

Ovarian and Pituitary Metastasis from Adenocarcinoma of the Lung – A Case Report –

Yun Kyung Kang

Department of Pathology, Inje University
Seoul Paik Hospital, Seoul, Korea

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Corresponding Author

Yun Kyung Kang, M.D.
Department of Pathology, Inje University, Seoul Paik
Hospital, 85 Jeo-dong 2-ga, Jung-gu, Seoul 100-032,
Korea
Tel: 02-2270-0153
Fax: 02-2270-0131
E-mail: jadepaka@hanmail.net

Ovarian metastasis as the first manifestation of a lung adenocarcinoma is an exceptionally rare condition and is often difficult to distinguish from primary ovarian carcinoma. Metastatic cancers of the pituitary gland are also very rarely recognized. This case concerns a 30-year-old woman who exhibited a unilateral ovarian mass that was initially diagnosed as a well- to moderately-differentiated mucinous adenocarcinoma. A month later, she was found to have a lung cancer. A year later, she developed a solitary pituitary mass. After immunohistochemical staining for thyroid transcription factor-1 (TTF-1), she was diagnosed with pulmonary adenocarcinoma with metastases to her right ovary and pituitary gland. This could be the first case of primary lung adenocarcinoma metastasis to two unusual secondary sites, the ovary and pituitary gland, without widespread systemic metastasis. In the differential diagnosis of an ovarian adenocarcinoma, metastatic carcinoma from the lung should be considered. Immunohistochemical staining for TTF-1 would be helpful as well.

Key Words : Adenocarcinoma; Lung; Metastasis; Ovary; Pituitary gland

Ovarian adenocarcinoma can be a primary occurrence or a result of metastasis from tumors of mullerian primaries and other sites such as the gastrointestinal tract, breast, pancreas, or appendix. Although metastasis of primary lung carcinoma to the ovary is a rare occurrence, reported cases have recently been increasing with the rising incidence of lung carcinoma in females.¹

Metastatic cancers of the pituitary gland are very rarely recognized clinically. They have been found in only 1% to 3% of patients, even in necropsy series. They are difficult to distinguish from primary pituitary tumors, especially when they are found as a solitary intracranial mass.²

The author presents a case of pulmonary adenocarcinoma metastasis to two unusual sites, the ovary and pituitary gland, without widespread systemic metastasis.

CASE REPORT

A 30-year-old woman was referred to our institution in August 2003 from the local hospital, where she was found to have a right ovarian mass. She had a history of pulmonary tuberculosis when she was 3 years old and was treated with medication for a year. Ten years ago, a pulmonary consolidation was noticed in a chest

radiograph at the local hospital. Subsequent needle biopsy revealed a benign process. Several years ago, she developed allergic asthma and rhinitis, which was managed with medication. She had a smoking history of 2.5 pack year. Her para was 0-0-0-0. She looked relatively healthy, but she complained of coughing, sputum, and hoarseness. Chest X-ray revealed a poorly defined parenchymal consolidation at the anterior segment of the left upper lobe, which was more suggestive of tuberculosis than a neoplastic lesion. Pelvic examination and sonography revealed a right adnexal mass the size of a woman's hand. Laboratory findings included an elevated CA19-9 of 286.9 U/mL, a CEA of 34.8 ng/mL, and normal levels of CA125, β -HCG, and α -FP. The patient underwent a right salpingo-oophorectomy. During the operation, the left ovary and pelvic peritoneum were grossly normal and there was no ascites. Grossly, the right ovary showed an 8.8 × 7.3 cm sized mass, mainly solid and partly cystic. It had a nodular, firm, and partly mucogelatinous cut surface, an intact capsule, and patchy areas of hemorrhage (Fig. 1A). Microscopically, the tumor showed acinar or cribriform architecture. The tumor cells showed complex gland architecture, cytoplasmic mucin, stromal invasion, and several foci of lymphatic invasions (Fig. 1B). They were diffusely positive for CEA (II-7, Dako, Glostrup, Denmark), CA19-9 (1116-NS-19-9, Signet, Dedham, MA, USA), CK-7

