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Endometrioid Carcinoma Metastasis and Minute Pulmonary Meningothelial-Like Nodules in the Lung: A Case Report

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Abstract:

Minute pulmonary meningothelial-like nodules (MPMN) are rare pulmonary lesions characterized by the proliferation of cells showing meningothelial differentiation and are most commonly detected incidentally. Their coexistence with pulmonary metastases is uncommon. We report a case of metastatic endometrioid carcinoma of the lung associated with incidentally identified MPMN. A 60-year-old woman with a history of endometrioid carcinoma presented with a soft tissue density lesion measuring 38×42 mm with ill-defined margins, causing mild narrowing of the right upper lobe bronchus on computed tomography. Surgical resection of the lung mass was performed. Intraoperative frozen section examination revealed a malignant epithelial neoplasm consistent with adenocarcinoma. On permanent sections, histopathological evaluation demonstrated an epithelial tumor composed of complex and cribriform glandular structures within a desmoplastic stroma, accompanied by loss of polarity and nuclear enlargement, consistent with metastatic endometrioid carcinoma. In the wedge resection specimen obtained after frozen section examination, multiple microscopic lesions were identified in the non-neoplastic lung parenchyma. These lesions consisted of bland cells with round to ovoid nuclei arranged in whorled patterns along the alveolar septa. Immunohistochemical analysis supported the diagnoses of metastatic endometrioid carcinoma and MPMN, respectively. Based on the histopathological, immunohistochemical, and clinical findings, the mass lesion was diagnosed as metastatic endometrioid carcinoma, while the incidental parenchymal lesions were diagnosed as MPMN. To our knowledge, coexistence of MPMN with metastatic endometrioid carcinoma is exceedingly rare and not well documented in the indexed English-language literature.

Keywords: Endometrioid Carcinoma, Minute Pulmonary Meningothelial-Like Nodules, Pulmonary Metastases

Minute pulmonary meningothelial-like nodules (MPMN), lesions formed by the proliferation of meningothelial-origin cells in the lung, may occasionally be observed. These benign lesions were described approximately six decades ago and are usually detected incidentally in autopsy series or surgical specimens [1].

In many retrospective studies, the most common malignant entity associated with MPMN is primary lung carcinoma [2, 3]. However, the lesions may also, though less frequently, accompany pulmonary metastases. The existing literature on MPMNs

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associated with metastatic tumors remains limited [3, 4]. By defining the current knowledge gap, this case aims to provide further context to the literature. We consider it noteworthy to present this case involving the coexistence of metastatic endometrioid carcinoma and incidentally detected MPMN in the lung.

CASE PRESENTATION

A 60-year-old woman with a history of endometrioid carcinoma diagnosed two years earlier was evaluated for a pulmonary lesion detected during routine follow-up. The patient's medical history was significant for diabetes mellitus, hypertension, and a remote history of surgery for endometriosis. Her primary malignancy had been staged as FIGO Grade 2, Stage IB, characterized by more than 50% myometrial invasion. She had previously completed adjuvant brachytherapy for this primary tumor. Non-contrast computed tomography (CT) of the chest revealed a 38×42 mm soft tissue density lesion with indistinct margins in the right upper lobe, causing mild stenosis of the right upper lobe bronchus (Figure 1). Additionally, the Positron Emission Tomography-Computed Tomography (PET-CT) performed on the patient was reported as showing a hypermetabolic soft-tissue mass in the anterior segment of the right upper lung lobe, obliterating the upper lobe bronchus; tissue diagnosis is recommended.

Surgical lung wedge resection was performed for the pulmonary lesion. Intraoperative frozen section analysis of the mass was reported as 'malignancy consistent with adenocarcinoma.' Subsequent examination of permanent hematoxylin and eosin (H&E) sections revealed an epithelial tumor characterized by a complex, cribriform architecture embedded within a desmoplastic stroma. The neoplastic cells exhibited loss of polarity, nuclear enlargement, and rounding.

Immunohistochemical analysis demonstrated focal positivity for CK7, while CK20, TTF-1, p16, and p53 were negative. The tumor cells showed nuclear expression of ER (40%, weak intensity) and PR (40%, weak intensity) (Figure 2). Evaluation of mismatch repair (MMR) proteins revealed retained expression of MSH2 and MSH6; however, there was a loss of nuclear expression for MLH1 and PMS2.

