



Metastatic Endobronchial Adenocarcinoma from the Uterine Cervix Verified by Human Papillomavirus Genotyping

Jisup Kim · Sungsoo Lee¹ · Heae Surng Park

Departments of Pathology and ¹Thoracic and Cardiovascular Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Endobronchial metastasis is defined by bronchoscopically visible extrapulmonary tumors with lesions histologically identical to the primary tumors. Carcinomas of the breast, kidney, and colorectum are the most commonly encountered solid tumors causing endobronchial metastases,¹ whereas such metastases arising from the tumors of uterine cervix are relatively rare. While there have been many case reports on endobronchial metastasis of uterine cervical squamous cell carcinoma, there is only one reported case of metastatic endobronchial adenocarcinoma from the uterine cervix² and this report focused only on endoscopic treatment. Herein, we report a case of metastatic endobronchial adenocarcinoma from the uterine cervix with discuss on the differential diagnosis.

CASE REPORT

A 59-year-old woman presented with cough, sputum, and dyspnea on exertion. Four years previously, she was diagnosed with uterine cervical cancer and had undergone radical hysterectomy and bilateral salpingo-oophorectomy with adjuvant radiotherapy in an overseas hospital. Chest computed tomography revealed an endobronchial mass in the distal right main bronchus. Whole body positron emission tomography (PET) showed intense 18F-fluorodeoxyglucose uptake in the endobronchial mass with no other abnormally hypermetabolic lesions. Bronchoscopic examination with biopsy was performed,

and the pathologic finding was poorly differentiated carcinoma with necrosis and focal mucin formation (Fig. 1A). The tumor had been considered as poorly differentiated pulmonary adenocarcinoma, but it was negative for thyroid transcription factor-1 (TTF-1) and napsin A immunostaining. The patient underwent right pneumonectomy with mediastinal lymph node dissection.

Macroscopically, a 6.5-cm-sized endobronchial mass was noted originating from the right lower lobar bronchus. Microscopically, the tumor showed large, confluent cribriform glands with focal papillary growth and intraluminal necrotic debris (Fig. 1B). The tumor cells were tall and columnar, showing elongated, vesicular nuclei and amphophilic cytoplasm. Metastases to the peribronchial and subcarinal lymph nodes were observed. Since the microscopic findings were unusual for primary lung adenocarcinoma and the patient had a history of uterine cancer, extensive immunohistochemical staining was performed. The tumor was positive for cytokeratin (CK) 7, carcinoembryonic antigen, and p16, and negative for TTF-1, napsin A, estrogen receptor, progesterone receptor, vimentin, CK20, and caudal-related homeobox gene 2 (Fig. 1C, D). Human papillomavirus (HPV) genotyping (GeneFinder HPV Liquid Bead Microarray Kit, Infopia, Anyang, Korea) revealed the presence of HPV type 18 genome in the tumor. The final pathological diagnosis was metastatic adenocarcinoma from the uterine endocervix.

DISCUSSION

Diffuse positive immunostaining for p16 is a good surrogate marker of high-risk HPV infection in uterine cervical and oropharyngeal cancer.³ Primary lung cancers can also overexpress p16, but mainly in a focal distribution in approximately 32% of cases.⁴ However, high-risk HPV genomes are nearly nonexis-

Corresponding Author

Heae Surng Park, M.D.
Department of Pathology, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 135-720, Korea
Tel: +82-2-2019-3545, Fax: +82-2-3463-2103, E-mail: turtle98p@yuhs.ac

