

Lack of BAP1 nuclear staining may help identify mesothelioma from other malignancies with similar morphology.

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BACKGROUND: The differential diagnosis of malignant mesothelioma(MM) and other malignancies with similar morphology is very difficult sometimes. BRCA-associated protein 1 (BAP1) has emerged as a promising biomarker for malignant mesothelioma. lack of BAP1 nuclear staining correlates with lack of Ino80 nuclear staining. It has been suggested that BAP1 mutations always result in loss of Ino80 nuclear staining

HYPOTHESIS: The central hypothesis of this proposal is that BAP1 nuclear staining may help in the difficult differential diagnosis between MM and metastasizing lung cancer to the pleura, and with carcinosarcomas, which are tumors that morphologically are difficult to distinguish from MM.

METHODS: We studied 22 MM, 10 primary lung adenocarcinomas, 10 primary lung squamous cell carcinomas, and 15 primary carcinosarcoma biopsies from Zhejiang Cancer Hospital in China. These biopsies were independently evaluated by pathologists experts in MM diagnosis at the Zhejiang Cancer Hospital (Dr. Guo) and at the University of Hawaii Cancer Center (Dr. Carbone) who concurred with the diagnosis. IHC analysis of BAP1 protein expression was performed using a mouse monoclonal anti-BAP1 antibody which recognizes the epitope between aa 430 and 739 and; therefore, it is predicted to detect BAP1 wild-type and mutant forms that retain the NLS. To decide whether the staining was real, we stained all these MM biopsies for Ino80 a protein that requires BAP1 for stabilization and localization on the DNA. .

RESULTS: Strong nuclear staining was detected in 100% of the tumor cells in all of adenocarcinomas, squamous cell carcinomas and primary carcinosarcomas. BAP1 was lost in 76.5%(13/17) of epithelioid cases. but was retained in all sarcomatoid cases (n=2); 33.3%(1/3) of biphasic cases showed loss. 4 out of 14 cases showed some cytoplasmic staining. A total of 8 MM showed nuclear staining, and 4/8 MM showed some weak staining in about 1-20% of tumor cells. Moreover, BAP1-negative cases demonstrated loss of staining in both the epithelioid and sarcomatoid components. BAP1-negative cases demonstrated loss of Ino80 nuclear staining, We conclude that BAP1 loss is frequent in epithelioid MM, and Ino80 lack of nuclear staining can be used to validate absence of BAP1 staining. .