In the lung wedge resection specimen submitted after the frozen section, multiple microscopic lesions were observed in the tumor-free lung parenchyma. These lesions consisted of bland cells with round to ovoid nuclei arranged in a whorled pattern between alveolar septa, accompanied by edema and congestion; the largest lesion measured 1.5 mm in maximum diameter. Immunohistochemical studies demonstrated positivity

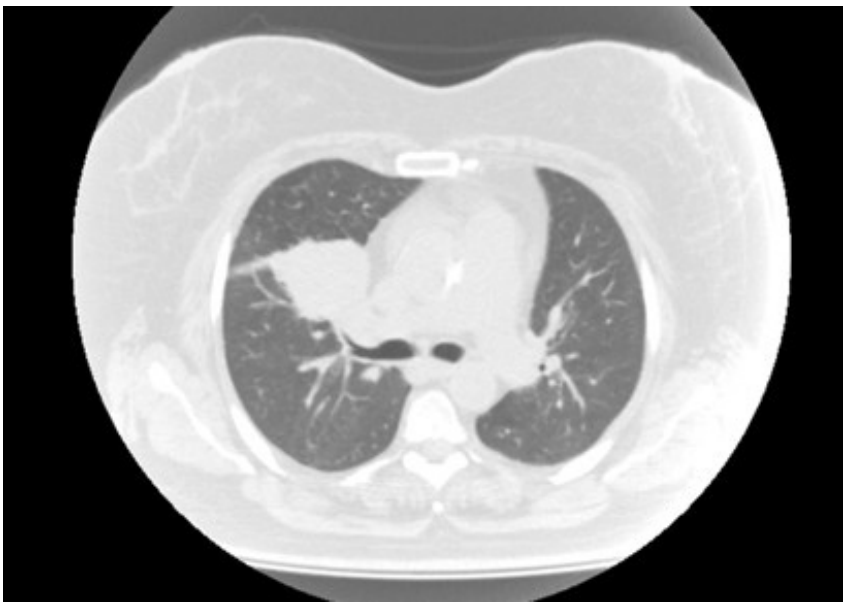

FIGURE 1. Non-contrast computed tomography (CT) of the chest revealed a 38×42 mm mass lesion.

for EMA, PR, and Vimentin, and negativity for S100, Pan-CK, Synaptophysin, Chromogranin, and TTF-1 (Figure 3).

Considering the histopathological and immunohistochemical findings together with the clinical history of the patient, the mass lesion was diagnosed as metastatic endometrioid carcinoma, while the multiple parenchymal nodules were diagnosed as MPMN. The patient received post-operative radiotherapy to the lung and at the 15-month follow-up, the patient showed no radiological or clinical evidence of recurrent or progressive disease.

Written informed consent was obtained from the patient for publication of this case report.

DISCUSSION

MPMN in the lung were first described by Korn *et al*. [1] as "chemodectoma-like tumors," identified in 19 cases among 3,635 autopsy specimens. These nodules are usually detected incidentally, and their reported incidence in autopsy or lung surgical specimens ranges from 0.07% to 13.8%. Notably, retrospective studies specifically conducted to investigate this entity have shown higher detection rates. In published case series, a marked female predominance has been observed [2, 5-7], consistent with the present case, which also involved a female patient.

The etiopathogenesis of MPMN remains unclear. The absence of detectable mutational damage in isolated MPMN may support a reactive origin, distinguishing them from meningiomas [8]. Pulmonary meningiomas can be differentiated from MPMN by their well-circumscribed, solid proliferation pattern, lack of prominent perivenular or interstitial distribution, and size greater than 4 mm [9].

In our case, the largest nodule measured 1.5 mm and did not exhibit a solid proliferative pattern. A distinct form known as diffuse pulmonary meningotheliomatosis, characterized by numerous disseminated bilateral nodules that may mimic interstitial lung disease on imaging, has also been described [10]. In our patient, there was no evidence of bilaterality, and a total of ten meningothelial-like nodules were identified within the lung parenchyma.

