Abstract. Although adenosquamous cell lung cancer (ASCLC) is included in the non-small-cell lung cancers (NSCLCs), the number of currently available studies on the response of this type of cancer to epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) is limited. This is the case report of a 66-year-old female who was referred to the Mito Medical Center (Mito, Japan) with hemoptysis and the chest computed tomography (CT) scan revealed a large cavitary mass in the lower lobe of the left lung. The patient underwent surgical resection of the lesion and the final pathological diagnosis was ASCLC staged as pT2bN2M0. Notably, an EGFR exon 19 deletion was identified in the adenocarcinomatous as well as the squamous cell carcinomatous components of the tumor. Despite adjuvant chemotherapy, the patient developed small cavitary metastases in the lungs bilaterally. Therefore, treatment with gefitinib was initiated. The chest CT scan revealed substantial regression of the metastatic cavitary tumors in both lungs, with thinning of the walls. The patient remains alive and recurrence-free 19 months following the initiation of gefitinib therapy. This case demonstrated an optimal clinical response to gefitinib treatment for EGFR mutation-positive ASCLC, suggesting that gefitinib is a therapeutic option for such a subset of patients with ASCLC.

Case report

Adenosquamous cell lung cancer successfully treated with gefitinib: A case report

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Key words: adenosquamous cell lung cancer, gefitinib, cavitary formation, non-small cell lung cancer

Introduction

Gefitinib, which is one of the highly promising epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs), is administered orally once daily for patients with non-small-cell lung cancer (NSCLC) (1). Among NSCLCs, adenosquamous cell lung cancer (ASCLC) is a morphologically mixed type of tumor, including two cell components, adenocarcinoma and squamous cell carcinoma, in varying proportions, each representing ≥10% of the entire tumor (2). Previous studies evaluated the possibility of monoclonality and similar biological characteristics, including the frequency of EGFR mutation, of the two components (3-12). However, the number of currently available studies on the response of EGFR-positive ASCLC to gefitinib therapy is limited (13). We herein report a case of metastatic ASCLC successfully treated with gefitinib.

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Introduction

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continued in the outpatient clinic without any signs of tumor progression 19 months after the initiation of the treatment.

**Discussion**

Lung cancer is the leading cause of cancer-related mortality worldwide (14). NSCLCs are the most frequent type of lung tumors, with two major histological subtypes: adenocarcinomas and squamous cell carcinomas. A less frequent subtype of NSCLCs, ASCLC, is a morphologically mixed type of tumor, including two cell components, adenocarcinoma and squamous cell carcinoma, in varying proportions, each representing ≥10% of the entire tumor (2). Previous studies have suggested that ASCLC represents 0.3-5% of NSCLCs (15,16). In certain ASCLC patients, cavitary formation was observed (17,18).
Kazerouni et al (18) reported that four of 30 cases exhibited cavitary formation. Cavities may be formed as a result of a unidirectional check-valve mechanism (17). Another mechanism of cavity formation may depend on the ischemic or colliquative tumor necrosis associated with neutrophil infiltration into the central portion of lesion. Cavitary formation due to tumor necrosis is common in squamous cell carcinomas, particularly in those developing peripherally in the lung (19). In our patient, the primary lesion exhibited cavitary formation and its wall was composed of the squamous cell carcinomatous component, which was pathologically confirmed. Certain metastatic lesions ≤10 mm also exhibited cavitation. Notably, the wall of the cavities, which were composed of the squamous cell carcinomatous component, were thinned with gefitinib therapy, although the cavities themselves did not change in size in the majority of the pulmonary lesions. The frequency of EGFR mutation-positive ASCLC patients was previously reported (3-12). However, the number of studies on the response of the lesions, either shrinkage or disappearance of pulmonary metastases with cavitary formation, specifically to gefitinib therapy is limited (13). Furthermore, there has been no report on long-term survivors who were successfully treated with gefitinib. Recently, Shukuya et al (13) reviewed the efficacy of gefitinib for non-adenocarcinoma NSCLC patients, including two ASCLC patients, and reported a response rate of 50%, a disease control rate 100% and a median progression-free survival of 5.3 months (13).

Although ASCLC is included in NSCLCs, the frequency of EGFR abnormalities has not been completely evaluated, due to the rarity of ASCLC (3-12). Two previous studies (4,5), reported EGFR abnormalities in ASCLC tumors identical to those previously described in primary lung adenocarcinoma: Ohtsuka et al (4) identified EGFR TK-domain gene mutations in 2 (50%) of 4 patients with ASCLC, whereas Kang et al (5) identified EGFR mutations in 11 (44%) of 25 ASCLC patients. However, Sasaki et al (11) reported that only four (15.4%) of 26 patients with ASCLC were positive for EGFR mutation.

The possibility of monoclonality and similar biological characteristics regarding genetic alterations, chromosomal abnormalities and immunohistochemical reactions in the two components of ASCLCs were evaluated in previous studies (3-12). With regard to EGFR mutations, Kang et al (5) demonstrated identical changes in the two components of ASCLC tumors, with of the nine mutations in 11 ASCLC patients being located in exon 19 (5). Furthermore, Toyooka et al (8) reported that three (27%) of the 11 ASCLC patients harboured EGFR mutations (two mutations in exon 19 and one in exon 21), which were identical in the two components. In our case, an EGFR mutation (exon 19 deletion) was identified in the two components of the surgically resected tumor. Taken together, the results of previous studies and our findings indicated that TKIs may be a reasonable therapeutic option for ASCLC patients harbouring EGFR mutations. Furthermore, identical EGFR mutations in the adenocarcinomatous and squamous cell carcinomatous components suggest the possibility of monoclonality and similar biological characteristics of the two components.

The present study suggested that gefitinib is a viable therapeutic option for EGFR mutation-positive patients with ASCLC. However, further investigations into the molecular determinants of tumor monoclonality in the histogenesis of ASCLC and response to EGFR-targeted therapies in patients with ASCLC are required.

References