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CASE REPORT

Lung Squamous Cell Carcinoma with De Novo c-Met Amplification

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SUMMARY

The study presented a case of lung squamous cell carcinoma (SCC) with de novo c-Met amplification. Four cycles of neoadjuvant chemotherapy were administered and partial response was achieved. Surgery was performed and the surgical margin was positive. Pathological diagnosis was lung SCC with c-ros oncogene 1 (ROS1) (+, 5%) and c-Met (++, 20%). The ROS1 rearrangement and c-Met amplification were detected using fluorescence in situ hybridization, and the result showed c-Met amplification positive and ROS1 negative. Four weeks after surgery, thoracic computed tomography scan showed a relapse of hilar and mediastinal lymph nodes. After three days, the patient died of hemoptysis.
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KEY WORDS

lung squamous cell carcinoma, c-Met, ROS1

LIST OF ABBREVIATIONS

SCC - squamous cell carcinoma
ROS1 - c-ros oncogene 1
NSCLC - non-small cell lung cancer
IHC - immunohistochemistry
CT - computed tomography
FISH - fluorescence in situ hybridization

INTRODUCTION

C-ros oncogene 1 (ROS1) rearrangement has been defined as a molecular subgroup of non-small cell lung cancer (NSCLC) for which Crizotinib showed marked antitumor activity. ROS1 rearrangements occurred in approximately 1% patients with NSCLC, mostly in those that were young never-smokers with adenocarcinomas [1]. The estimated positive rate of c-MET immunohistochemistry (IHC) was 44%, primarily in non-squamous cell carcinomas and tumors with stage III - IV [2]. Go et al. included 451 patients with resected

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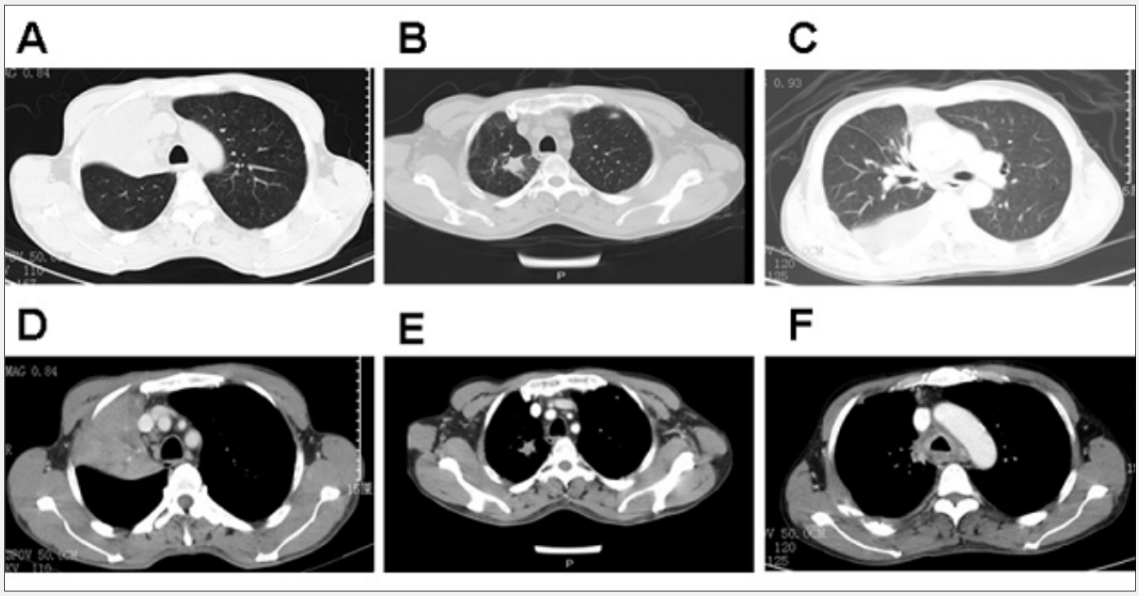

Figure 1. CT scan of the patient.

(A, D) Chest CT scan before chemotherapy. (B, E) Chest CT scan after four cycles of chemotherapy. (C, F) Chest CT scan four weeks after surgery.

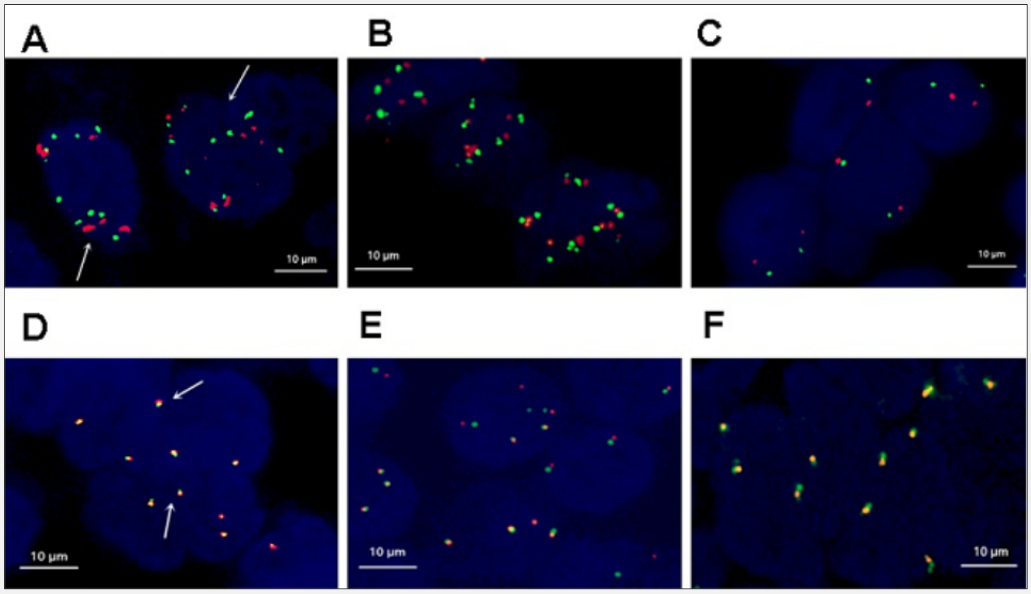

Figure 2. The result of FISH detection for the patient.

