Mucin-producing Lung Cancer and Response to Gefitinib

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Abstract

A 53-year-old woman who was hypoxemic due to primary lung adenocarcinoma with both pleuritis and pericarditis carcinomatosa was treated with gefitinib, an inhibitor of the epithelial growth factor receptor (EGFR) tyrosine kinase. The tumor seemed to produce mucin because the extremely high serum KL-6 and almost normal SP-D values on admission. After 3 days of treatment, the patient became asymptomatic and oxygen was discontinued. The response to this drug was remarkable on chest CT findings. Mucin overproduction could offer a candidate marker to determine the patient subset displaying good response to gefitinib.

A 53-year-old woman was referred in June 2004 with abnormal shadows on chest radiography and was admitted. The patient reported palpitations and breathlessness over the preceding 10 days, and was a never-smoker. Her mother had died of interstitial pneumonia. Hypoxemia was identified and oxygen therapy was started immediately. Chest computed tomography (CT) (Fig. 1A, B) revealed both pericardial and pleural effusion, a round nodule in the left lower lobe of the lung, and hilar and mediastinal lymph node swelling. Consolidation was noted with CT angiogram and air bronchogram signs in the left upper lobe, appearing compatible with a bronchioloalveolar carcinoma component. Serum CEA level was high, at 471・8 ng/ml. Serum KL-6 level was 4858 U/ml, which was extremely high, whereas SP-D level was 121・2 ng/ml, slightly above normal range. The day after admission, 750 ml of pericardial fluid was drained. Cytology yielded positive results for adenocarcinoma cells in the sputum, and in pleural and pericardial fluids. Stage IV (T4N2M1) adenocarcinoma of the lung was diagnosed, with a possible bronchioloalveolar component. Gefitinib, an inhibitor of the epithelial growth factor receptor (EGFR) tyrosine kinase was started on hospital day 6 at 250 mg/day, and response was impressive. After 3 days of treatment, the patient became asymptomatic and oxygen was discontinued. Chest CT on day 18 of treatment (Fig. 1C, D) revealed marked improvements to initial findings. On day 28 of treatment, serum CEA was 322・4 ng/ml and serum KL-6 was 1982 U/ml.

Serum KL-6 offers a clinically useful marker for detecting interstitial pneumonia, and reportedly represents MUC1, a member of mucin glycoproteins. In the present case, serum KL-6 was high on admission and decreased in response to gefitinib, with concomitant improvements in CT findings. High serum KL-6 thus seems attributable to overproduction by the lung cancer itself. The importance of EGFR members in cell proliferation, decreasing apoptosis and angiogenesis is well recognized in various solid tumours. Gefitinib was recently approved for the treatment of non-small-cell lung cancer (NSCLC). However, this drug is only effective for a subset of NSCLC patients. Large-scale studies have shown that pretreatment characteristics for radiographic improvement include being Japanese,

female, a never-smoker and pathological type of adenocarcinoma, particularly with a bronchioloalveolar subtype.[1] The present patient displayed overproduction of KL-6 in addition to all of these characteristics. The EGFR system has been shown to regulate mucin production,[2] and MUC1 interacts with EGFR and activates the EGFR system.[3] These may implicate mucins as autocrine ligands for the EGFR system. A subset of patients with NSCLC has recently been reported to display specific mutations in the EGFR genes, correlating to clinical responsiveness to gefitinib.[4] However, to obtain sufficient tumour samples for gene-evaluation is sometimes clinically difficult. Mucin overproduction could offer a candidate marker to determine the patient subset displaying good response to gefitinib, although further studies are clearly needed.

