Endotracheal and Endobronchial Metastases in a Patient With Stage I Lung Adenocarcinoma

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Endotracheal or endobronchial metastasis from primary lung cancer is extremely rare. We report a case of endotracheal and endobronchial metastases from peripheral early lung adenocarcinoma 7 months after complete resection. The patient harbored the same gene mutation in both primary and metastatic lesions. This report highlights that enough attention on endotracheal metastases should be paid no matter what the pathologic TNM stage of primary lung cancer is.


The incidence of endotracheal or endobronchial metastasis from peripheral primary lung cancer thus far has not been known. In this paper we present a case of endotracheal and endobronchial metastases from an early stage peripheral lung adenocarcinoma after the right upper lobectomy, and first clarify the gene mutation status of epidermal growth factor receptor (EGFR), Kirsten rat sarcoma viral oncogene homolog (KRAS), and the anaplastic lymphoma kinase (ALK).

A 57-year-old Chinese female patient presented with repeated nonproductive cough after upper respiratory tract infection for approximately 5 months prior to her admission. A chest computed tomography (CT) scan revealed a peripheral nodule (ground glass opacity lesion) less than 1 cm in diameter with non-homogeneous density located in the right upper lobe of the lung. The recommendation of follow-up for 3 months and anti-inflamatory therapy was made. A repeated chest CT was done 4 months afterwards (Fig 1), and the lesion showed a progressive change with mild consolidation in the center. This characteristic indicated the possibility of a lung cancer, and the patient was advised to have an operation on February 14, 2012.

Preoperative examination results were in favor of operation. The clinical TNM stage was cT1aN0M0. A right upper lobectomy and systemic lymph node dissection was performed smoothly on the patient 3 days after admission. The excised lesion was $1.2 \times 1.1 \times 0.7 \, \text{cm}^3$ and pathology demonstrated a primary moderately differentiated adenocarcinoma of the lung, with acinar growing principally and micropapillary growing partially; visceral pleura was not affected. The pathologic stage was pT1aN0M0 (stage Ia). Therefore, the patient did not receive any chemotherapy or radiotherapy, and was informed of follow-up at 3 to 6 months postoperative. Any sign of metastasis was not shown in the examinations 3 months postoperatively. However, 7 months postoperatively a CT was performed again due to continuous hemoptysis and cough for 2 weeks, and several irregular endotracheal nodules approximately 0.8 cm in diameter with eccentric thickening in the tracheal were found (Figs 2A–2C), but no enlarged lymph node and parenchymal abnormalities were detected. No relief of the above symptoms and strong anxiety prompted the patient to take bronchoscopic examination. Unfortunately, multiple endotracheal and endobronchial polypoid lesions located in the upper and lower trachea and the left main bronchus (Figs 3A–3B) were detected. Pathologic results of the biopsy demonstrated moderately differentiated adenocarcinoma with micropapillary growing principally, identical to the pathologic features of previously resected lung cancer. Endotracheal and endobronchial metastases from the primary lung cancer were confirmed.

Gene testing was performed both in primary and metastatic lesions, EGFR mutations at exons 18, 19, 20, 21 and KRAS mutations were detected by DNA sequencing, and EML4-ALK was identified by using fluorescent in situ hybridization for ALK rearrangement. It presented that this patient harbored EGFR exon 20 insertions without KRAS mutation and ALK rearrangement. Gefitinib was administered orally only for 2 weeks and the patient decided not to undergo further chemotherapy and went to the another institution for transbronchial cryotherapy. The patient is still alive after transbronchial cryotherapy.
cryotherapy and some type of chemotherapy in another institution.

Comment

The frequency of endobronchial metastasis from non-pulmonary malignancies (primary lung cancer and lymphomas were excluded) ranged from 2% to 50%, and usually the cancer of the breast, kidney, colorectal, uterine cervix, sarcoma, and skin predominate. However, the incidence of endotracheal or endobronchial metastasis from peripheral primary lung cancer thus far has not been reported. According to what has been reported in literature, including this case, only 10 cases in total with metastases from pathologically proven primary lung cancer after radical surgical resection have been reported from 1984 to 2012 [1–4], but gene mutation status was informative. The pathologic types of the primary lung cancer were squamous cell carcinoma (n = 7), adenocarcinoma (n = 2), and adenosquamous cell carcinoma (n = 1).

It is inconceivable that the multiple endotracheal metastases originated from a peripheral early-stage lung cancer (stage Ia) within 7 months after complete surgical resection. Moreover, the preoperative radiology findings was only a “ground glass opacity” lesion, the lymph nodes were negative in metastasis, and tumor cells were only moderately differentiated, although the micropapillary growth variant carries a poor prognosis according to the new adenocarcinoma classification. This case highlighted the rarity.

Some scholars [4] put forward the possibility of cancer cell implantation due to the endoscopic examination and biopsy preoperatively; however, the bronchoscopy was not performed preoperatively for this patient due to her refusal and an early stage peripheral lesion and negative CT scan. If the location classification of tracheal abnormalities (nodules or wall thickening) into the upper or lower trachea suggested by the literature [2], drawing a horizontal line tangential to the upper margin of the aortic arch on CT, all 10 cases are shown: 5 in the upper trachea; 5 in the lower trachea; 2 in the left main bronchus; and 1 in the right intermediate bronchus (2 cases both had tracheal and bronchial lesions). It was found that there was no apparent predilection of the location of the metastatic neoplasms based only on these 10 cases.

To our knowledge, we have reported, herein, the first case of endotracheal metastases from primary lung cancer, which was confirmed by using gene mutation and first clarified the gene mutation status of EGFR, KRAS, and ALK for the patient. Gene mutation testing from primary tumor demonstrated that this patient was EGFR mutant while KRAS and EML4-ALK mutation were
negative, and the metastatic lesions were exactly the same. Previous studies [5] showed that EML4-ALK and EGFR mutation are mutually exclusive, and patients with EGFR exon 20 insertions would show low sensitivity to EGFR tyrosine kinase inhibitors such as gefitinib, which indicates a poor prognosis [6].

Clinicians should be attentive to endotracheal or endobronchial metastasis when the patient constantly complains of the respiratory symptoms postoperatively, no matter what the pathologic TNM stage of primary lung cancer is.

References