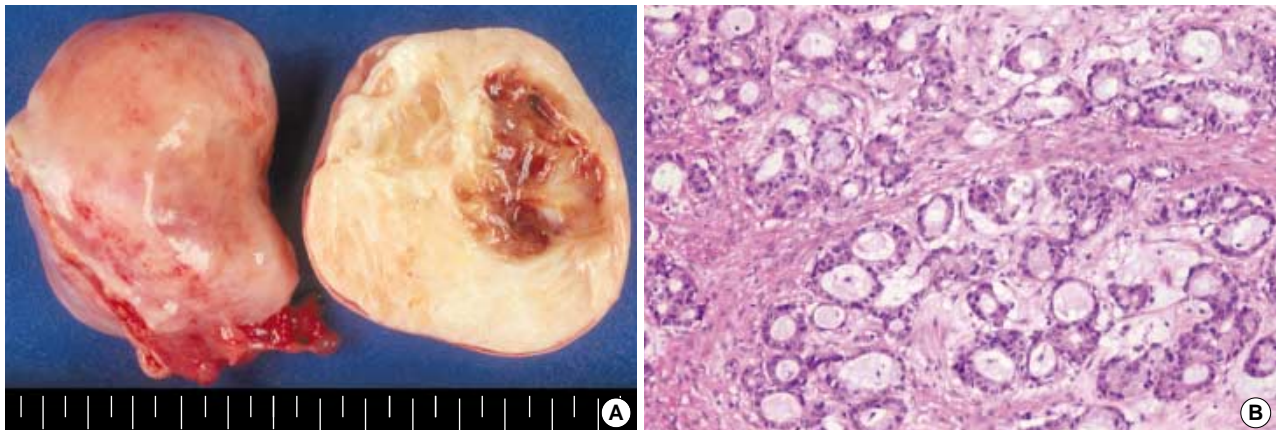


Fig. 1. (A) The right ovarian tumor is a mainly solid and partly cystic mass with firm and mucinous cut surface. (B) The tumor shows a complex glandular architecture with prominent cytoplasmic mucin.

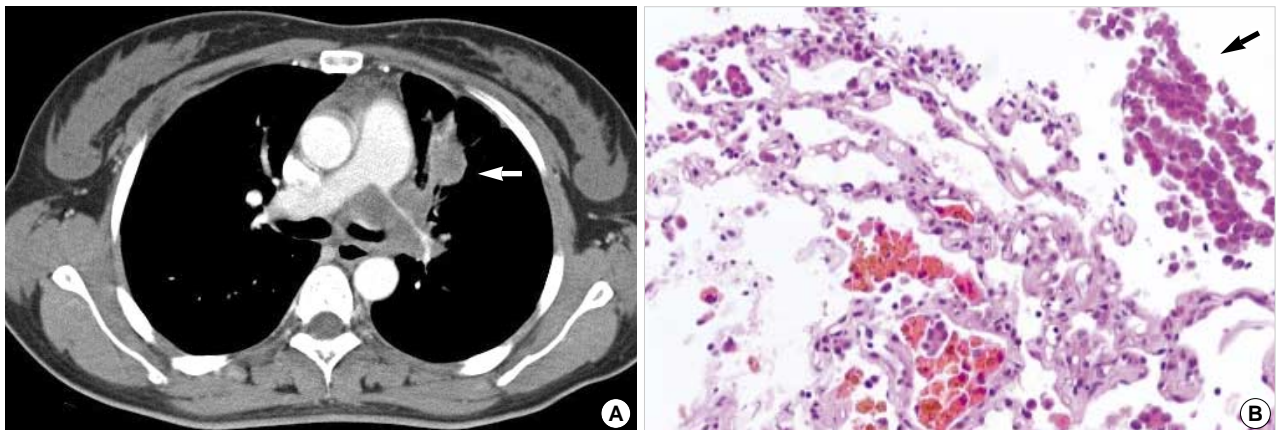


Fig. 2. (A) A 2.5 cm mass (arrow) with hilar lymphadenopathy appears on computerized tomography. (B) Percutaneous needle aspiration biopsy reveals a few clusters of atypical cells (arrow) suspicious of adenocarcinoma.

(OV-TL, Dako), focally positive for CA125 (OC 125, Signet), and negative for CK-20 (Ks20.8, Dako). The pathologic findings raised the possibility of metastatic carcinoma, which prompted further diagnostic work up. Clinical and radiographic studies such as gastroduodenoscopy, colonoscopy, abdominal sonography, and bone scan all proved negative. Therefore, it was diagnosed as an unusual type of ovarian carcinoma with features of well- to moderately-differentiated mucinous adenocarcinoma. However, follow-up chest X-rays and computerized tomography (CT) a month later showed a 2.5 cm mass in the lung with hilar lymphadenopathy which was suspected to be either primary or metastatic carcinoma (Fig. 2A). A percutaneous needle aspiration biopsy revealed only a tiny amount of atypical cell clusters, highly indicative of adenocarcinoma (Fig. 2B). The immunohistochemical staining for TTF-1 (SPT24, Novocastra, Newcastle upon Tyne, UK) revealed focal positivity in the atypical

cells, so the possibility of primary adenocarcinoma was suggested. With a clinical diagnosis of synchronous lung and ovarian carcinoma, systemic chemotherapy was performed with taxotere and diamminedichloro-platinum.

