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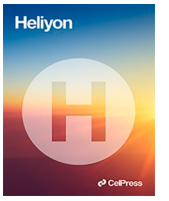

Pulmonary primary meningioma: A report of two cases and review of the literature

Xibo Liu [a,1], Xia Xu [b,*,1], Yi Zou [b]

[a] Department of Pathology, Shaoxing People's Hospital, No. 568, Zhongxing North Road, Shaoxing, Zhejiang, 312000, China
[b] Department of Pathology, The Second Affiliated Hospital of Zhejiang University School of Medicine, No. 88, Jiefang Road, Hangzhou, Zhejiang, 310009, China

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ABSTRACT

Introduction: Primary pulmonary meningioma (PPM) is rare, mostly asymptomatic, and difficult to recognize preoperatively. In this report, we describe two new cases of PPM and provide an updated review of the literature to enhance our understanding of PPM.

Case presentation: The first patient was a 53-year-old woman with an asymptomatic solitary pulmonary nodule in the right lower lobe on chest computed tomography (CT). Wedge resection of the right lung was performed and histological features of benign PPM were pathologically confirmed, which was further supported by immunohistochemistry. The second patient was a 63-year-old man who had a left pulmonary nodule during routine physical examination. CT revealed a solid nodule in the outer basal segment of the left lower lobe. The patient underwent a wedge resection of the left lower lobe and mediastinal lymph node dissection. Postoperative pathology confirmed the presence of two tumors: one adenocarcinoma and one PPM. Both cases were confirmed to be benign PPM (grade I) by pathological examination, with histological subtypes of fibrous and psammomatous.

Conclusions: Radiological imaging is crucial for the early detection of PPM, while pathological examination is necessary to confirm the diagnosis. Surgical treatment is recommended, and intraoperative frozen sections are essential for determining the extent of the operation.

1. Introduction

Meningiomas are the most frequently occurring primary tumors of the central nervous system (CNS) and comprise more than one-third of all primary CNS tumors [1]. They rarely appear in extracranial and extraspinal organs but commonly in the head, neck, skin, and peripheral nerves [2]. Since the first description by Kemnitz et al., in 1982 [3], fewer than 60 cases of primary pulmonary meningioma (PPM) have been reported in English literature over the past four decades. Except for isolated "coin lesions" visible on imaging [4], PPM typically presents as asymptomatic or with nonspecific respiratory symptoms, making correct diagnosis difficult before surgery and leading to the misdiagnosis of metastases [5]. This article presents two new cases of incidental PPM, along with a review of the literature to provide a better understanding of PPM.

* Corresponding author.
E-mail address: xuxia12345@zju.edu.cn (X. Xu).
[1] Xibo Liu and Xia Xu have the same contribution to this paper.

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2. Case presentation

2.1. Case 1

In December 2016, a 53-year-old Chinese woman was admitted to the hospital because of a nodule in her right lung that was discovered during a routine health examination at a local hospital ten days prior. The patient reported no respiratory symptoms and was otherwise healthy. She had no family history of hereditary diseases or tumors. A physical examination revealed no significant findings. A computed tomography (CT) scan indicated a small, 6 mm nodule in the dorsal segment of the right lower lobe, with a clear boundary and visible calcification (Fig. 1a and b). Two days later, the patient underwent thoracoscopic wedge resection of the dorsal segment of the right lower lung. An intraoperative frozen pathological examination was conducted, and the initial diagnosis was a spindle cell tumor in the dorsal segment of the right lower lobe, suspected to be a solitary fibrous tumor or meningioma.

Gross examination revealed a nodule with a diameter of 1.1 cm and a well-circumscribed boundary under the pleura of the lung. The cut surface was grayish-white in color and hard in texture. Microscopic examination indicated that the tumor was composed of spindle cells of moderate to high density. Spindle cells had elongated nuclei, forming parallel or striated fascicles. Abundant collagen fibers were intertwined with tumor cells. Additionally, psammomatous calcification and nodules of epithelioid cells were occasionally observed (Fig. 2a and b). Immunohistochemistry revealed positive staining for β-catenin, CD56, EGFR, PR and CD117. Locally positive staining for CD10, EMA, and S100 and weakly positive for P53 were also observed. Ki-67 demonstrated a low proliferative index (Fig. 2c, d, and S1). However, the tumor cells were negative for CD34, CD99, AE1/AE3, ER, TTF-1, STAT6 and SOX10. The postoperative pathological diagnosis was primary pulmonary meningioma, fibrous, grade I. The postoperative magnetic resonance imaging (MRI) scans of the head showed no evidence of primary CNS meningiomas. The patient was in good physical condition five years after surgery.

