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Case report

Primary pulmonary meningioma mimicking a carcinoid tumor in a middle-aged female

Federica Pezzuto, Chiara Giraudo, Matteo Baldi, Andrea dell'Amore, Fiorella Calabrese

University of Padova, Medical School, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, Padova, Italy

Summary
A 46-year-old female complained of cough and dyspnea. A chest X-ray and CT scan showed a solitary subpleural pulmonary nodule in the left upper lobe. Surgical resection was performed. The frozen examination was presumptive of a benign/low grade lesion, likely a carcinoid. Definitive histology revealed uniformly sized eosinophilic cells arranged in solid nests, immunoreactive for epithelial membrane antigen and progesterone receptors. The diagnosis of grade 1 meningothelial meningioma was finally achieved. This case of a meningioma mimicking a carcinoid tumor highlights its rarity and warns diagnostic specialists of the potential for misdiagnosis and overtreatment.

Key words: meningioma, primary pulmonary meningioma, carcinoid tumor

Case summary

A 46-year-old female was admitted to our hospital due to cough and dyspnea. She underwent a chest X-ray which demonstrated a well-defined opacity in the left upper lobe. A whole-body computed tomography (CT) confirmed the presence of a solitary, subpleural pulmonary nodule of 22 mm, with homogeneous contrast enhancement (Fig. 1A). The lesion demonstrated high ^{18}F-fluorodeoxyglucose uptake (SUV max 4.3) at the PET/CT (Fig. 1B). No pathological mediastinal and/or hilar lymph nodes were detected. Based on the characteristics at imaging, the patient underwent surgery. The frozen examination of the specimen showed small, uniformly sized cells with eosinophilic cytoplasm, occasionally fusiform, arranged in solid nests, separated by collagen bundles (Fig. 1C, D). The tumor exhibited low mitotic activity and mild atypia. The intraoperative diagnosis was presumptive of a benign/low grade lesion (likely carcinoid). Due to the location of the lesion, a lobectomy with hilar and mediastinal lymphadenectomy was performed. At gross examination, the nodular mass measured 26 mm, with a greyish surface and well-defined borders. Histological examination revealed a lobulated architecture (Fig. 2A), with solid whorled nests of small eosinophilic cells, uniformly ovoidal and fusocellular, indistinct membrane borders and isolated syncytial cells (Fig. 2B). Occasional psammomatous bodies were also detected. Immunostainings were negative for cytokeratin and all neuroendocrine markers, and positive for epithelial membrane antigen (Fig. 2C) and progesterone receptors (Fig. 2D). The diagnosis of grade 1 meningothelial meningioma was finally achieved. The patient had a reg-

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Correspondence
Fiorella Calabrese
E-mail: fiorella.calabrese@unipd.it

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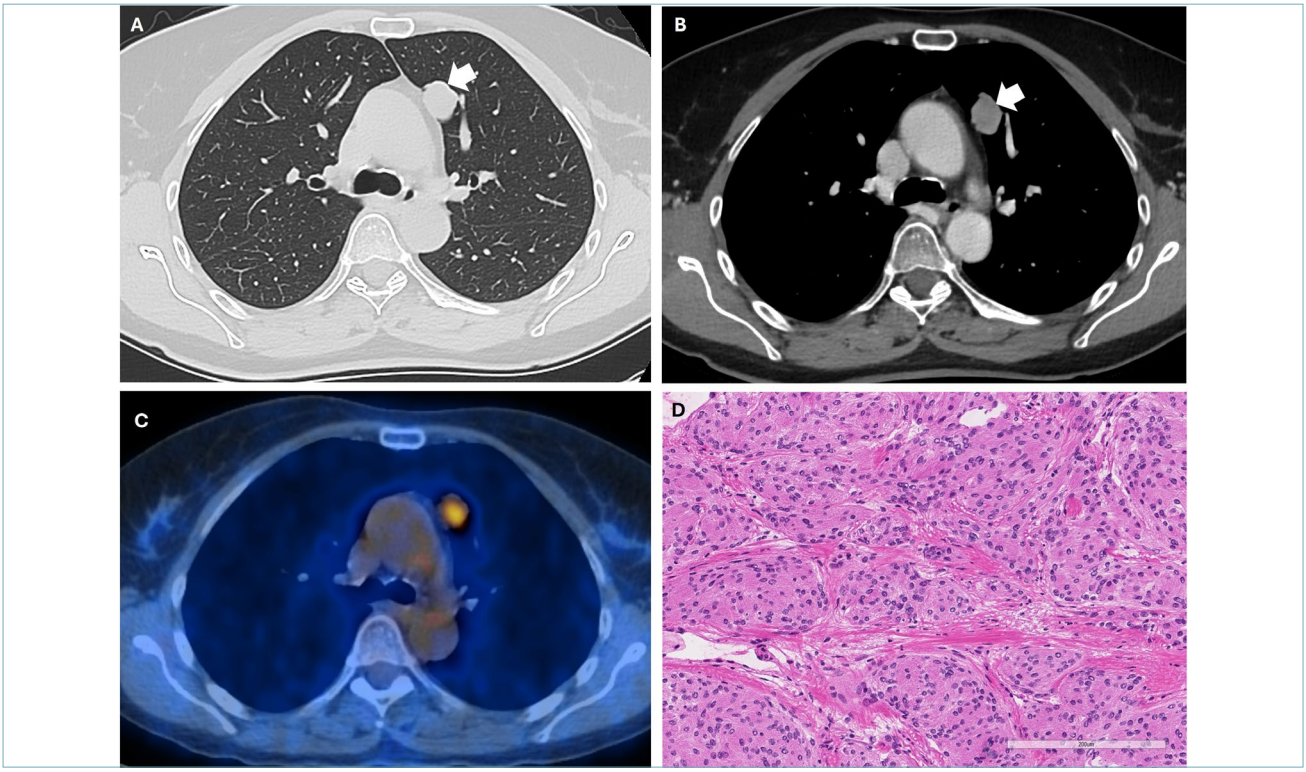

