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Utility of homozygous p16/CDKN2A deletion by fluorescence in-situ hybridization analysis and P16 immunohistochemistry in malignant pleural mesothelioma in Egyptian patients.

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Abstract

Background: Malignant pleural mesothelioma (MPM) is an aggressive cancer caused basically by environmental exposure to asbestos and has limited overall treatment options and poor prognosis. The current standard diagnosis of MPM requires the testing of multiple immunohistochemical (IHC) markers on formalin-fixed paraffin-embedded tissue to differentiate MPM from other lung malignancies. Owing to the lack of a single, accurate IHC biomarker for MPM, recent studies have focused on identifying new diagnostic modalities.
Objective : Homozygous deletion of 9p21 is one of the most common genetic alterations in malignant mesotheliomas. In this work, we evaluated homozygous 9p21 (p16/ CDKN2A) deletion by fluorescence in-situ hybridization (FISH) analysis in Egyptian patients with MPM using paraffin-embedded tissue specimens. We also studied the status of p16 expression by IHC, and results of both were analysed separately and in relation to each other.
Patients and methods : Thoracoscopic pleural or true-cut needle biopsies from 42 cases of primary MPM were examined pathologically on routine hematoxylin and eosin histology. Age matched and sex-matched 12 cases diagnosed as having non mesothelioma diseases were included as controls. IHC markers to differentiate epithelioid MPM from metastatic lung adenocarcinoma were Carcino Embryonic Antigen (CEA) and calretinin. Representative tissue blocks were selected for p16 expression by IHC and 9p21 deletion by FISH.

Results : Deletion of 9p21 was demonstrated in 39 (92.8%) of 42 MPM cases, whereas it was not detected in any of the controls (P=0.002). Evaluating the diagnostic accuracy of P16 detected by FISH showed a positive sensitivity of 92.8%, specificity of 100%, and a power of performance of 0.93, with an overall accuracy to classify MPM correctly of 94.4%. However, p16 inexpression by IHC showed a sensitivity of 57.1%, specificity of 25%, with a very low power of performance of −0.1, and an overall accuracy of 50%. The discrepancy between the results of both techniques was analysed.
Conclusion : Detection of homozygous p16 deletion by FISH is more sensitive and specific to distinguish MPM from others compared with IHC p16 inexpression and may represent an alternative diagnostic tool for MPM, especially in challenging cases. IHC p16 may be of prognostic value.

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