Expression of Protein Kinase EML4-ALK Gene in Non-Small Cell Lung Cancer (NSCLC) in a University Hospital of Reference in Latin America

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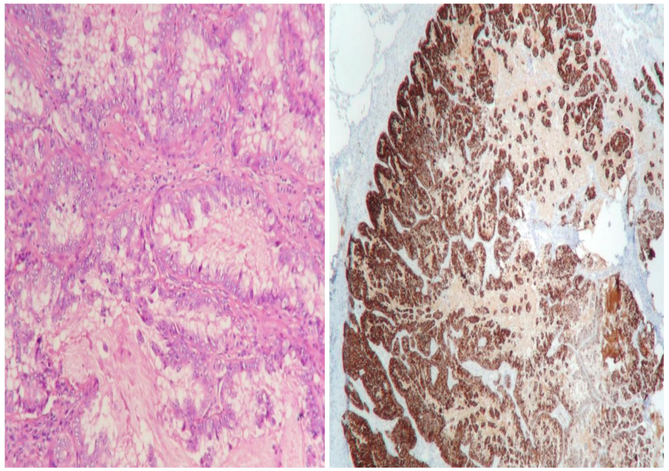
Background

Lung cancer is the leading cause of cancer deaths worldwide and exists in two distinct entities: small and non-small cell lung cancer, representing 85% of lung cancers, and generally presents at diagnosis with locally advanced or metastatic disease. The rare genetic changes, such as anaplastic lymphoma kinase (ALK) gene rearrangements, most often consisting in a chromosome 2 inversion leading to a fusion with the echinoderm microtubule-associated protein like 4 (EML4) gene, results in the abnormal expression and activation of this tyrosine kinase in the cytoplasm of cancer cells. This rearrangement occurs in 2–5% of NSCLC, predominantly in young patients (50 years or younger) and in non-smokers or former smokers with adenocarcinoma. This aberration most commonly occurs independent of EGFR and KRAS gene mutations. Inmunohistochemical (IHC) analysis is a cost-effective alternative for the detection of ALK gene rearrangements and recent guidelines from the College of American Pathologists, International Association of the Study of Lung Cancer, and The Association for Molecular Pathology supports the use of IHC screening as long as it has been appropriately validated.

Methods

Between November 2014 and March 2015, 20 tumor samples were obtained in Fundacion Valle del Lili, Cali-Colombia. The Ventana anti-ALK (D5F3) assay was performed using OptiView DAB IHC detection kit and OptiView Amplification Kit, with external controls rated with positive and negative cell lines (H2228 and CALU-3 respectively), with appropriate expression.



A. Mucinous adenocarcinoma histological variant (H & E) B. Positive expression for the detection of protein kinase gene of EML4-ALK (IHC)

Results

We analyzed the samples of 20 patients with NSCLC using immunohistochemistry. We found tumor cells in 100% of the samples. The average age was 62.8 years ± SD, 45% (9) women and 55% (11) men. The protein kinase expression of EML4-ALK gene was found in 20% (4) of the cases, which included 3 females. Thirteen cases were adenocarcinoma and fourteen patients were diagnosed in stage IV. Fourteen of twenty patients received chemotherapy. During this time in our hospital began the Phase Three Study of the molecule specific for this tumor rearrangement. The mortality in this group of patients was 3 of 20.

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Conclusions

Knowledge of cancer biology and oncogenic drivers has led to a better understanding of lung cancer and the development of very active targeted therapies. ALK rearrangements have been identified as oncogenic drivers for a subgroup of lung adenocarcinoma. The clinical benefit gained by targeted therapies has led to transition from a standardized therapeutic approach to a personalized approach based on molecular tumor characteristics in current clinical practice.

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