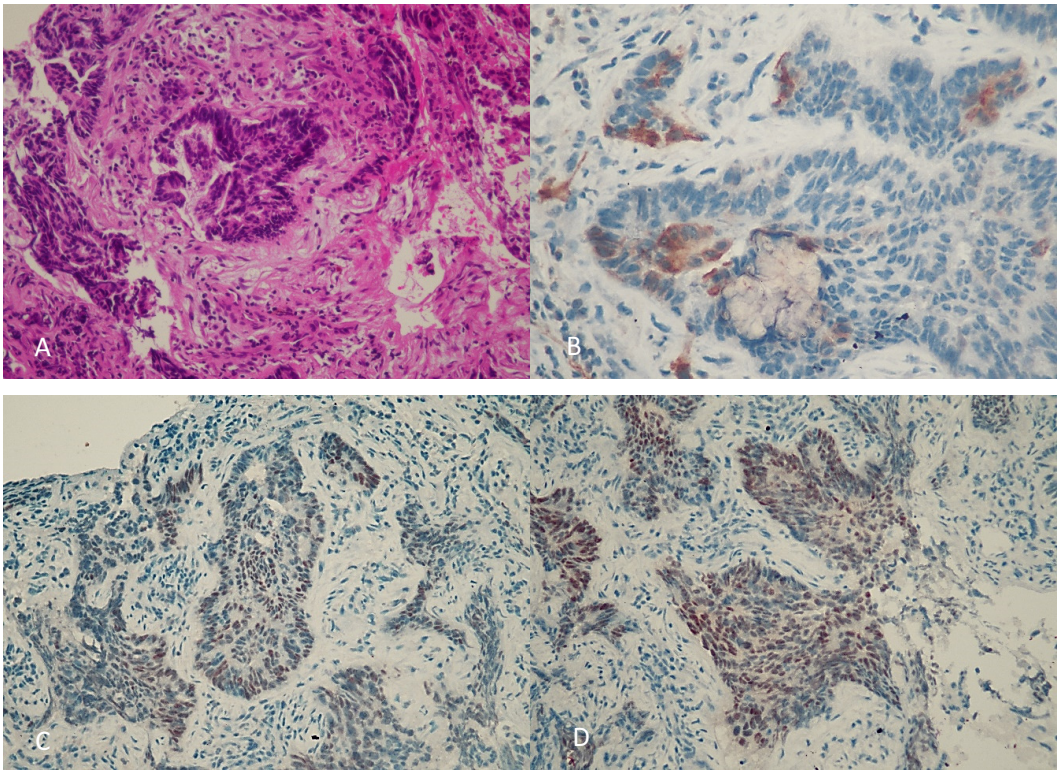

FIGURE 2. (a) Metastatic endometrioid carcinoma in the lung, H&E, ×200; (b) Focal CK7 positivity, ×200; (c) ER positivity, ×200; (d) PR positivity, ×200.

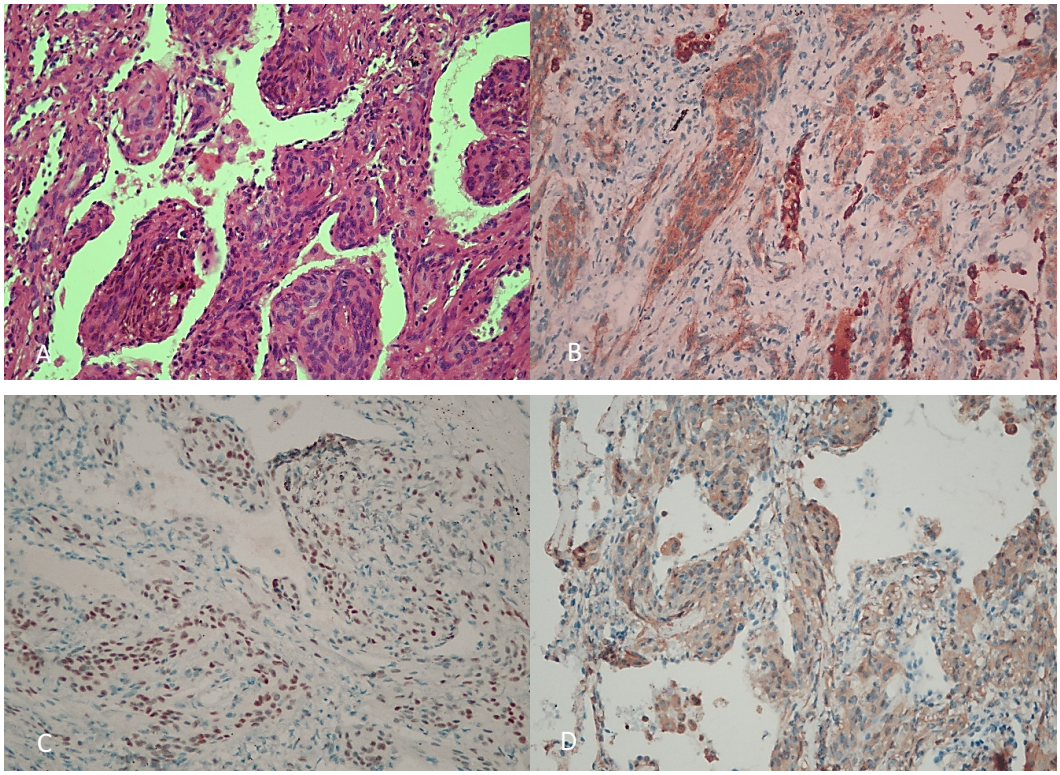

FIGURE 3. a) Meningothelial cells exhibiting a whorled pattern, H&E ×200; (b) Epithelial membrane antigen (EMA) positivity, ×100; (c) Progesterone receptor (PR) positivity, ×200; (d) Vimentin positivity, ×200.

