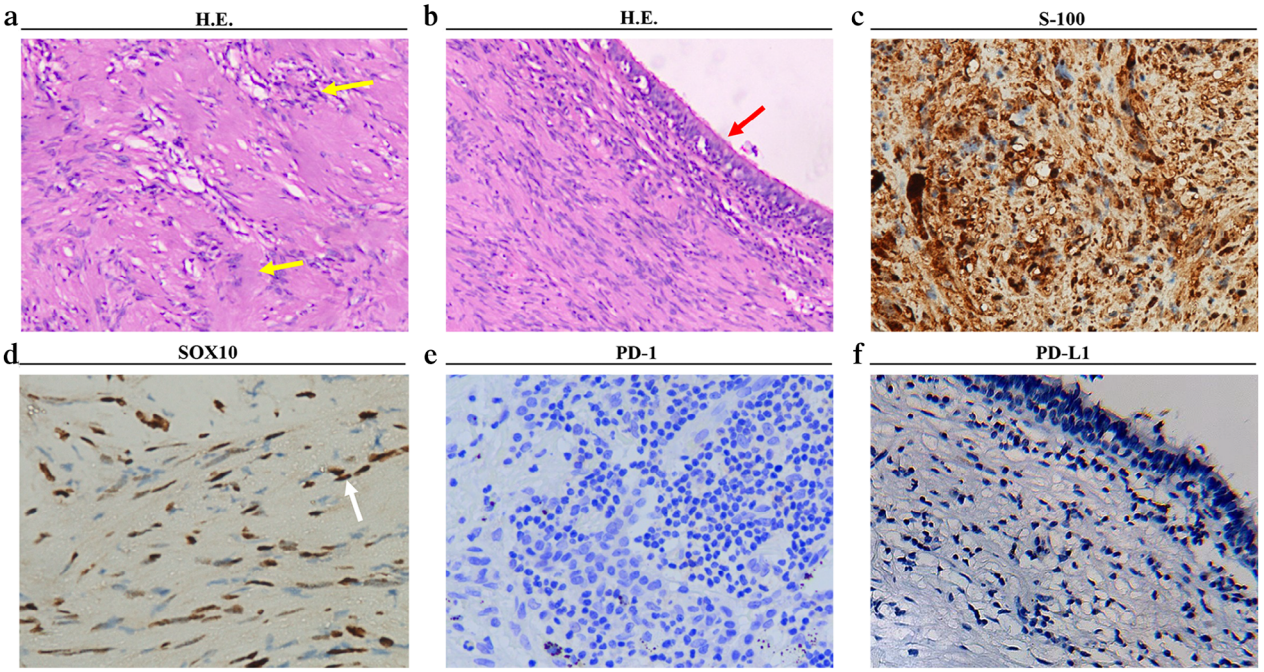

Figure 3 Histopathological characteristics of the bronchial schwannoma. (**a**) Typical spindle cells are arranged in Verocay bodies with nuclear palisading (yellow arrows). (**b**) The tumor is covered with ciliated airway epithelium lining (red arrows). ABC immunostaining shows tumor cells positive for S-100 (**c**) and SOX10 (**d**, white arrow), but negative for PD-1 (**e**) and PD-L1 (**f**). Magnification × 200. ABC, avidin-biotin complex; PD-1, programmed cell death protein 1; PD-L1, programmed cell death protein-ligand 1.

up to 17.3.[8] Our report of bronchial schwannoma has a SUV_{max} of 8.5, in agreement with others that benign schwannomas may present with high SUV_{max} and mimic malignancy. High SUVs in schwannomas may be attributable to hypercellularity in the Atoni A area or local infiltration of inflammation, the latter was demonstrated in repeat biopsies in this patient. Therefore, SUV value alone in PET-CT scan has limited value in diagnosis of schwannoma. The diagnostic gold standard for bronchial schwannoma is histopathological examination to confirm spindle cells with positive staining for S-100 protein. The postoperative histological examination in this case showed typical features such as spindle cells with a palisading arrangement of the nuclei consistent with Verocay bodies, Antoni A and irregularly spaced Antoni B area. However, schwannomas are typically encapsulated by an outer fibrous sheath of connective tissue. A nonencapsulated schwannoma is more prone to hemorrhage as seen in this patient. The reason(s) for the absence of a capsule is unknown but it has been hypothesized to be related to an origin from autonomic nerves.[9,10] Autonomic fibers from pulmonary plexus descend in parallel to the bronchial tubes to stimulate bronchial smooth muscle cells and submucosal glands to cause airway bronchoconstriction and mucus production. Indeed, pulmonary schwannomas cases mainly located centrally in trachea and main bronchi, rarely appeared in lung parenchyma.[11,12] This may suggest autonomic nerve origins for pulmonary schwannomas.

In normal adult tissue, PD-L1 constitutively expresses in normal schwann cells of peripheral nerve bundles and diffuse cytoplasmic PD-L1 expression was found in 89% of peripheral schwannomas.[13] Normal lung parenchyma lacks PD-L1 expression, while lung carcinomas express varying levels of PD-L1.[13,14] However, PD-1/PD-L1 expression has never been examined in pulmonary schwannomas. Given the recent use of immune checkpoints inhibitors, as well as different levels of PD-1/PD-L1 expression in schwannomas in different organs, we were intrigued to investigate PD-1/PD-L1 pathway in this patient. Surprisingly, PD-1/PD-L1 immunoreactivity was negative for this tumor suggesting that potential adjuvant treatment with immune checkpoints inhibitors would not have been useful in this particular case.

In summary, we present a case of PD-1/PD-L1 negative schwannoma whose initial presentation and PET scan was suggestive of a bronchial malignant tumor. The mass was confirmed as a benign schwannoma only after surgical resection allowed adequate histopathological diagnosis. Histological characterization with molecular markers indicates novel pathological characters. This case raises awareness that schwannomas should be considered in the differential diagnosis of lung neoplasm because nonsurgical options and novel targeted molecular drugs may exist.

Disclosure

The authors declare that they have no competing interests.

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