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Case Report

Unexpected endometrial metastasis of a primary lung adenocarcinoma

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ABSTRACT

Following diagnosis of primary malignancies, subsequent workup includes evaluation for metastasis. Each malignancy, both location and histologic features, have statistically common and less common metastatic patterns. Metastatic lung adenocarcinoma typically involves lymph nodes, liver, brain, and bone. Very rarely can it involve the reproductive tract. Specifically, in females, multiple reported cases include ovarian metastasis. Even rarer, endometrial metastasis, such as this case report, has been reported. Even with usual staging utility of PET/CT, common things remain common; knowledge of common metastatic patterns can bias overall interpretation. This case is a reminder that despite our tendencies to focus on frequent patterns, even the rarest of metastatic patterns are still possible.

1. Case report

A 73-year female without history of malignancy presented to the emergency department for sinusitis. A chest x-ray was obtained and an incidental nodule was detected in the lingula. On computed tomography (CT) follow-up 2 months later, a 1.5 cm lingular nodule was again seen. Subsequent positron emission tomography (PET)/CT confirmed abnormal metabolic activity. An additional focus of radiotracer uptake was noted involving the uterus (Fig. 1). Soon after, the patient reported spotting which prompted further investigation in the setting of aforementioned PET/CT findings. Hysteroscopy was performed approximately 2 months later with excision of pathologically confirmed benign cervical and endometrial polyps. Around that time, bronchoscopy was also performed with unsuccessful biopsy and negative cytology from bronchoalveolar lavage. The patient opted for imaging surveillance despite physician recommendation for CT-guided biopsy.

CT of the chest performed approximately 1 year after initial chest x-ray demonstrated a stable lingular nodule. PET/CT follow-up 6 months later showed increased size of the pulmonary nodule with persistent abnormal hypermetabolic activity (Fig. 1). No abnormal radiotracer uptake was present in the uterus. The patient again opted for imaging surveillance and was recommended to follow up in 4 months.

Follow-up chest CT was performed 8 months later. There was continued growth of the nodule. The patient was then agreeable to a CT-guided biopsy of the nodule. Within the following month, the biopsy was obtained and pathology was

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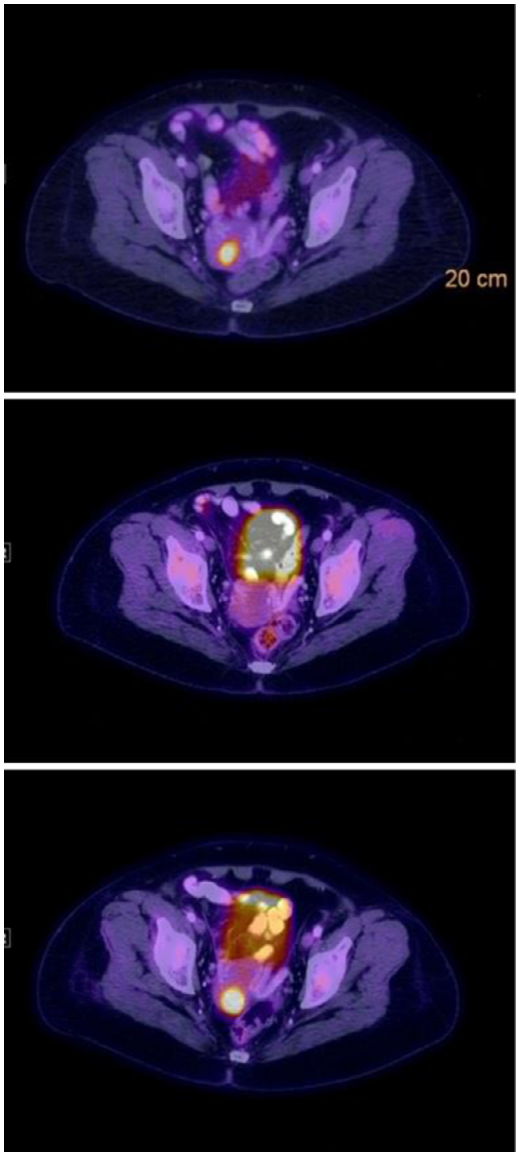

Fig. 1 – *Top:* Axial PET/CT from July 2013 through the level of the uterus demonstrates a hypermetabolic focus within the uterus.
***Middle:* Axial PET/CT from October 2014 through the level of the uterus demonstrates no uterine hypermetabolic focus at a similar slice through the uterus.**
***Bottom:* Axial PET/CT from April 2017 through the level of the uterus demonstrates a hypermetabolic focus within the uterus, similar to PET/CT of July 2013**

consistent with lung adenocarcinoma. Left upper lobe wedge resection was performed with negative margins. Mediastinal lymph node sampling demonstrated no evidence of metastasis. The lung adenocarcinoma was staged as T1a and routine surveillance of the thorax was recommended.