In July 2004, she complained of headache and dizziness. She also developed bitemporal hemianopsia and a decrease in visual acuity of her left eye. Brain CT and magnetic resonance images revealed a 1.7 cm pituitary mass suggestive of macroadenoma. The other area of brain parenchyma was negative for any lesion (Fig. 3A). She underwent a trans-sphenoidal exploration and subsequent histological examination revealed metastatic adenocarcinoma. The histological findings of pituitary adenocarcinoma were similar to those of ovarian adenocarcinoma, except that there were fewer mucin-containing carcinoma cells (Fig. 3B). After thorough immunohistochemical staining for TTF-1 revealed strong nuclear positivity for the marker in both the ovarian and

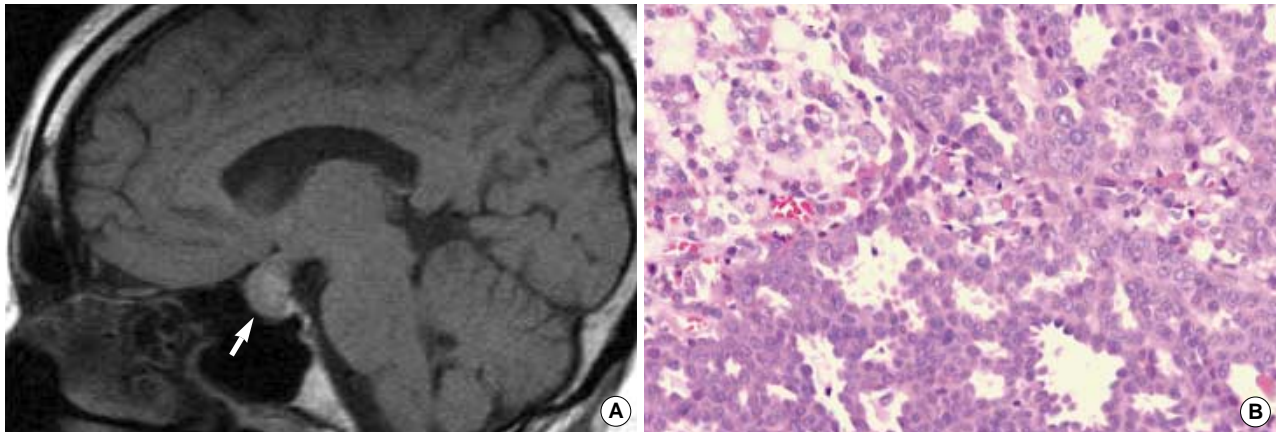


Fig. 3. (A) A pituitary mass (arrow) is noted on brain magnetic resonance image taken after a year of follow up. (B) The resected tumor has features of metastatic adenocarcinoma.

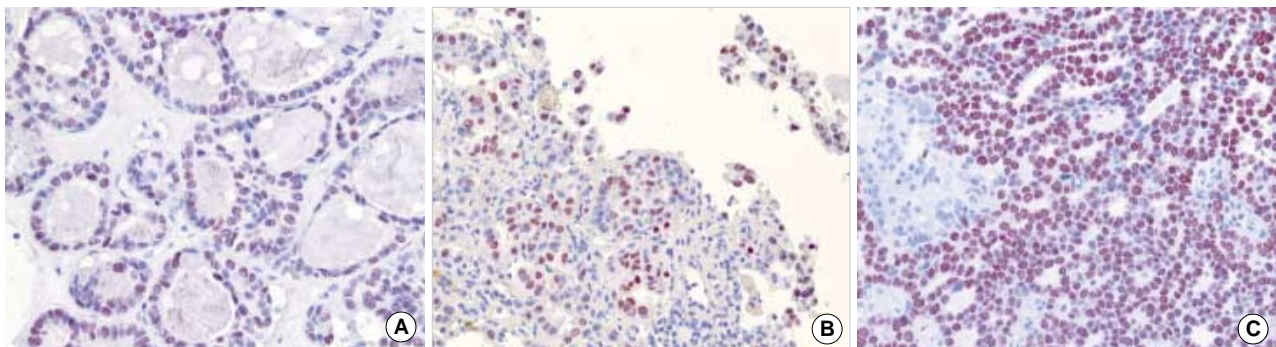


Fig. 4. The ovarian (A), pulmonary (B) and pituitary (C) tumors disclose nuclear TTF-1 positivity.