(A) The result of c-Met (positive). (B) Positive contrast of c-Met. (C) Negative contrast of c-Met. (D) The result of ROS1 (negative). (E) Positive contrast of ROS1. (F) Negative contrast of ROS1.

NSCLC and 64 with advanced pulmonary adenocarcinoma with no known oncogenic aberrations; the ROS1-positive adenocarcinomas in all patients revealed no alterations in c-Met amplification [3]. The present study reported a case of lung squamous cell carcinoma (SCC) with ROS1-positive (IHC), c-Met overexpression, and de novo amplification, who underwent surgery.

CASE PRESENTATION

A 57-year-old heavy smoker in good physical condition was diagnosed with a mass in the right lung through computed tomography (CT) scan during the health examination (Figure 1). Fludeoxyglucose positron emission tomography scan showed a mass in the right upper lung with hilar lymph nodes and mediastinal lymph nodes. No distant or cerebral metastasis was found. Bronchoscopy examination revealed lung SCC. Four cycles of chemotherapy were administered (Docetaxel combined with Nedaplatin), and partial response was achieved (Figure 1). Four weeks after completing the chemotherapy, surgery was performed. The surgical margin was positive and the pathological diagnoses for SCC and IHC analysis were as follows: ALK (D5F3) (-), ALK-NC (-), ROS1 (+, 5%), c-Met (++, 20%), Ck5/6 (+), Napsin A (-), P40 (+), P63 (+), TTF1 (-), and CK7 (+) (Supplementary Figure 1). The postoperative pathological stage was IIIA (T1cN2M0) according to the eighth edition of TNM classification for lung cancer. The result of ROS1 rearrangement and c-Met amplification detected by fluorescence in situ hybridization (FISH) showed c-Met amplification and ROS1 without rearrangement (Figure 2). Four weeks after surgery, the CT scan showed a relapse of hilar lymph nodes and mediastinal lymph nodes (Figure 1). Three days after the scan, the patient died of hemoptysis. This case report was approved by the Medical Ethical Committee of Zhejiang Cancer Hospital. The patient signed the informed consent for publication of this case report and accompanying images.

DISCUSSION

C-Met overexpression occurs more frequently than amplification, particularly in high-grade lung adenocarcinoma; c-Met amplification was correlated with c-Met expression. A majority of the patients with c-Met overexpression or amplification present lung adenocarcinoma [2,4]. In the current patient, both c-Met overexpression and amplification were demonstrated while the pathology was lung SCC. c-Met overexpression was an independent prognostic factor for overall survival in non-smoker NSCLC in univariate ($p = 0.01$) and multivariate ($p= 0.01$) analyses [4]. The disease progressed for one month after surgery and rapidly led to mortality in the patient. The poor prognosis of the patient might be correlated to c-Met overexpression and amplification. ROS1 rearrangement may also be a poor prognostic factor. Both IHC and FISH are efficient methods for the detection of ROS1 rearrangement. IHC would be a useful screening method in routine pathological laboratories while FISH is the “gold standard” for ROS1 detection [5]. For this patient, ROS1 was positive as assessed by IHC while ROS1 rearrangement was negative as detected by FISH.

CONCLUSION

c-Met overexpression and amplification can also be seen in lung SCC, which might be a poor prognosis factor. Although IHC is suitable for screening ROS1 rearrangement, the result needs to be substantiated further by FISH.

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Declaration of Interest:
All authors declare that they have no conflicts of interest.

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Supplementary Figure

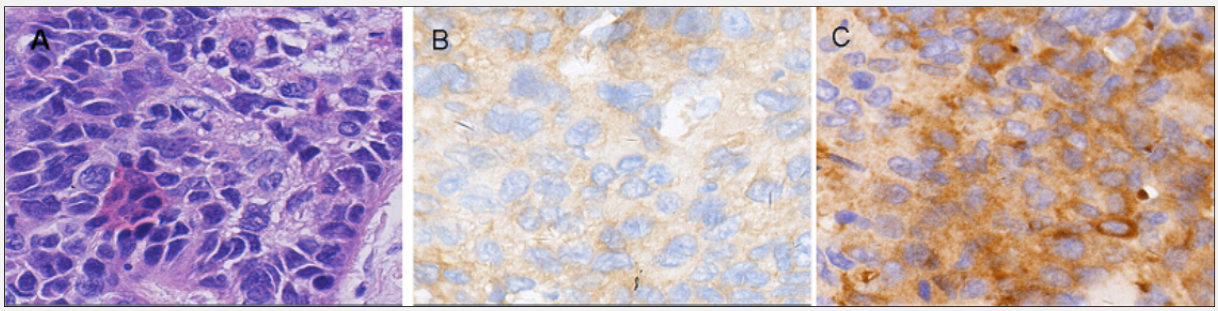

Figure 1. The results of pathology and IHC detection.

(A) Hematoxylin and eosin staining. (B) IHC of c-Met. (C) IHC of ROS1.