2.2. Case 2

In October 2020, a 63-year-old Chinese man was admitted to the hospital because a left pulmonary nodule was found during routine physical examination more than a month ago. He lost 5 kg of weight within 10 months and requested further examination. He did not experience any significant respiratory discomfort, although he had a history of hypertension for over 5 years and had been a smoker for 30 years, smoking approximately 20 cigarettes per day. Additionally, he had been drinking moderately for 30 years, but this did not affect his daily life or work.

Chest CT showed a solid nodule in the outer basal segment of the left lower lobe, measuring approximately 10 mm◊8 mm in size (Fig. 3a and b). Brain CT and MRI showed no space-occupying lesions. The patient underwent surgery a few days after admission. During the surgery, two nodules were found in the left lower lung, and the frozen section of each nodule was examined. The pathological report identified the first nodule as adenocarcinoma and the second nodule as nodular hyperplasia of epithelioid cells with psammoma. Consequently, the patient underwent thoracoscopic wedge resection of the left lower lobe and mediastinal lymph node dissection.

On the gross examination, 2 Gy-white nodules were observed on the cut surface, measuring 0.8 cm ◊0.6 cm and 1 cm◊0.7 cm respectively. The distance between them was 0.5 cm, and the latter was adherent to the visceral pleura. On microscopic examination, the first nodule was diagnosed as adenocarcinoma, whereas the second nodele showed characteristics of meningioma, psammomatous, and grade I. The second nodule exhibited numerous psammomas and spiral lesions composed of spindle cells and nests of meningeal epithelial cells that lacked nuclear atypia and mitosis. Atypical glandular epithelial cells were also observed around the second nodule (Fig. 4a and b). Immunohistochemically, the second nodule showed positive reactions for EMA, SMA, PR, and SSTR2 (Fig. 4c–f), and

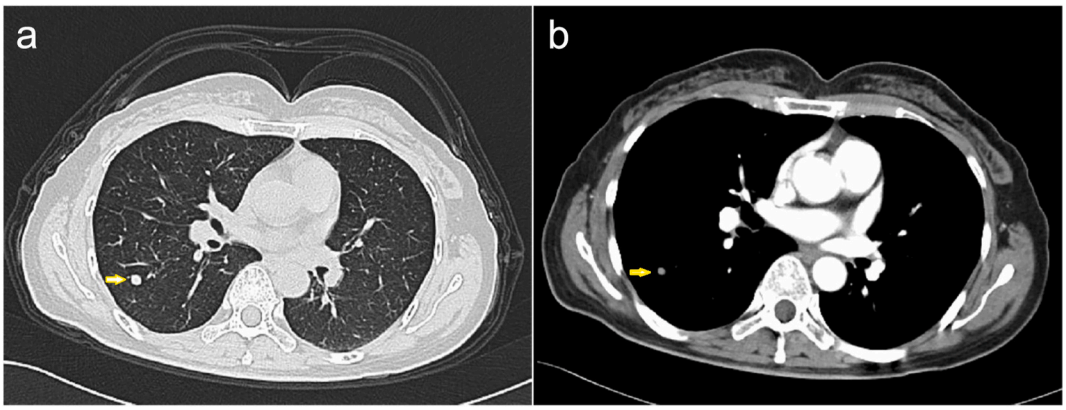

Fig. 1. CT scan of the primary pulmonary meningioma in Case 1. An enhanced spiral CT scan of the chest revealed a single nodule 6 mm in diameter in the dorsal segment of the right lower lobe, with a solitary, well-circumscribed margin and calcification (yellow arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

