

Complementary Value of Electron Microscopy and Immunohistochemistry in the Diagnosis of Non-Small Cell Lung Cancer

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Background: Pathological classification of lung cancer has been redefined by cytogenetics and molecular data. Consequently, therapeutic targets have been identified for pulmonary adenocarcinoma (ADK). Thus, it is crucial to accurately distinguish between ADK and squamous cell carcinoma (SQCC) in poorly differentiated cases. Immunohistochemistry (IHC) is very helpful in making this differential diagnosis. However, a subset of cases remains classified as Non-Small Cell Lung Carcinoma, NOS (NSCLC-NOS), after IHC. In these cases, Electron Microscopy (EM) can be a useful tool, as it objectively identifies glandular differentiation. The aim of this study was to determine the value of EM and IHC in the NSCLC-NOS subclassification.

Design: Forty-eight NSCLC-NOS cases were selected from the files of Parc de Salut Mar Biobank, Barcelona, Spain. IHC panel consisted of TTF-1 and p40 antibodies, and for older cases, p63 was available. Tissue was retrieved from paraffin blocks and processed for EM. The results of each technique were compared to the final diagnosis (gold standard), that was derived from the combination of light microscopy, IHC, EM, cytogenetics, molecular studies and data of the resection specimen if available.

Results: IHC concurred with the final diagnosis in 38 cases (79.2%) (Kappa=0.517). The identification of ADK by IHC had a sensitivity of 73%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 52.4%. EM results agreed with the final diagnosis in 35 cases (72.9%) (Kappa=0.471). For the diagnosis of ADK, IHC failed to recognize 10 cases (TTF1, P40 negative) and in all of them EM was conclusive, while in 10 cases with inconclusive EM, IHC gave the diagnosis. Thus, the values obtained for EM were identical to those of IHC: sensitivity 73%, specificity 100%, PPV 100% and NPV 52.4%. Combining results of IHC and EM, 47 cases (97.9%) were coincident with the final diagnosis (Kappa=0.943).

Conclusions: The results of this retrospective study support that EM can provide useful information in the diagnosis of NSCLC, mainly in recognizing poorly differentiated ADK, and that it has a particularly helpful role in cases in which IHC provides inconclusive results.