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中国肿瘤临床 2012, Vol. 39 Issue (14): 970-973 DOI: doi: 10.3969/j.issn.1000-8179.2012.14.008

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非小细胞肺癌原发灶与淋巴结转移灶中KRAS和EGFR基因状态的比较及其临床意义

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Comparison of KRAS and EGFR Gene Statuses between Primary Non-Small Cell Lung Cancer and Local Lymph Node Metastases and Their Clinical Significance

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摘要 比较表皮生长因子受体(EGFR)基因和KRAS基因在非小细胞肺癌原发灶及其淋巴结转移灶之间突变状态的差异,并分析其与吉非替尼治疗非小细胞肺癌(NSCLC)疗效之间的关系。方法:收集天津医科大学附属肿瘤医院2010年5月至2010年11月间手术切除的80例NSCLC病例标本,利用直接测序和实时荧光定量PCR的方法分别检测原发灶和相应淋巴结转移灶中EGFR基因第18、19、20、21外显子及KRAS基因第12、13密码子的突变情况;其中5例在淋巴结转移灶中检出EGFR酪氨酸激酶抑制剂(EGFR-TKI)敏感型基因突变的患者接受了吉非替尼的新辅助靶向治疗。结果:80例患者中,检出原发灶携带KRAS和EGFR基因突变分别为1例和21例,检出转移灶携带KRAS和EGFR基因突变分别为7例和26例;分别有6例(7.50%)和7例(8.75%)患者其KRAS和EGFR基因状态在原发灶和转移灶之间不一致。直接测序法和实时荧光定量PCR法的检测结果一致。在5例接受吉非替尼治疗的患者中仅1例原发灶中未检出EGFR-TKI敏感型基因突变,并表现为疾病进展。结论:部分NSCLC患者中KRAS和EGFR的基因状态在肿瘤转移过程中会发生改变,在给予患者靶向治疗时不应忽视这一现象的存在。实时荧光定量PCR法比直接测序法更适用于临床的快速检测工作。

关键词: 表皮生长因子受体 KRAS基因 基因突变 非小细胞肺癌 EGFR酪氨酸激酶抑制剂 实时荧光定量PCR

Abstract: This study compares the differences of KRAS and epidermal growth factor receptor (EGFR) gene statuses between primary non-small cell lung cancer (NSCLC) and lung cancer with local nodal metastasis. Methods: The mutation of KRAS and EGFR between primary tumors and local lymph node metastases in 80 Chinese NSCLC patients were analyzed using direct sequencing and real-time polymerase chain reaction (RT-PCR), respectively. Five patients were given gefitinib as neoadjuvant therapy after the EGFR-tyrosine kinase inhibitor (TKI) sensitive mutations were detected in their metastasized mediastinal lymph node biopsy. McNemar's test was then used to compare the EGFR and KRAS mutation statuses between primary tumors and homologous local lymph node metastases. Data evaluation was carried out using SPSS-13.0 statistical software. Results: Among the 160 samples, 1 case with primary tumor and 7 metastases were identified with KRAS mutations, whereas 21 primary tumors and 26 metastases were recognized with EGFR mutations. The KRAS and EGFR mutation statuses were different between the primary tumors and the corresponding metastases that occurred in 6 (7.5%) and 7 (8.75%) patients, respectively. Moreover, consistent results were obtained through direct sequencing and RT-PCR. Among the five patients who received targeted therapy, primary tumor disease progression was observed in the patient with no TKI-sensitive mutations. Conclusion: Our results show a discrepancy in KRAS and EGFR mutation statuses between primary tumors and corresponding metastases in the small number of Chinese NSCLC patients tested. This observation may have important implication for the use of targeted TKI therapy in treating NSCLC patients. Moreover, RT-PCR is more convenient for clinical examination compared with direct sequencing.

Key words: Epidermal growth factor receptor KRAS gene Gene mutation Non-small cell lung cancer Epidermal growth factor receptor tyrosine kinase inhibitor

收稿日期: 2011-11-23; 出版日期: 2012-07-30

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·非小细胞肺癌原发灶与淋巴结转移灶中KRAS和EGFR基因状态的比较及其临床意义[J]. 中国肿瘤临床, 2012, 39(14): 970-973.

· Comparison of KRAS and EGFR Gene Statuses between Primary Non-Small Cell Lung Cancer and Local Lymph Node Metastases and Their Clinical Significance[J]. Chinese Journal of Clinical Oncology, 2012, 39(14): 970-973.

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