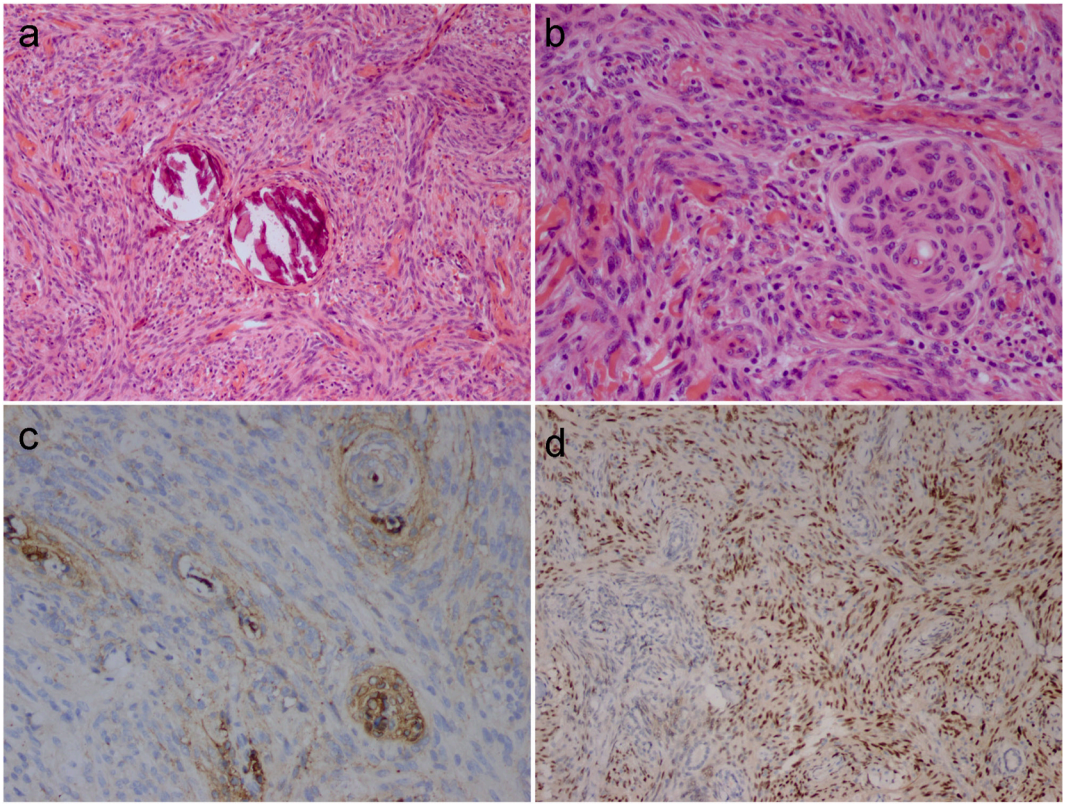

Fig. 2. Histological and immunohistochemical examination of the primary pulmonary meningioma in case 1. (a) The tumor is composed of spindle cells, forming storiform and interlacing bundlesand structures, with multifocal psammomatous calcifications. HE, × 100. (b) Occasionally, epithelioid cells formed whorls. HE, × 200. Immunohistochemical staining of the tumor cells in case 1 was positive for EMA (c, × 200) and PR (d, × 100).

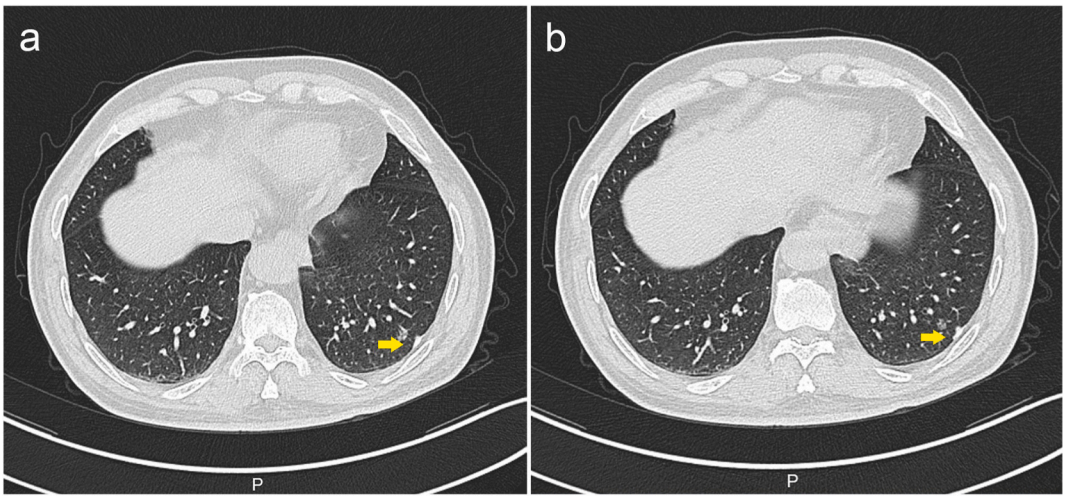

Fig. 3. CT scan revealed a solid nodule in the outer basal segment of the left lower lobe in Case 2, with a size of approximately 10 mm × 8 mm (yellow arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

sporadic positive expression of P53. STAT6, CD34, S-100, and SOX10 were negative. The proliferation index of Ki-67 was low. The patient was diagnosed with adenocarcinoma in the first nodule without lymph node metastasis and meningioma, psammomatous, and grade I in the second nodule. Two years later, the patient was in good physical condition.

