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CASE REPORT

Afatinib treatment of a squamous lung cancer after tumor progression of nivolumab

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Keywords
Afatinib; anti-programmed death-1 monoclonal antibody; immunotherapy; lung cancer; nivolumab.

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Abstract

Nivolumab prolonged disease control in a patient with advanced squamous lung cancer that was refractory to multiple treatments. The rapid eradication of cancer after the administration of nivolumab caused hemoptysis and repeated infection. Six months after immunotherapy, mediastinal lymph node metastasis developed and afatinib effectively relieved dysphonia associated with nerve paralysis.

Introduction

Nivolumab, an anti-programmed death-1 monoclonal antibody, has not only proven to be of benefit in refractory squamous non-small cell lung cancer (NSCLC), but also provides a durable response for first-line advanced NSCLC.[1,2] The potential of afatinib was demonstrated in the LUX-Lung 8 study for the treatment of squamous NSCLC, independent of epidermal growth factor receptor (EGFR) mutational status.[3] We present a case of a heavy smoker with no EGFR or anaplastic lymphoma kinase (ALK) mutations who had undergone two lines of platinum-based chemotherapy, radiotherapy, and radiosurgery, coughed out the cancer tissue after taking nivolumab (which left a cavity in the lung), and then suffered hemoptysis. Nivolumab provided six months of tumor control. After the disease progressed, afatinib was introduced and showed a beneficial effect after 12 days.

Case presentation

In December 2014, a 68-year-old male patient was diagnosed with squamous lung cancer with contralateral mediastinal lymph node metastasis by percutaneous supraclavicular lymph node biopsy. He received five cycles of paclitaxel/cisplatin chemotherapy, followed by radiotherapy. One year later, as a result of lung tumor progression, the patient started a three-cycle gemcitabine/nedaplatin chemotherapy course. After the third cycle of chemotherapy, positron-emission tomography revealed high fluorodeoxyglucose uptake in the left lung hilus only. CyberKnife therapy was performed on May 14, 2016. In November 2016, the patient returned reporting bloodstained sputum. A computed tomography (CT) scan revealed tumor progression at the left pulmonary hilum (Fig 1a,b). A biopsy was performed during bronchoscopy and confirmed squamous cell carcinoma. Tumor tissue DNA was reevaluated but showed no EGFR or ALK mutations. Tumor tissues used for the first diagnosis and the new biopsy samples were evaluated for programmed death ligand 1 (PD-L1). The original tumor tissue obtained for diagnosis was PD-L1 positive, but the tissue taken after radiotherapy was negative. After evaluation by doctors, the patient was administered three doses of nivolumab (3 mg/kg of body weight every 2 weeks) and experienced a significant reduction in coughing; the only adverse effect at that time was mild fatigue. However, in January 2017, the patient started coughing out charcoal-like sputum, and a CT scan

