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Diagnosis Discrepancy from Different Original Specimen in PCR EGFR Mutation Test

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Abstract

Epidermal growth factor receptor (EGFR) mutation status guides treatment in non-small cell lung cancer; del E746-A750 in exon 19 and p.L858R in exon 21 are the most common mutations. We present a patient whose initial lymph node and computed tomography-guided pathology led to a suspicion of poorly differentiated carcinoma; however, during the clinical course, no obvious tumor origin was noted, and the pathologic morphology favored the squamous type. Not until the EGFR mutation status of secondary sites was checked did we confirm the disease origin as the lung.

Keywords: p.L858R mutation; EGFR-mutated; Non-small cell lung cancer

Introduction

Somatic mutations in the epidermal growth factor receptor (EGFR) gene have guided treatment of non-small cell lung cancer based on the response of EGFR to specific kinase inhibitors [1,2]. A recent study also described some EGFR mutations that were observed in non-adenocarcinoma lung cancer [3]. Further, EGFR mutation status has been explored in other types of cancer [4]. However, the treatment response is still not reliably predicted by mutation status. Even with this molecular diagnostic tool, clinical decisions are largely based on the patient's clinical presentation.

Case Report

A 52-year-old Chinese woman with a history of uterine myoma 10 years after an abdominal total hysterectomy and a T11 compression fracture from a traumatic fall underwent polymethyl metamethacrylate vertebroplasty. Post-surgery, she experienced ongoing dyspnea, and x-ray imaging showed massive right side pleural effusion. The thoracocentesis and pleural effusion led to a suspicion of adenocarcinoma, but her EGFR mutation status was negative. The initial evaluation of tumor markers revealed only mild CE-153 elevation (CEA: 2.0 and CA-153: 43.6). A chest computed tomography (CT) scan showed that metastatic carcinoma with right side pleural seeding, massive right side pleural effusion, and as well as bone and liver metastases.

For confirmation of the malignancy, pathological analysis of her lymph nodes, CT-guide liver biopsy was arranged, and the results showed poorly differentiated metastatic carcinoma. EGFR mutation test of the lymph node specimen by polymerase chain reaction (PCR) was done but showed negative. Pathology report of lymph node demonstrated CK(+), CK(7), TTF-1(-), CK20(-), ER(-), PR(-), and HER(-), there for no definite cancer origin can be made.

Sonography of her abdomen and a breast echocardiogram to survey for malignancies were negative. Later she developed massive right pleural effusion and had a pigtail catheter inserted times. Thoracoscopic surgery for chest tube insertion and pleural biopsy were arranged. Pathology report of pleural biopsy still presented poorly differentiated carcinoma.

We repeated the EGFR mutation analysis by PCR from the pleural biopsy specimen, confirming the presence of the p.L858R mutation in exon 21. Repeat tumor marker analysis showed the following results: CEA, 1.9; CA-153, 245.4; CA-125, 754.5; and C1-199, 73.8.

After the diagnosis was confirmed, we prescribed the tyrosine kinase inhibitor (TKI), erlotinib. After one month of treatment, she had stable x-ray findings. However, her dyspnea progressed, she had a fever on and off, and her sputum culture confirmed *Acinetobacter baumannii* pneumonia. The patient died due to hypoxia and hypercapnia. Our result suggested that EGFR mutation should be done on the primary origin in addition to the metastatic site (Figures 1 and 2).

Discussion

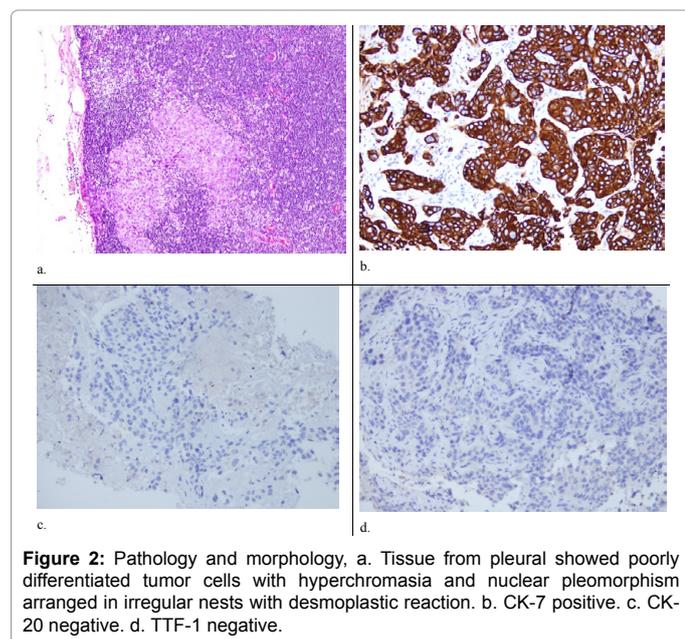EGFR is the cell-surface receptor for members of the epidermal
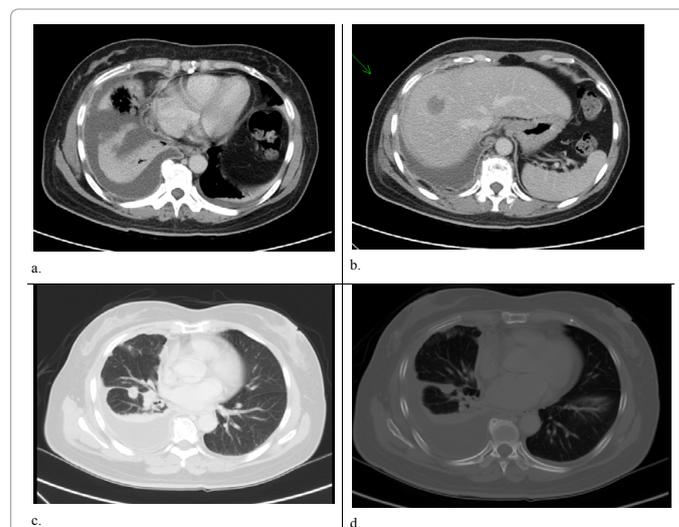
Figure 1: Chest computed tomography (CT) at diagnosis. a. Initial Chest CT with massive pleural effusion on the right side. b. Liver nodule suspected to be liver metastasis. c. View of the lungs showing some pleural seeding. d. View of the bones showing a suspected T11 pathological fracture.