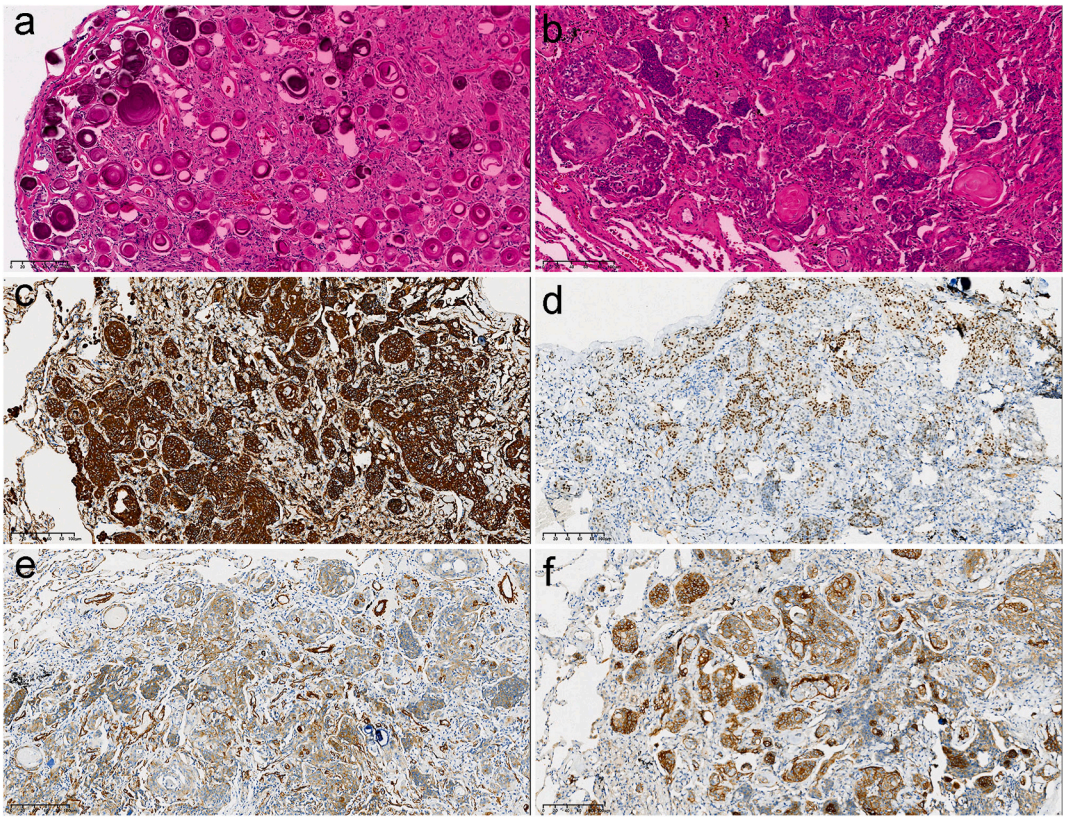

Fig. 4. Histological and immunohistochemical examination of the primary pulmonary meningioma in case 2. (a) There are numerous psammoma bodies on the pleural side of the nodule. (b) There are numerous nests of epithelioid cells in the nodule adjacent to the lung forming a whorl structure. Immunohistochemical staining was positive for vimentin (c), PR (d), SMA (e), and SSTR2 (f).

3. Discussion and conclusions

Central nervous system (CNS) meningiomas are common primary intracranial tumors believed to originate from arachnoid cap cells [6]. Pulmonary meningiomas are identical to meningeal (arachnoid) cell tumors, which typically arise from the dura mater of the CNS but without significant lesions in the CNS. PPM has no specific anatomical site preference and is slightly more common in females with a median age of 56 years. Most cases are incidental, although some patients may present with respiratory symptoms, including hemoptysis [7]. The pathogenesis of PPM remains unknown. The origin of PPM has been suggested to be either the proliferation of ectopic embryonic nests of arachnoidal cells or minute pulmonary meningothelial-like nodules (MPMN) [8,9]. Another theory suggests that the histological origin of PPM is pluripotent subpleural mesenchyme [10]. MPMN is similar to the PPM but differs in size [9]. Morphological and immunostaining studies have revealed similarities between normal arachnoid cells and meningioma cells [11]. MPMN and PPM are related lesions that may arise from the same precursor cells [4]. No mutations were found in solitary meningioma nodules, whereas multiple meningioma nodules showed increased genetic alterations, indicating a transition to tumorigenesis [7].

