

Relationship of Epidermal Growth Factor Receptor Gene Mutations And serum Levels of Ligands in Non-Small Cell Lung Carcinoma Patients

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Abstract : Non-Small Cell Lung Carcinoma (NSCLC) is associated with a number of gene mutations in epidermal growth factor receptor (EGFR). The prognostic significance of mutations in exons 19 and 21, together with serum levels of EGFR, amphiregulin (AR), and Transforming Growth Factor-alpha (TGF- α) are implicated in diagnosis and treatment. The aim of this study was to examine the relationship of EGFR mutations in selected exons with the expression of relevant ligands in sera samples of NSCLC patients. For this, a group of NSCLC patients (n=98) referred to the hospital for lung surgery with a mean age of 59 ± 10.5 were enrolled (M/F: 75/23). Blood specimen was collected from each patient. Besides, formalin fixed paraffin embedded tissues were processed for DNA extraction. Gene mutations in exons 19 and 21 were detected by direct sequencing, following DNA amplification which was done by PCR (Polymerase Chain Reaction). Also, serum levels of EGFR, AR, and TGF- α were measured by ELISA. The results of our study show that EGFR mutations were present in 37% of Iranian NSCLC patients. The most frequently identified mutations were deletions in exon 19 (72.2%) and substitutions in exon 21 (27.8%). The most frequently identified alteration, which is considered as a rare mutation, was the E872K mutation in exon 21, which was found in 90% (9 out of 10) cases. EGFR mutation detected in exon 21 was significantly ($P < 0.05$) correlated with the levels of its ligands, EGFR and TGF- α in serum samples. Furthermore, it was found that increased serum AR ($> 3 \text{ pg/ml}$) and TGF- α ($> 10.5 \text{ pg/ml}$) were associated with shorter overall survival ($P < 0.05$). The results clearly showed a close relationship between EGFR mutations and serum EGFR and serum TGF- α . Increased serum EGFR was associated with TGF- α and AR and linked to poor prognosis of NSCLC. These findings are implicated in clinical decision-making related to EGFR-Tyrosine kinase inhibitors (TKIs).

Keywords : lung cancer, Iranian patients, epidermal growth factor, mutation, prognosis

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