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Figure 2: Pathology and morphology, a. Tissue from pleural showed poorly differentiated tumor cells with hyperchromasia and nuclear pleomorphism arranged in irregular nests with desmoplastic reaction. b. CK-7 positive. c. CK-20 negative. d. TTF-1 negative.

growth factor family of extracellular protein ligands [5]. Mutations affecting EGFR expression have been related to cancer formation. In the past decade, the superior response of pulmonary adenocarcinoma with EGFR mutations to TKIs has changed the treatment guidelines, especially for elderly patients and those with locally advanced or metastatic pulmonary adenocarcinoma [6]. More recent research has also confirmed the presence of EGFR mutations in other types of lung cancer [7] and in triple negative breast cancer [4]. However, the EGFR mutation rate is extremely low in non-adenocarcinoma NSCLC. The treatment response of other EGFR mutation-positive cancer types was described in the OPTIMAL study [8]. In most hospitals, EGFR mutations are detected with mutation-specific IHC; however, the quality of the sample and the number of cancer cells greatly impact the quality of the result. Using commercially available monoclonal antibodies, the specificity may be increased to 99.8%, but the sensitivity is variable [9,10]. The two most common mutations are del E746-A750 in exon 19 and p.L858R in exon 21 [11], which account for up to 80% to 90% of all mutations [12]. However, these mutations are rarely observed in other malignancies. In our patient, we assumed that the negative EGFR mutation result was due to inadequate specimen quality. Due to the persisting massive pleural effusion and clinical features consistent with adenocarcinoma, we reexamined the EGFR mutation status in the pleural biopsy specimen and detected the commonest p.L858R mutation.

We have no data to confirm that the metastatic site had the same EGFR mutation as the primary site or that all of the tumor tissue had the same EGFR mutation. In patients with multiple metastases, it is important to check the EGFR mutation status of the primary site.

Conclusion

Determining the EGFR mutation status is essential in the diagnosis and treatment of pulmonary adenocarcinoma, but an adequate and high-quality sample is essential. In some cases, repeat testing may be indispensable to establish the correct diagnosis.

References

1. Lynch TJ, Bell DW, Sordella R (2004) Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. N Engl J Med 350: 2129-2139.

2. Paez JG, Janne PA, Lee JC (2004) EGFR mutations in lung cancer: Correlation with clinical response to gefitinib therapy. Science 304: 1497-1500.

3. Han B, Tjulandin S, Hagiwara K (2015) Determining the prevalence of EGFR mutations in Asian and Russian patients with advanced non-small-cell lung cancer (ANSCLC) of adenocarcinoma (ADC) and non-ADC histology: Ignite study. Ann Oncol 26: i29-i30.

4. Hui-Fang Teng Y, Tan WJ, Thike AA, Cheok PY, Man-Kit Tse G, et al. (2011) Mutations in the epidermal growth factor receptor (EGFR) gene in triple negative breast cancer: possible implications for targeted therapy. Breast Cancer Res 13: R35.

5. Herbst RS (2004) Review of epidermal growth factor receptor biology. Int J Radiat Oncol Biol Phys 59: 21-26.

6. Zhang H, Berezov A, Wang Q, Zhang G, Drebin J, et al. (2007) ErbB receptors: From oncogenes to targeted cancer therapies. J Clin Invest 117: 2051-2058.

7. Xu J, Zhang Y, Jin B, Chu T, Dong X, et al. (2016) Efficacy of EGFR tyrosine kinase inhibitors for non-adenocarcinoma lung cancer patients harboring EGFR-sensitizing mutations in China. J Cancer Res Clin Oncol 142: 1325-1330.

8. Zhou C, Wu YL, Chen G, Feng J, Liu XQ, et al. (2011) Erlotinib versus chemotherapy as first-line treatment for patients with advanced EGFR mutation-positive non-small-cell lung cancer (OPTIMAL, CTONG- 0802): A multicentre, open-label, randomized, phase 3 study. Lancet Oncol 12:735-742.

9. Kozu Y, Tsuta K, Kohno T (2011) The usefulness of mutation-specific antibodies in detecting epidermal growth factor receptor mutations and in predicting response to tyrosine kinase inhibitor therapy in lung adenocarcinoma. Lung Cancer 73: 45-50.

10. Brevet M, Arcila M, Ladanyi M (2010) Assessment of EGFR mutation status in lung adenocarcinoma by immunohistochemistry using antibodies specific to the two major forms of mutant EGFR. J Mol Diagn 12: 169-176.

11. Seo AN, Park TI, Jin Y (2013) Novel EGFR mutation-specific antibodies for lung adenocarcinoma: Highly specific but not sensitive detection of an E746 A750 deletion in exon 19 and an L858R mutation in exon 21 by immunohistochemistry. Lung Cancer.

12. Shigematsu H, Gazdar AF (2006) Somatic mutations of epidermal growth factor receptor signaling pathway in lung cancers. Int J Cancer 118: 257-262.