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 1*A*) that stained positive, by immunohistochemistry, for thyroid transcription factor 1 (Figure 1*B*), transformation-related protein 63 (P63; Figure 1*C*), and cytokeratin (CK5/6; Figure 1*D*). 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[1]; 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.[2,3] 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.[3] However, tumors with squamous cell carcinoma or adenosquamous histologies, albeit at a much lower frequency than adenocarcinomas, have been reported to harbor *ALK* translocations.[4,5] One report described 3 cases on non-adenocarcinoma (with 1 squamous cell carcinoma and 1 adenosquamous carcinoma) among 82 *ALK* translocated NSCLCs,[4] and another 1 case of nonadenocarcinoma (1 adenosquamous carcinoma) among 19 *ALK* translocated NSCLCs.[5] Because the ALK tyrosine kinase inhibitor crizotinib is highly effective in *ALK* translocated NSCLC,[4] 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[1] 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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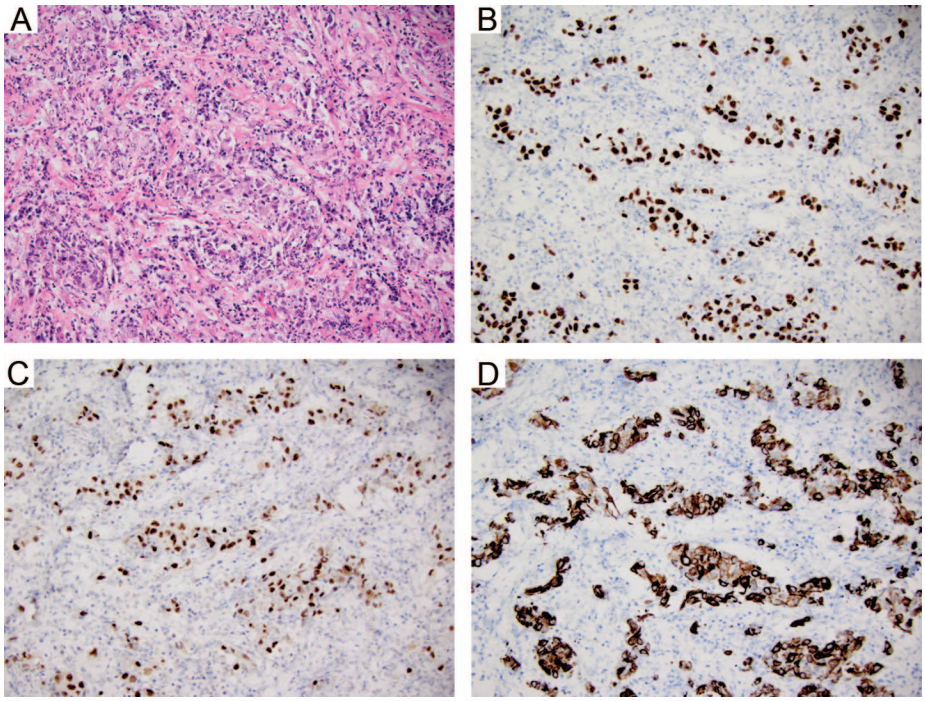

FIGURE 1. *A*, Level 7 mediastinal lymph node with carcinoma (hematoxylin and eosin). *B*, Immunohistochemical (IHC) staining for thyroid transcription factor-1. *C*, IHC staining for P63. *D*, IHC staining for CK5/6. Magnification, ×200.