Figure 1. Findings at pre-surgical diagnostic imaging and intraoperative histological features. Axial computed tomography images demonstrating the presence of the subpleural solitary pulmonary nodule in the left upper lobe (arrow, in A) characterized by homogeneous contrast enhancement (arrow, in B). The lesion showed high metabolic activity at 18F-FDG PET/CT performed a few days later (C). Intraoperative examination of the specimen showed clusters of small, uniformly sized cells with eosinophilic cytoplasm, separated by collagen bundles (D, hematoxylin and eosin staining, scale bar: 300 μm).

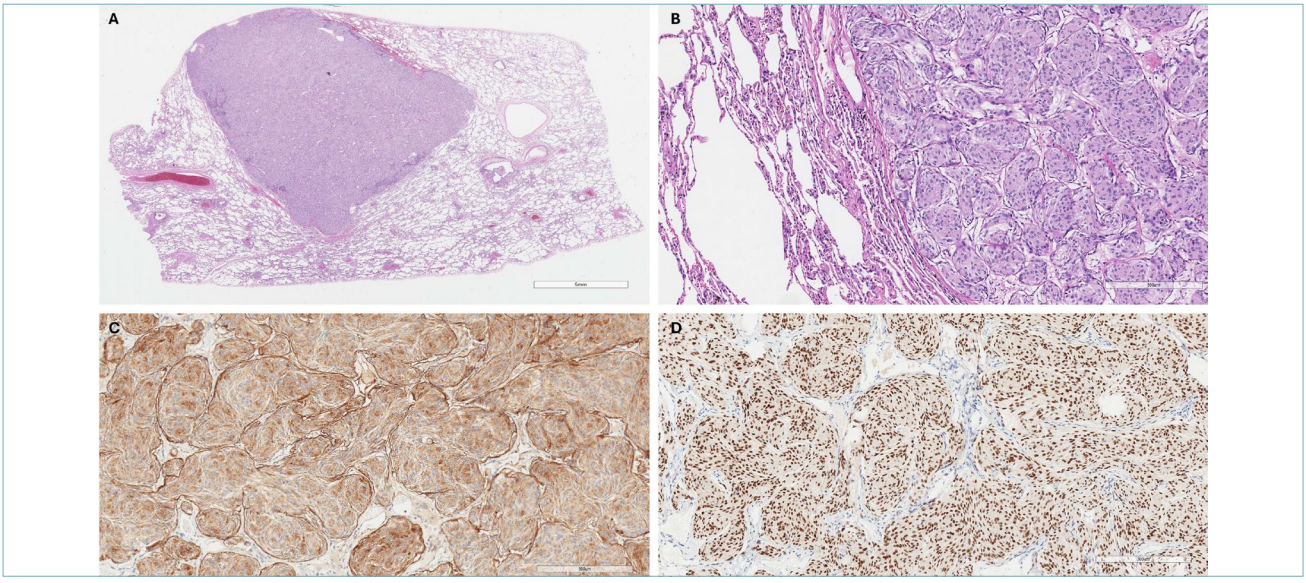

Figure 2. Histological features on FFPE sections. Histological examination demonstrated a well-delimitated mass with lobulated architecture (A, hematoxylin and eosin staining, scale bar: 5 mm). At higher magnification, solid whorled nests of small eosinophilic cells, uniformly ovoidal and fusocellular, with indistinct membrane borders and occasional syncytial cells were detected (B, hematoxylin and eosin staining, scale bar: 300 μm. In the inset, a syncytial cell). Immunohistochemical analysis showed positivity for epithelial membrane antigen (C, EMA immunostaining, scale bar: 300 μm) and progesterone receptors (D, PR immunostaining, scale bar: 300 μm).

ular post-operative course and was discharged after three days. The patient underwent a head and whole-spine magnetic resonance which excluded any other meningioma.

Comment

Meningioma is the most common tumor of the central nervous system, predominantly affecting middle-aged females [1]. According to the WHO, meningiomas are classified in three groups with grade 1 the most common [1]. They can also arise in ectopic sites but rarely occur in the lungs [2]. Patients are usually asymptomatic or complaining of mild respiratory symptoms [2]. The tumor can cause partial airway obstruction and compression, resulting in reduced ventilation and triggering a cough. Additionally, the presence of the tumor likely induces local inflammation, leading to irritation of the airways and pleura, exacerbating respiratory symptoms [2].

