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Human papillomavirus type-16 positive endobronchial metastasis from uterine cervical cancer

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Keywords
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Abstract

Although the lung is the most common site of metastasis from extrapulmonary malignancies, endobronchial metastases (EBM) are relatively rare. EBM typically originate from breast, colorectal, or kidney cancer. EBM from uterine cervical cancer is relatively rare and is difficult to confirm. In this study, we report a case of EBM in a patient with previously treated uterine cervical cancer. In this case, differentiation of the EBM from primary bronchogenic carcinoma with clinical, radiological, and pathologic findings was difficult. As identical human papillomavirus (HPV)-16 DNA was detected in both the EBM and in previously resected tissues from the prior uterine cervical cancer, the patient was diagnosed with EBM from uterine cervical cancer. HPV genotyping may aid in discriminating EBM from primary bronchogenic carcinoma in patients with uterine cervical cancer.

Introduction

Uterine cervical cancer is a common gynecologic cancer and prevailing cause of cancer death in the United States. Uterine cervical cancer often invades adjacent organs and occasionally metastasizes to extrapelvic areas such as the lung. Pulmonary metastasis has been reported in 3.1%–8.2% of patients with uterine cervical cancer.

Endobronchial metastases (EBM) from an extrapulmonary malignancy such as breast, colorectal, or kidney cancer occasionally occur, while EBM from uterine cervical cancer is relatively rare.

Because bronchoscopic biopsy specimens are usually small, it is very difficult to differentiate EBM from primary bronchogenic carcinoma by pathology alone. If carcinoma in situ is determined in the bronchial epithelium located adjacent to the tumor, the endobronchial tumor can be regarded as a primary bronchogenic carcinoma. Additional immunohistochemical staining, together with specific clinical manifestations, can occasionally help in differential diagnosis; however, there are no clear criteria to distinguish between the two.

We report a case of EBM in a patient with uterine cervical cancer. We performed human papillomavirus (HPV) genotyping in the endobronchial tumor of the uterine cervical cancer patient and found identical HPV-16 DNA in both the EBM and the primary uterine cervical cancer. Therefore, HPV genotyping may aid in diagnosis of EBM from uterine cervical cancer by differentiating between EBM and primary bronchogenic carcinoma.

Case

A 46-year-old woman presented to our institution with exertional dyspnea and dry cough. One year previously, she had undergone radical hysterectomy for stage IIb uterine cervical cancer and had received adjuvant chemotherapy and radiotherapy. Before presentation, there was no evidence of local recurrence or distant metastasis. A plain chest radiograph showed increased opacity in the left

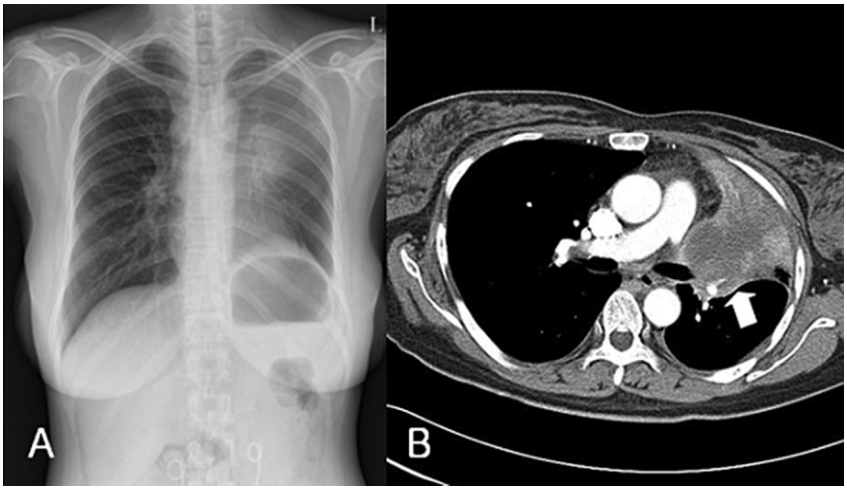

Figure 1. (A) A plain chest radiograph showed increased opacity in the left perihilar area. (B) A chest CT scan revealed a 6.1 × 5.1 × 5.1 cm sized ill-defined large mass in the left upper lobe and the left hilum. Left upper lobar bronchus was obstructed with the mass (arrow).

perihilar area (Fig. 1A). A chest computed tomography scan revealed a 6.1 × 5.1 × 5.1 cm, ill-defined mass obstructing the left upper lobar bronchus (Fig. 1B), and a positron emission tomography scan revealed a large hypermetabolic mass in the left upper lobe, with no other site of uterine cervical cancer metastasis. Fiber optic bronchoscopy revealed complete obstruction of the left upper lobar bronchus by a tumor, and the pathologic findings of the endobronchial mass were consistent with invasive squamous cell carcinoma. Immunohistochemical staining for thyroid transcription factor-1 was negative. Pathological findings were similar between previously resected uterine cervical cancer specimens and the endobronchial mass (Fig. 2A,B). We used an HPV DNA chip® (provided by Biomedlab Company, Seoul, South Korea), a polymerase chain reaction-based DNA microarray system, according to the manufacturer's protocol as a genotyping method for HPV infection. An identical subtype (HPV-16) of HPV was identified in the bronchoscopically biopsied endobronchial mass and the previously resected uterine cervical cancer tissues (Fig. 2C,D). On the basis of these findings, the patient was diagnosed as having EBM from uterine cervical cancer.