Imaging examinations are important for detecting pulmonary meningioma; however, for an accurate diagnosis, pathological examination is required. Benign PPMs exhibit consistent histopathology and immunophenotypes that closely resemble their benign primary intracranial counterparts. These benign PPMs can be multiple and show no malignancy after 20 years of follow-up [12]. If malignant or atypical PPM is suspected, it must be differentiated from benign PPM. However, there are no specific histopathological guidelines for the diagnosing malignant lung PPM. In such cases, it is recommended to refer to the diagnosis and grading of CNS meningioma [1].

Immunohistochemical staining can be used to verify the diagnosis of PPM and rule out any lung tumors that resemble it histologically. The positive expression of Vimentin, EMA, PR and CD56 can aid in diagnosis of PPM [9]. Recent research have confirmed that SST2A is a more effective immunostaining target [13]. Benign meningioma has a lower MIB-1 (Ki-67) proliferative index, and evaluation of Ki-67 proliferation can have prognostic significance in meningiomas [14].

This study revealed, for the first time, positive expression of β-catenin and EGFR in PPM. Previous research on CNS meningiomas has suggested that the expression level of β-catenin correlates with meningioma grade, and is significantly reduced in atypical or malignant meningiomas [15]. EGFR has been associated with the grade of CNS meningiomas, with expression levels in grade I being higher than in grades II and III [16]. S-100 has been reported to be predominantly negatively expressed in PPMs, but up to 70% of fibrous meningiomas are positive [17]. The patchy expression pattern of CD10 may reflect the distribution of clear cells in

meningiomas [18]. Although both calretinin and CD117 are generally negatively expressed [19], case 1 in this study showed positive expression of both. In the CNS, most meningiomas exhibit allelic loss and NF2 mutations on chromosome 22. However, due to limitations in research conditions, relevant molecular detection was not performed in two of the cases in this study.

To prevent misdiagnosis, pathologists should have a thorough understanding of the essential characteristics of the pathological diagnosis. The main pathognomonic features of PPMs are circumscribed solid proliferation of tumor cells that grow in whorls and lobular nests, most commonly transitional or fibrous. They lack a major stromal or perivenular distribution, with ill-defined borders. PPMs also exhibit histological and immunohistochemical features of CNS meningiomas, without evidence of CNS meningiomas. Their sizes were generally greater than 4 mm [7].The differential diagnosis of PPM includes various primary and metastatic spindle cell tumors in the lungs. CT or MRI of the brain and spinal cord are necessary to exclude pulmonary metastases from CNS meningiomas [20]. Immunohistochemistry can be safely used to differentiate PPM from morphologically similar tumor such as schwannoma, solitary fibrous tumour (SFT), sclerosing pneumocytoma, pulmonary chemodectoma/neuroendocrine tumor, mesothelioma, thymoma, and carcinoma [20]. SFT expresses CD34 and nuclear STAT6 but not EMA. EMA and TTF1 were positive in the surface and round cells of sclerosing pneumocytoma. Pancytokeratin, CAM5.2, CK7 and Napsin A diffused to the surface cells; however, round cells were usually negative or weakly positive. Pulmonary chemoreceptor tumors/neuroendocrine tumors express neuroendocrine markers such as CgA and Syn. Mesothelioma expresses keratin, mesothelial markers, and GATA3. Type A thymoma expressed p63/p40. Carcinoma always exhibit variable atypia and keratin expression.

Both patients expressed satisfaction with the effectiveness of their treatments. The first patient underwent a chest X-ray examination the year after discharge, which did not reveal any abnormalities. For the second patient, regular outpatient follow-ups were conducted after discharge, with the latest chest CT examination performed in June 2022 revealing no signs of tumor recurrence. Despite being diagnosed with adenocarcinoma in one patient at the time, both patients are currently in good health.

To summarize, PPM is a rare and mostly asymptomatic benign lung tumor. Early detection of PPM relies on radiological imaging, and its diagnosis must be confirmed through pathological examination. If a well-circumscribed nodule is found in a patient's lung, biopsy should be performed to avoid unnecessary chemotherapy. Surgery is the recommended treatment for PPM, with wedge resection being a reasonable approach. Intraoperative pathological examination is critical for determining the scope of surgery and avoiding unnecessary lobectomy in patients with benign peripheral PPM.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed consent was obtained from the patients for publication of this report and accompanying images.

Authors' contributions

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e16705.

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