References

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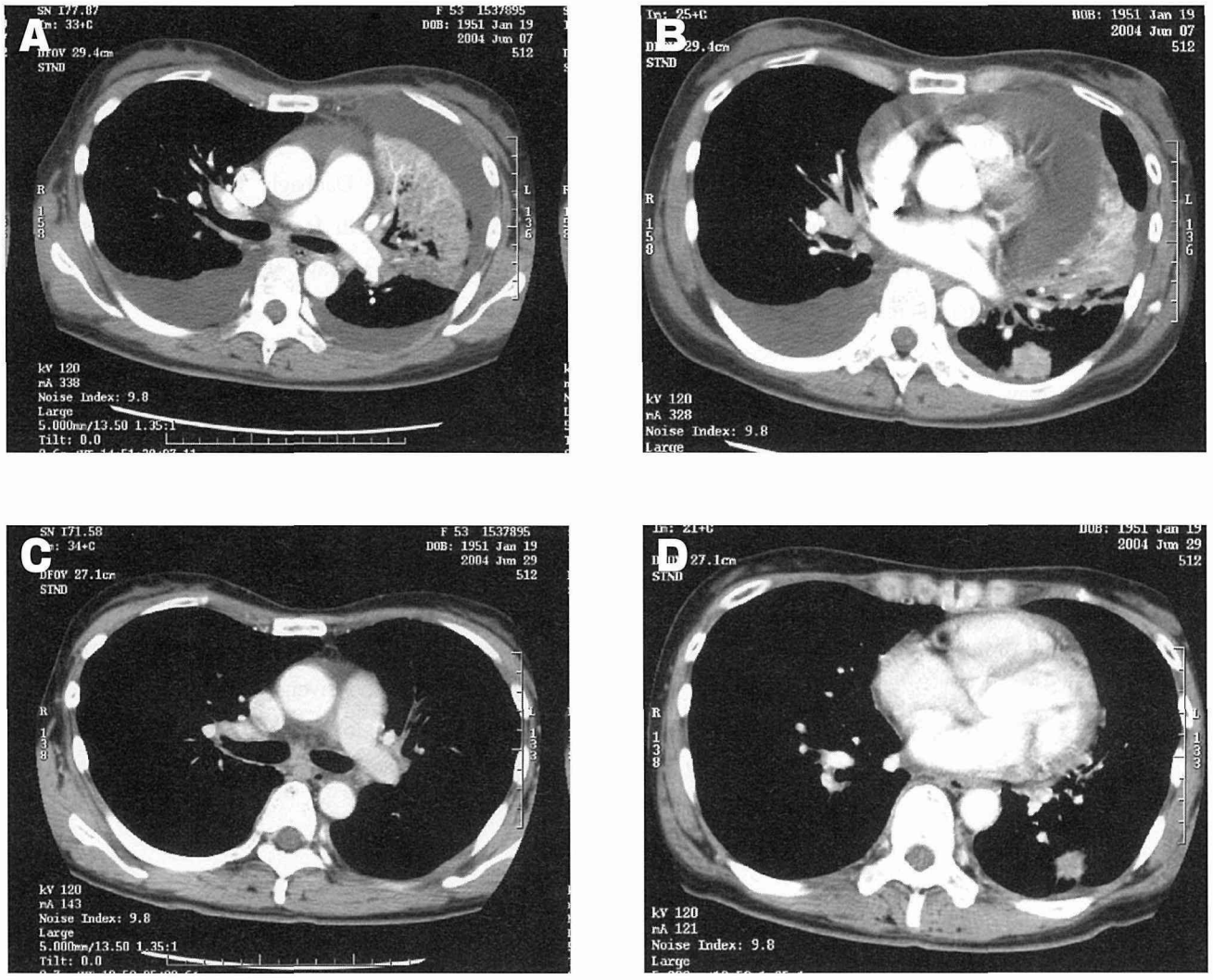

Figure 1: Contrast-enhanced CT of the chest.

A, B) CT on admission revealed massive pericardial effusion, bilateral pleural effusion, consolidation with CT angiogram and air bronchogram signs in the left upper lobe, a nodule in the left lower lobe, and hilar and mediastinal lymph node swelling. C, D) On day 18 of gefitinib treatment, consolidation in the left upper lobe and both pleural and pericardial effusion had resolved. The nodule in the left lower lobe and lymph nodes became much smaller.

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