Radiologically, MPMNs are rarely detected and are usually identified incidentally. On CT, they may present as ground-glass opacities or, less commonly, as semi-solid or solid nodules. Establishing a diagnosis of MPMN based solely on imaging findings appears to be quite challenging [11]. In our case, no nodules were detected radiologically in the preoperative evaluation. MPMN may appear as either single or multiple lesions [3-5]. In our patient, the nodules were multiple.

Although MPMNs have been reported in association with both primary pulmonary and metastatic malignancies, the available literature suggests that their coexistence with metastatic carcinomas is considerably less well characterized than with primary lung neoplasms. Previous series have documented occasional associations with metastatic tumors, including colorectal, breast, and unspecified metastatic carcinomas [3-5]. However, compared with the relatively frequent coexistence reported with primary lung adenocarcinoma, metastatic lesions appear to represent a distinctly less common setting. In the seven-case series reported by Wang *et al*. [12], lung adenocarcinoma was the most frequently associated malignancy. Similarly, Li *et al*. [13], in their study comprising 167 cases of minute meningothelial-like nodules and 13 cases of diffuse pulmonary meningotheliomatosis, found that the majority of cases were associated with lung adenocarcinoma, whereas no coexistence with metastatic carcinoma was identified. These findings suggest that MPMNs may have a stronger association with primary pulmonary epithelial malignancies, particularly adenocarcinoma, than with metastatic tumors. In this context, the coexistence observed in our case with metastatic endometrioid carcinoma represents an uncommon and diagnostically noteworthy presentation that further broadens the currently limited spectrum of reported metastatic associations.

These all data suggest that MPMNs may show a stronger association with primary pulmonary epithelial neoplasms than with metastatic tumors.

The histopathological differential diagnosis of MPMN includes tumorlet, carcinoid tumor, and paraganglioma. Compared with MPMN, tumorlets

and carcinoid tumors exhibit an increased nucleus-to-cytoplasm ratio and a characteristic "salt-and-pepper" chromatin pattern. Immunohistochemical staining for synaptophysin and chromogranin may be useful in their distinction. In paraganglioma, the presence of a classic zellballen pattern and S100 positivity in sustentacular cells on immunohistochemical analysis are helpful distinguishing features [13].

In our case, tumorlet and carcinoid tumors were excluded based on histopathological findings along with negative immunoreactivity for Pan-CK, synaptophysin, and chromogranin, while S100 negativity ruled out paraganglioma. Additionally, considering the progesterone receptor positivity observed in this case, endometrioid carcinoma—which may present a diagnostic pitfall—was excluded by the absence of Pan-CK expression. The loss of MMR (mismatch repair) expression was also a feature that supported the diagnosis of endometrioid carcinoma and was observed in the patient's primary endometrial tumor as well.

In this case, immunohistochemical and histomorphological evaluation contributed to establishing the diagnosis of meningothelial-like nodules. In the differential diagnosis, other entities such as myogenic, neural, vascular, PEComa, and primitive respiratory-origin tumors should also be considered. In our patient, both the histomorphological and immunohistochemical findings excluded these differential possibilities. In this context, the coexistence of MPMNs with pulmonary metastasis of endometrioid carcinoma in this case represents a particularly uncommon finding. Given the limited number of previously documented metastatic associations and the apparent predominance of primary lung tumors in the literature, our case expands the existing spectrum of neoplastic conditions associated with MPMNs.

CONCLUSION

In conclusion, MPMN of the lung are rare lesions, even in resection specimens. Although their clinical significance remains unclear, particularly since they are often not radiologically detectable, they should be kept in mind in the histomorphological differential diagnosis. To our knowledge, the coexistence of MPMN with metastatic endometrioid carcinoma is exceedingly rare and not well documented in the indexed English literature.

Ethics Approval and Consent to Participate

Ethics committee approval was not required for this study as it is a single case report. The authors confirm that all procedures were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the principles of the Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Data Availability

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

Authors' Contribution

Study Conception: MK, BBA, ÇÖ; Study Design: MK, BBA, ÇÖ; Supervision: MK, BBA, ÇÖ; Funding: MK, BBA, ÇÖ; Materials: MK, BBA, ÇÖ; Data Collection and/or Processing: MK, BBA, ÇÖ; Statistical Analysis and/or Data Interpretation: MK, BBA, ÇÖ; Literature Review: MK, BBA, ÇÖ; Manuscript Preparation: MK; and Critical Review: MK.

Conflict of Interest

The author(s) disclosed no conflict of interest during the preparation or publication of this manuscript.

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Generative Artificial Intelligence Statement

ChatGPT (OpenAI) was used solely for language translation support in this article. No intellectual content or scientific conclusions were generated by the

tool. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication. The all content of the study was produced by the author(s) in accordance with scientific research methods and academic ethical principles.

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