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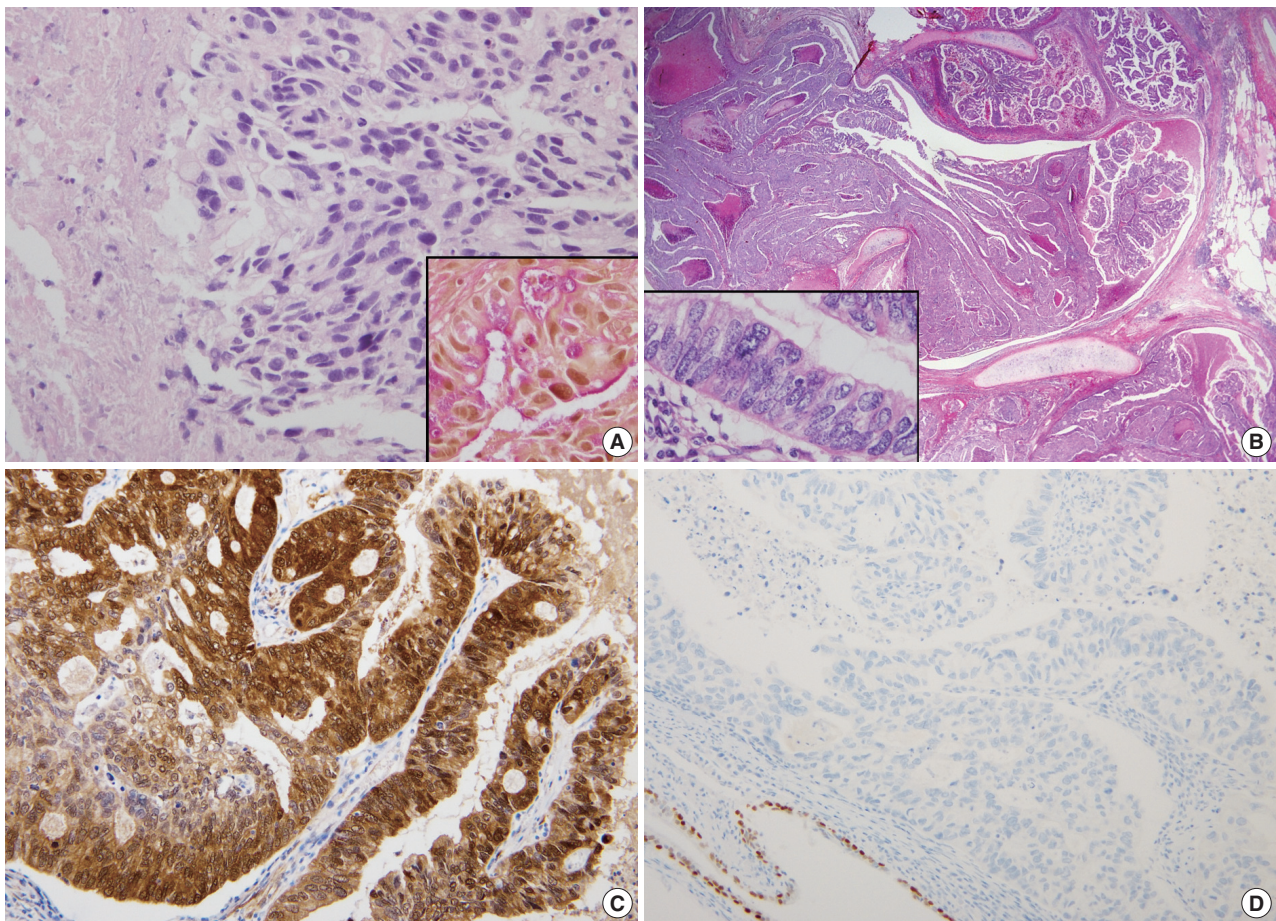


Fig. 1. (A) Histology of bronchoscopic biopsy shows poorly differentiated carcinoma with necrosis and focal mucin production (inset, mucicarmine stain). (B) Histology of the pneumonectomy specimen shows confluent cribriform glands with focal papillary growth and intraluminal necrotic debris. Tall columnar tumor cells have elongated, vesicular nuclei and amphiphilic cytoplasm (inset). (C) Immunohistochemical staining for p16 shows diffuse strong nuclear and cytoplasmic positivity in tumor cells. (D) Immunohistochemical staining for thyroid transcription factor-1 shows non-reactivity of tumor cells.

tent in lung cancer.^{4,5} Accordingly, confirmation of HPV infection is important to determine whether lung tumor has metastasized from an HPV-associated primary cancer elsewhere in the body, such as the uterine cervix. In this case, HPV type 18 was detected in the tumor and a diagnosis of metastatic endocervical adenocarcinoma was made although the primary cancer tissue was no longer available.

At the time of bronchoscopic biopsy, the patient's history of uterine cancer was not known and whole body PET showed no other abnormal lesions except the endobronchial mass. Retrospective pathologic review of the biopsy showed no specific histologic findings to suggest uterine endocervical adenocarcinoma. While positive immunostaining for both TTF-1 and napsin A is highly specific and relatively sensitive for primary lung adenocarcinoma, negative immunostaining for both TTF-1 and napsin A has been reported in a small fraction of primary lung

adenocarcinoma.⁶ Therefore, primary lung adenocarcinoma could not be excluded from the biopsy specimen alone. Since the tumor was an endobronchial lesion, mucoepidermoid carcinoma was considered in the differential diagnosis. We retrospectively performed immunohistochemical staining for p16 as well as paired box 8 (PAX8), which is expressed in carcinomas arising in the endometrium, endocervix, ovary, thyroid, kidney, and urothelium. The tumor from the bronchoscopic biopsy showed positive immunoreactivity for p16, but negative immunoreactivity for PAX8.

Diagnosis of an extrapulmonary malignancy in a small biopsy is challenging in the absence of information on the patient's history of cancer. A combination of TTF-1 and napsin A immunostaining is useful to differentiate between pulmonary and extrapulmonary carcinoma in a proper clinical setting. When a non-squamous carcinoma from the bronchus is negative for both

TTF-1 and napsin A, the possibility of an extrapulmonary lesion may be considered and ancillary testing with clinical correlation should be pursued.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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