ALK Translocation in Non-small Cell Lung Cancer with Adenocarcinoma and Squamous Cell Carcinoma Markers

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A 47-year-old white Hispanic man with a never smoking history was incidentally found to have a right-sided pulmonary nodule, hilar, and mediastinal adenopathy. Sampling of level 10R, 11R, and 7 nodal stations disclosed a carcinoma (Figure 1A) that stained positive, by immunohistochemistry, for thyroid transcription factor 1 (Figure 1B), transformation-related protein 63 (P63; Figure 1C), and cytokeratin (CK5/6; Figure 1D). By using the newly accepted International Association for the Study of Lung Cancer (IASLC)/European Respiratory Society (ERS) classification for lung cancers, the tumor was best classified as a non-small cell lung cancer (NSCLC), not otherwise specified; because it had both adenocarcinoma (thyroid transcription factor 1) and squamous cell carcinoma (P63, CK5/6) markers. There was no evidence of extrathoracic tumor involvement, and the patient was felt to have stage III NSCLC. The tumor had no epidermal growth factor receptor or V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS) gene mutations. A break-apart fluorescence in situ hybridization probe for the anaplastic lymphoma kinase (ALK) demonstrated an ALK translocation.

ALK translocated NSCLCs account for approximately 5% of all NSCLCs and 20% of NSCLCs from never smokers. The main clinicopathologic characteristics of these NSCLCs, to date, include younger age at diagnosis, never or light smoking history, adenocarcinoma histology, and signet-ring cells. However, tumors with squamous cell carcinoma or adenosquamous histologies, albeit at a much lower frequency than adenocarcinomas, have been reported to harbor ALK translocations. One report described 3 cases on non-adenocarcinoma (with 1 squamous cell carcinoma and 1 adenosquamous carcinoma) among 82 ALK translocated NSCLCs, and another 1 case of nonadenocarcinoma (1 adenosquamous carcinoma) among 19 ALK translocated NSCLCs. Because the ALK tyrosine kinase inhibitor crizotinib is highly effective in ALK translocated NSCLC, it may be imperative to identify all NSCLCs that harbor ALK translocations in the near future. Our case is instructive and highlights that tumors with squamous cell carcinoma (P63 and CK5/6) immunohistochemical markers also need to be screened for ALK translocations—especially in never smokers—if all cases of ALK translocated NSCLC are to be identified.

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