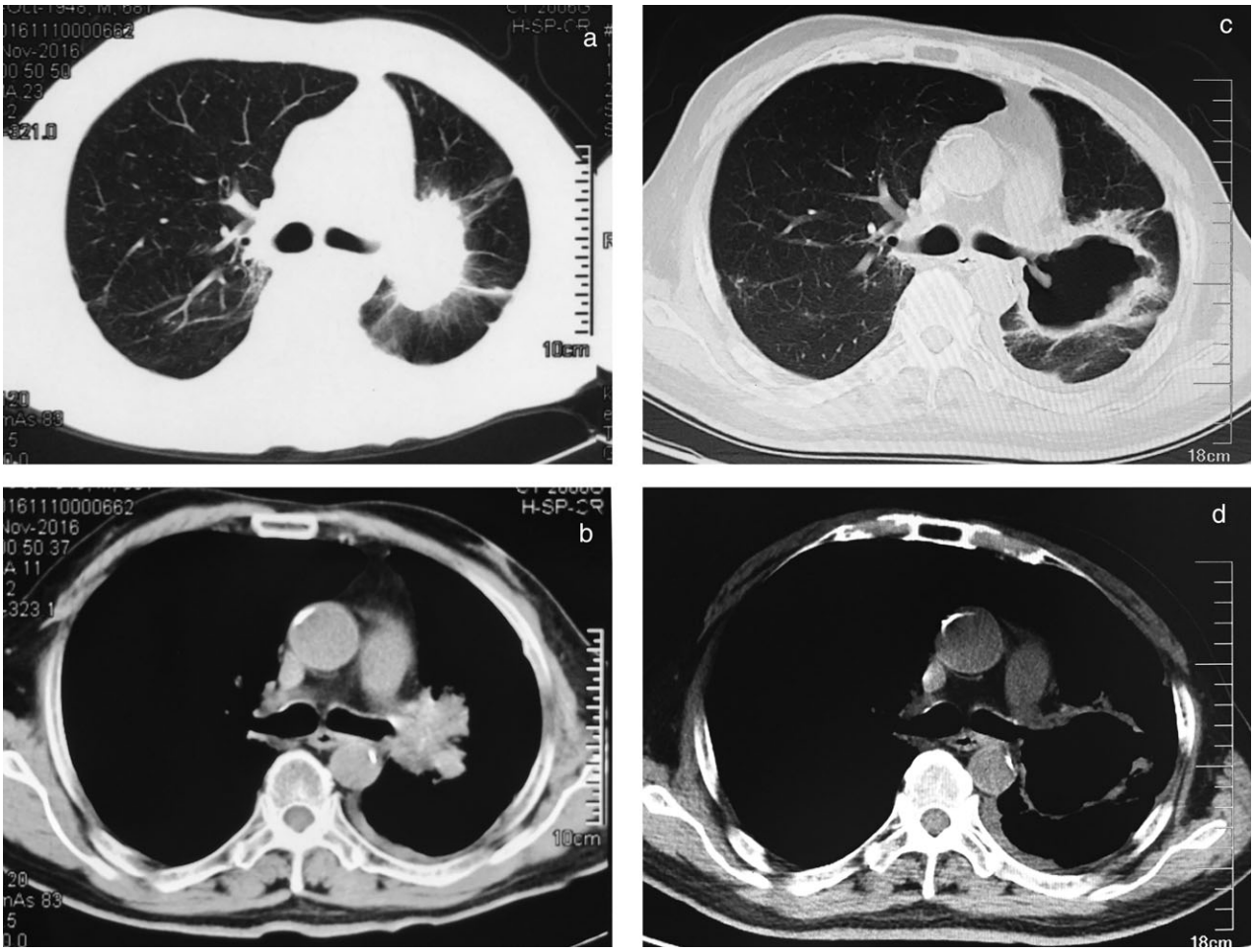

Figure 1 (**a,b**) A pretreament computed tomography scan shows the tumor at the left pulmonary hilum. (**c,d**) After three doses of nivolumab, the tumor disappeared and a cavity was left.

demonstrated a cavity in the left pulmonary hilum, where the tumor was located (Fig 1c,d). Cytological examination of the sputum for malignant cells came back negative. Two weeks later, the patient was hospitalized for massive hemoptysis (nearly 500 mL) and recovered after several days of treatment. The patient returned to the hospital several times up to May 2017 because of bloody sputum or respiratory infection. On May 22, 2017, the patient presented with dysphonia (hoarse voice) and dyspnea. CT imaging revealed significant pleural effusion and an enlarged mediastinal lymph node. Thoracocentesis was then performed. Nedaplatin was injected after depletion of pleural effusion. A follow-up CT scan was performed one month later, which revealed no pleural effusion. In order to screen to determine further treatment options, a blood-based genetic test was performed, which revealed no mutation. Considering the constant bloodstained sputum and repeated infection, afatinib (30 mg orally every day) was prescribed on July 6, 2017. Twelve days after commencing afatinib, the patient experienced relief of the dysphonia and no obvious side effects.

Discussion

This case suggests the potential of afatinib treatment for squamous lung cancer patients with no EGFR or ALK mutations, particularly those who have undergone several lines of chemotherapy, radiotherapy, radiosurgery, and anti-PD1 monoclonal antibody treatments. We present this case not only because physicians need to be aware of the possibility of hemoptysis caused by nivolumab, but also because the results in this case suggest an alternative treatment for patients who cannot endure or are resistant to nivolumab.

Acknowledgment

We are grateful to the patient for kindly sharing his case information.

Disclosure

No authors report any conflict of interest.

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