pituitary adenocarcinomas, the patient was diagnosed with pulmonary adenocarcinoma metastasis to the right ovary and pituitary gland (Fig. 4).

The patient refused additional radio- or chemotherapy and accepted a regular follow-up. Her condition was stable until July 2005, when she became nearly blind on her left side. In October 2005, she underwent a pericardiostomy to relieve the malignant effusion. She suffered from severe headache and visual disturbance and was found to have a recurrent pituitary mass. Craniotomy was performed to reduce the volume of the tumor, but she developed postoperative cerebral hemorrhage and pneumonia. The patient ultimately died in December 2005.

DISCUSSION

This could be the first case of primary lung adenocarcinoma metastasis to two unusual secondary sites, the ovary and pituitary gland, without widespread systemic metastasis.

It is uncommon for lung carcinoma to spread to the ovaries.

According to previous studies on the site distribution of secondary ovarian neoplasia, primary lung carcinoma has accounted for only 4 out of over 900 cases.³⁻⁹ There have been only two case reports of pulmonary adenocarcinoma metastasis to ovary without widespread systemic metastasis.^{10,11} In the only case documented in Korea, a large cell neuroendocrine carcinoma of the lung presented as an ovarian mass.¹² Irving and Young¹ have recently reported in a clinicopathologic study of 32 cases that cases of lung carcinoma metastasis to the ovary have been increasing, often in relatively young women. This pattern is presumably a consequence of statistical trends, as lung carcinoma is increasing in females. In about a half of their cases, a history of prior lung carcinoma was documented. However, in 15 cases, the ovarian tumors occurred synchronously, or were detected prior to the lung tumors as in the present case. Ovarian metastasis was unilateral in about 2/3 of the patients, a higher frequency than is usually encountered. Tumors were limited to the lung and one or both ovaries in 40% of the cases, and ovarian surface involvement was infrequent. This suggests that the mode of spread is hematogenous or lymphangitic, rather than the peritoneal seed-

ing that occurs frequently in metastases of gastrointestinal origin. They also shared the common features of metastatic tumors: multinodular growth, lymphovascular invasion, and necrosis. The present case showed the corresponding features of unilateral nodular growth, absence of capsular involvement, and presence of lymphovascular invasion. The most frequent histologic subtypes of lung carcinoma metastasis to the ovary were small cell carcinoma, followed by adenocarcinoma, and large cell carcinoma.¹ In metastatic adenocarcinoma, diverse morphologic features have been described, including acinar, cribriform, papillary, and mucinous patterns mimicking most types of surface epithelial tumors.¹ Prominent cytoplasmic mucin mimicking mucinous adenocarcinoma in this case was frequently noted in metastasis from the gastrointestinal tract. In the present case, the histopathology of the lung carcinoma was not thoroughly evaluated. However, immunohistochemical staining for TTF-1 provided irrefutable evidence of metastasis from primary lung adenocarcinoma to the ovary, since none of the ovarian carcinomas examined in previous studies showed TTF-1 positivity.^{13,14}

Secondary tumors of the pituitary gland are very rarely recognized clinically. It is often difficult to distinguish them from primary pituitary tumors, especially in the absence of multiple intracranial metastases.^{2,15} Even in the presence of a primary carcinoma, the possibility of pituitary metastasis is less likely suggested both clinically and radiographically in the patient with pituitary mass.² In the present case, pituitary metastasis of pulmonary adenocarcinoma was confirmed by pathologic examination.

In the differential diagnosis of an ovarian adenocarcinoma, metastatic carcinoma from lung should be considered since the incidence of lung cancer in women has been increasing. The possibility of metastatic disease must also be considered in suspected cases of non-functioning pituitary adenoma. Immunohistochemical staining for TTF-1, as with CK-7 and CK-20, may help identifying whether a metastasis has arisen from a pulmonary or nonpulmonary site as well as discrimination between primary and metastasized malignancy.^{1,13,16}

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