Like in our case, primary pulmonary meningioma often appears at imaging as a solitary nodule with homogeneous contrast enhancement and has high metabolic activity; very large lesions have been reported especially in case of a malignant grade [3]. Extracranial meningiomas might be metastases from primary intracranial lesions, usually in cases of advanced disease [4]. Several hypotheses about the origin of ectopic meningiomas have been proposed. It has been suggested that they are due either to ectopic arachnoid cells migrating during embryonic development or to the presence of pluripotent stem cells in extracranial tissues that differentiate into meningioma cells through still unknown mechanisms [4]. A potential role of recurrent genetic mutations and chromosomal abnormalities has also been described [4]. Although histological features and immunophenotype are quite characteristic [1], diagnosing meningiomas in extracranial sites can be challenging.

In the thorax, primary pulmonary meningiomas must be differentiated from several other types of tumors.[2,5] This distinction can be particularly challenging, especially when dealing with small biopsy samples and frozen sections. Schwannomas are nerve sheath tumors that can present similarly to primary pulmonary meningiomas. Histologically, schwannomas are composed of spindle cells arranged in Antoni A (cellular) and Antoni B (less cellular, myxoid) areas, often with characteristic Verocay bodies (palisading nuclei). Immunohistochemically, schwannomas are positive for S-100 protein, which is a crucial marker for identifying these tumors. In contrast, primary pulmonary meningiomas are typically negative for S-100 but positive for epithelial membrane antigen. Solitary fibrous tumors (SFTs) represent another diagnostic challenge. These tumors often show a patternless architecture with a mixture of hypocellular and hypercellular areas, separated by thick bands of collagen. The presence of staghorn blood vessels is a characteristic feature of SFTs. Immunohistochemically, SFTs are usually positive for CD34 and STAT6, which are not expressed in meningiomas. Sclerosing pneumocytomas can also mimic primary pulmonary meningiomas. These tumors often exhibit a combination of solid, papillary, sclerotic, and hemorrhagic patterns, containing both surface cuboidal cells and round stromal cells. Immunohistochemically, sclerosing pneumocytomas typically express TTF-1 and EMA. The presence of these two distinct cell populations is a key feature that helps distinguish sclerosing pneumocytomas from meningiomas, which lack this dual cell population. Pulmonary neuroendocrine tumors, mainly typical and atypical carcinoids, are another important group to consider in the differential diagnosis. These tumors exhibit neuroendocrine morphology, often with organoid nesting, trabecular patterns, and rosettes. Immunohistochemically, they are positive for neuroendocrine markers such as chromogranin, synaptophysin, and CD56. In contrast, primary pulmonary meningiomas do not express these neuroendocrine markers but are positive for EMA and progesterone receptors.

Thymomas can also be misdiagnosed with primary pulmonary meningiomas when they present as anterior mediastinal masses. Histologically, thymomas are characterized by a mixture of epithelial cells and immature T-lymphocytes. Immunohistochemically, thymomas express markers such as cytokeratins, CD3, and Tdt, which are not found in meningiomas.

Meningothelial-like nodules (MLNs) represent another entity to consider in the differential diagnosis of primary pulmonary meningiomas [2]. MLNs are small, incidental nodules usually found during autopsy or in resected lung specimens. They are benign proliferations of meningothelial cells that can resemble meningiomas microscopically [2]. Histologically, MLNs appear as well-circumscribed nests of epithelioid cells with oval nuclei and a syncytial arrangement, like meningothelial meningiomas [2]. Immunohistochemically, they express markers such as EMA and vimentin [2]. The pathogenesis of MLNs remains speculative, but several hypotheses have been proposed [6]. One hypothesis suggests that MLNs may originate from misplaced embryonic arachnoid cells, similar to ectopic meningiomas, during early development [7]. Alternatively, these nodules may arise from mesothelial or submesothelial cells that undergo metaplasia, differentiating into meningothelial-like cells [8]. Chronic inflammation or recurrent injury to the lung parenchyma may play a role in stimulating this differentiation process [9]. They

can be considered as a reactive process in response to local injury or inflammation, where pluripotent stem cells in the lung tissue differentiate into meningothelial-like cells as part of a reparative mechanism [9].

Avoiding an erroneous interpretation of tumors as having an excessively aggressive form is important for managing patients correctly. Indeed, while primary pulmonary meningiomas have already been described in the literature [1], this case emphasizes the practical challenges in diagnosing this rare tumor. In reporting this case of a meningioma mimicking a carcinoid tumor, we would like to highlight its rare occurrence and alert specialists involved in the diagnostic procedures to this possible unexpected pitfall that might lead to potential overtreatment when a malignant neoplasia is suspected.

Conflicts of interest statement

The authors declare they have no conflict of interest.

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Authors' contributions

FP drafted the article. FP, FC performed histological examination. AD, MB, CG performed the operation and acquired the clinical data. FP, FC critically read and revised the article. All authors approved the final version of this article for publication.

Ethical consideration

The study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient.

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