Approximately four surveillance chest CTs were performed throughout the following 20 months without evidence of recurrence. At 20 months post-wedge resection, the patient reported an 8 month history of intermittent spotting. Dilation and curettage of the uterus was performed with pathologic samples demonstrating moderately differentiated adenocarcinoma with a suspicion of a metastasis from patient's known primary pulmonary adenocarcinoma. Further evaluation with PET/CT was performed which once again demonstrated abnormal metabolic activity of the uterus (Fig. 1). A week later, total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed with pathologic samples demonstrating adenocarcinoma which was histologically similar to the previously diagnosed pulmonary adenocarcinoma (Fig. 2). Confirmatory immunohistochemical stains showed reactivity to thyroid transcription factor 1 (TTF-1) and Napsin A with no reactivity to estrogen receptor or PAX-8 (Fig. 3). Immunohistochemical staining findings were consistent with metastatic adenocarcinoma from a lung primary.

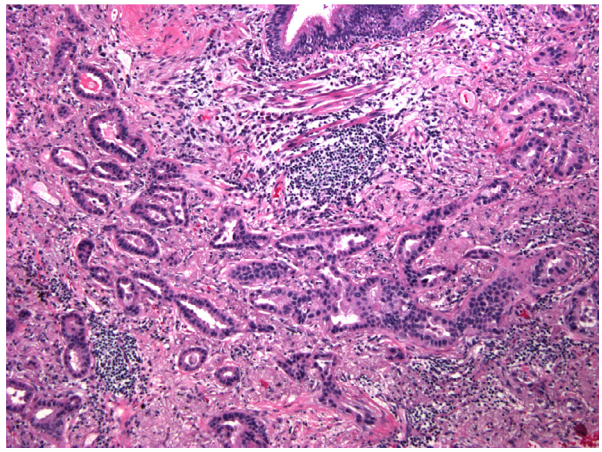

Fig. 2 – Primary adenocarcinoma of the lung (hematoxylin and eosin, original magnification 100×)

Lung adenocarcinoma was upstaged to IV. The patient declined adjuvant chemotherapy and once again opted for imaging surveillance.

2. Discussion

Common metastatic sites for lung adenocarcinoma include lymph nodes, liver, brain, and bone [4]. Nodal metastatic locations include, but are not limited to, hilar, mediastinal, and supraclavicular lymph nodes. Metastasis to the gynecologic tract is rare with several studies showing metastasis to the ovary as well as two cases reporting metastasis to a uterine leiomyoma [5]. On literature review, only four cases were found reporting metastasis to the endometrium [1].

Our case demonstrated a unique characteristic in that the uterus showed abnormal metabolic activity on the initial PET/CT. In the interval time period between the first two PET/CTs, our patient underwent a hysteroscopy and two pathologically confirmed benign polyps were excised. This added an additional alternative explanation to the differences in metabolic activity. Aside from the known possibility of false negative results on a PET/CT, whether it involves the small size of the lesion or its relative proximity to the bladder or bowel,