Discussion

HPV infection is a traditional risk factor for the development of uterine cervical cancer, and HPV DNA genotyping can help diagnose, treat, and estimate the prognosis of uterine cervical cancer [1]. Recently, HPV vaccines have become clinically useful for preventing uterine cervical cancer.

HPV infection has been also identified in metastatic uterine cervical cancer lesions. Nagai et al. analyzed the pattern of HPV infection in specimens of primary uterine cervical cancer and metastatic uterine cervical cancer tissues and found the positive rate of HPV infection in squamous cell carcinoma of uterine cervical cancer to be 89%. Many subsequent metastatic lesions of uterine cervical cancer also presented as positive for HPV DNA [2].

Pulmonary metastasis of uterine cervical cancer has been reported. Weichert et al. analyzed the status of HPV infection in metastatic squamous cell carcinoma of uterine cervical cancer in the lung and found that the overall frequency of HPV positivity of uterine cervical cancer that metastasized to the lung was 100%. Moreover, five patients with uterine cervical cancer and concomitant or subsequent lung tumors had identical HPV genotyping in both tumors (HPV-16, HPV-45) [3]. The utility of HPV genotyping in pulmonary metastases of uterine cervical cancer has been reported [4]. In our case, we performed HPV genotyping on the endobronchial mass biopsy according to a report of HPV infection in the primary uterine cervical cancer. Identical HPV-16 DNA was isolated from both the endobronchial mass and the primary uterine cervical cancer. HPV genotyping aided our clinical and pathological diagnosis of EBM from uterine cervical cancer, and, to our knowledge, this is the first report of HPV genotyping in EBM from uterine cervical cancer.

The occurrence of HPV infection in primary bronchogenic malignancy is possible as the rate of HPV infection in non-small lung cancer in the Western world is approximately 3%; however, there are currently no reports concerning HPV infection and the development of primary lung cancer [5]. Additionally, the same strain of HPV that causes uterine cervical cancer may not cause lung cancer. It is more reasonable to consider that HPV-infected cancer cells metastasize to the bronchial tree from the uterine

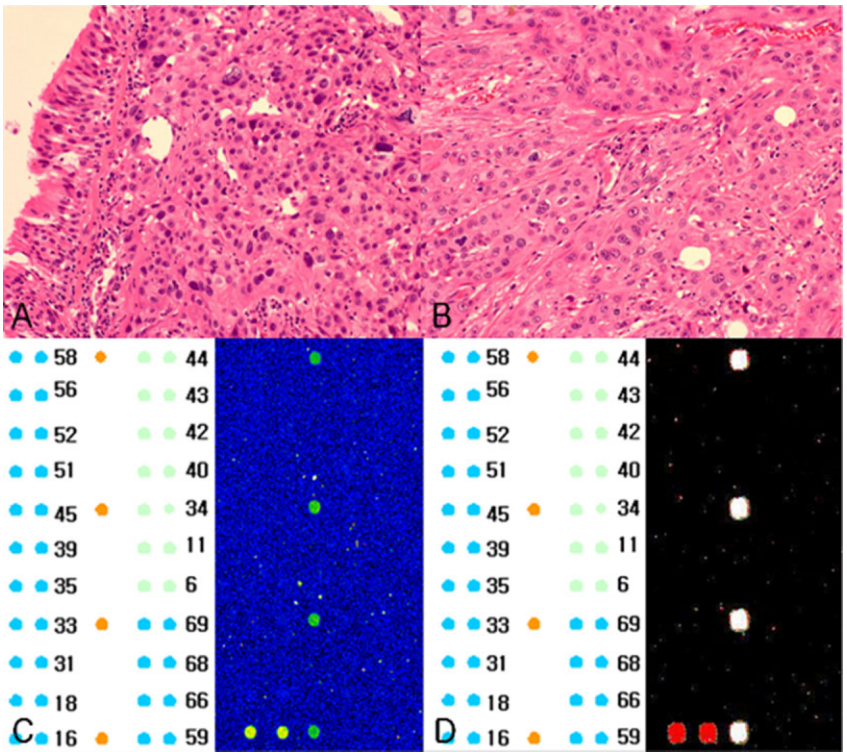

Figure 2. Histology of the endobronchial mass and uterine cervical cancer. (A) Bronchus; invasive squamous cell carcinoma (H&E, ×400). (B) Cervix; invasive keratinizing squamous cell carcinoma (H&E, ×400). (C) HPV genotyping of the biopsy of the endobronchial mass using the HPV DNA chip® shows positive high risk 16. (D) HPV genotyping by HPV DNA chip® from the cervical brushing specimen shows strongly positive high risk 16.

cervix. Here, we report a case of EBM from uterine cervical cancer, which was validated by HPV genotyping.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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