Successful Treatment of Lung Cancer with Gefitinib and EGFR Mutation Status Determination Using EBUS-TBNA Samples in an Extremely Old Patient

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Abstract

We report a 90-year-old woman who had complained of bloody sputum and for whom a chest CT showed a nodular lesion on the right lower lobe. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed and adenocarcinoma was revealed in both a subcarinal lymph node (#7) and in the primary lung tumor. Epidermal growth factor receptor (EGFR) gene mutation status was evaluated, and an exon 21 point mutation (L858R) was identified by direct sequencing. Two weeks after administration of gefitinib, the tumor size decreased and bloody sputum disappeared. The patient has remained in good condition for 6 months.

Key words: endobronchial ultrasound-guided transbronchial needle aspiration, nonagenarian, epidermal growth factor receptor mutation, gefitinib

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Introduction

While the number of lung cancer patients within the elderly population is increasing, elderly individuals have limited treatment options due to their generally diminished physical status. Furthermore, advanced lung cancer is difficult to cure by conventional chemotherapy—the response rate of combined chemotherapy, including platinum-containing agents, remains low at approximately 30%. Recently, epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), including gefitinib and erlotinib, have been developed as molecularly targeted therapies. Treatment with EGFR-TKIs has resulted in dramatic effects in some lung cancer patients. Furthermore, the sensitivity to gefitinib is known to be associated with the status of certain EGFR gene mutations.

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a novel and promising modality for evaluating mediastinal and hilar lymph node metastasis in patients with lung cancer (1). Histological as well as cytological samples can be obtained by EBUS-TBNA under local anesthesia with mild conscious sedation. No severe complications have been reported in association with the EBUS-TBNA procedure (1). Herein, we report that samples obtained by EBUS-TBNA can be used not only for diagnosis, but also for determination of EGFR mutation status.

Case Report

A 90-year-old woman was referred to our department due to complaints of bloody sputum. Sputum cytology results were negative for malignant cells. A chest X-ray showed a nodular shadow in the right lower lung field. Computed tomography (CT) scanning revealed a nodule in the right lower lobe and mediastinal lymphadenopathy (Fig. 1A, B). However, the nodule was located close to the right inferior lobar bronchus, and there were no direct findings in the airway. EBUS-TBNA was performed for diagnosis and staging of the lung tumor. Convex probe endobronchial ultrasonography equipped with a 7.5-MHz linear probe on its tip (BF-UC260F-OL8; Olympus Ltd., Tokyo, Japan) and a dedi-
Figure 1. (A) Chest CT showing a tumor shadow (arrow) in the right lower lobe adjacent to the right basal lobar bronchus, as well as (B) subcarinal lymphadenopathy (#7, arrow). (C) Endobronchial ultrasound (EBUS) (arrow) was performed for both the subcarinal lymph node and the primary lung tumor. (D) Histological findings revealed adenocarcinoma (Hematoxylin and Eosin staining ×100). (E) Detection of an EGFR exon 21 point mutation (L858R) by direct sequencing (arrow). (F) Two weeks after administration of gefitinib, the tumor decreased in size (arrow). It was judged as partial response (PR) according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria (2).

cated 22-gauge needle (NA-201SX-4022; Olympus Ltd) were used for EBUS-TBNA.

First, we punctured a subcarinal lymph node (#7), and then we punctured the primary tumor from the basal bronchus of the right lung (Fig. 1C). Adenocarcinoma was revealed in both the subcarinal lymph node and the primary tumor (Fig. 1D), which together were diagnosed as primary lung cancer with mediastinal lymph node metastasis (N2 disease). Because the patient maintained a good performance status (PS1), we considered her eligible for gefitinib treatment. DNA was extracted from formalin-fixed, paraffin-embedded samples, and EGFR mutations were analyzed by direct sequencing. An EGFR exon 21 point mutation (L858R) was identified (Fig. 1E).

We discussed different treatment options with the patient and her family. She finally selected gefitinib treatment; hence, gefitinib was administered as first-line therapy. Two weeks after gefitinib administration, the tumor decreased in size and bloody sputum disappeared (Fig. 1F). This was judged as a partial response (PR) according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria (2). The only adverse event experienced was skin hyperpigmentation on both legs. She remains in stable condition without tumor re-growth for 6 months after gefitinib administration.

Discussion

Herein we reported a 90-year-old woman who was successfully treated with gefitinib for lung cancer. EBUS-TBNA is a novel, promising approach for the evaluation of mediastinal and hilar lymph node metastases in lung cancer patients (1). Furthermore, EBUS-TBNA can be used to evaluate intrapulmonary tumors located adjacent to the central airway (3). EBUS-TBNA is a real-time procedure that can be performed under local anesthesia with mild conscious sedation. No severe complications associated with EBUS-TBNA have been reported in the literature (1). We were able to safely perform EBUS-TBNA in this case. Histological as well as cytological samples can be obtained by EBUS-TBNA, and high-quality cores can be used for EGFR mutation analysis (4). EBUS-TBNA provides not only diagnostic information, but also information on EGFR mutation status, which is critical when considering treatment with EGFR-TKIs.

Gefitinib, a recently developed EGFR-TKI, has demonstrated dramatic effects in some non-small cell lung cancer patients. Sensitivity predictors for this type of molecularly targeted therapy have been evaluated, and EGFR mutation status was determined to be the most important independent predictor for response to gefitinib treatment (5). First-line treatment with gefitinib for non-small cell lung cancer patients with EGFR mutations has been described, and the utility of gefitinib as first-line treatment has also been reported (6). Therefore, when considering administration of gefitinib, assessment of EGFR mutation status is critical for ensuring that patients receive the most effective treatment (5).

Currently, effective treatments can be given to extremely old patients who have a good performance status. Furthermore, if more effective, less toxic treatments can be selected on an individual basis, patients can maintain a good quality of life for a long period. EBUS-TBNA, a safe and highly precise diagnostic modality, also appears to have a potentially important role to play in the era of molecularly targeted therapy.

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References