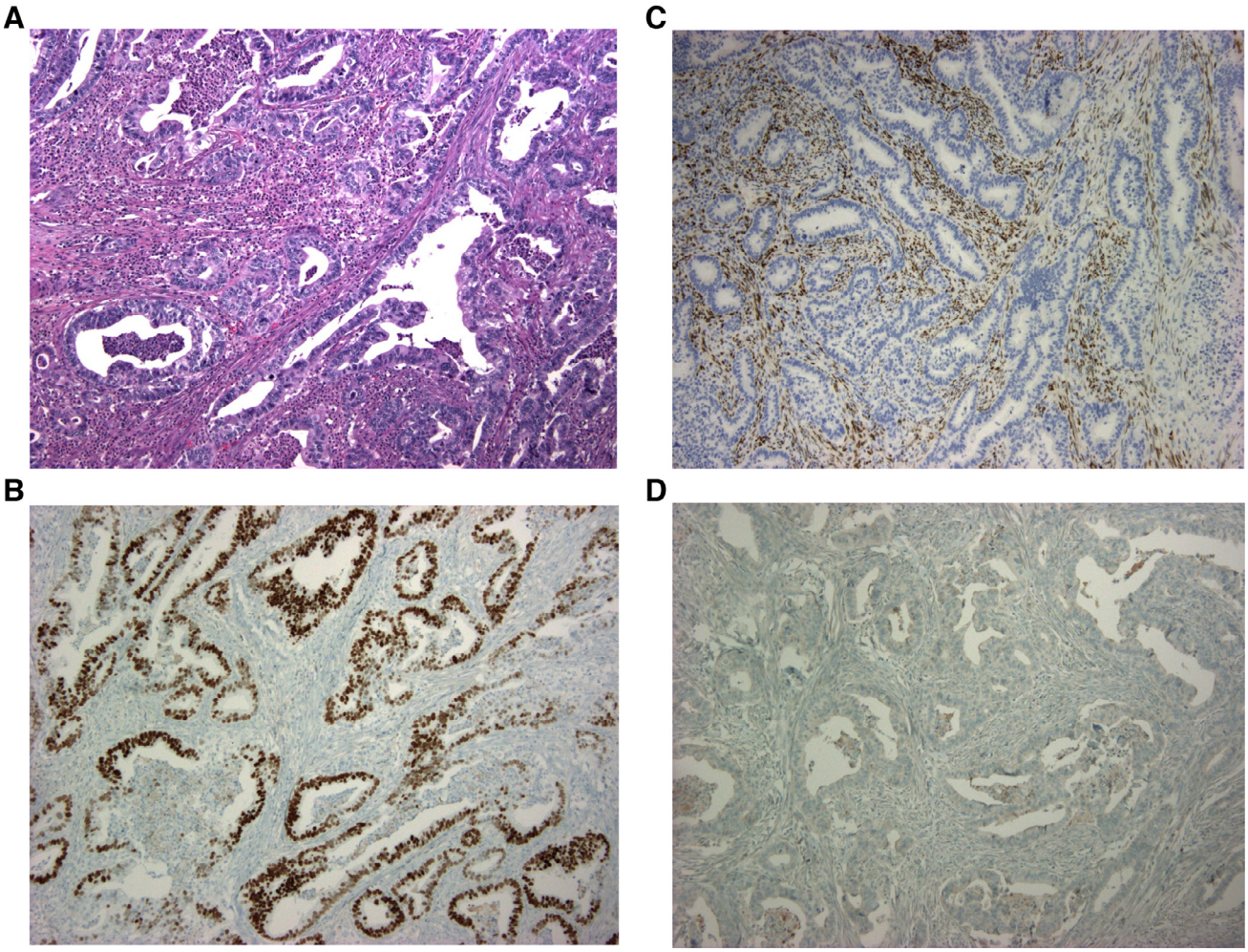

Fig. 3 – (A) Endometrial adenocarcinoma with myometrial invasion (hematoxylin and eosin, original magnification 100×). (B) Tumor cells are immunoreactive for TTF-1 (original magnification 100×). (C) estrogen receptor immunohistochemical stain showing negative staining in the malignant glands while positive in the endometrial stroma (original magnification 100×). (D) PAX-8 IHC stain showing no reactivity in the malignant glands (original magnification 100×)

there is the likelihood that one or both of the polyps may have demonstrated increased metabolic activity [2,3]. Additionally, it is important to remember that since the lung adenocarcinoma was initially staged T1a, adjuvant chemotherapy was not indicated therefore is not considered as a reason for the false negative.

Given the rarity of primary lung adenocarcinoma metastasizing to the endometrium, pathologic confirmation was of the utmost importance. TTF-1 immunoreactivity is used to distinguish adenocarcinoma of the lung from other origins but a small percentage of endometrial adenocarcinomas have shown similar immunoreactivity [8]. Napsin A immunostaining has been found to be more sensitive and specific differentiating lung primary from others [7]. Furthermore, the malignant cells failed to show estrogen receptor immunoreactivity while surrounding endometrial tissue did. Finally, PAX8 expression is seen in carcinomas of Mullerian origin; the absence of PAX8 expression was further confirmation of the lung origin [6].

In all cases of malignancy, it is especially important to identify distant metastasis as it drastically alters staging of the malignancy. While this patient did report postmenopausal bleeding, a hysteroscopy failed to show malignancy. Lung metastasis to the endometrium was not included in the differential of this patient's postmenopausal bleeding given its rarity.

Appropriate imaging follow-up should always be stressed to patients with history of malignancy and questionable PET/CT findings.

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