Evidence-Based Immunohistochemical Panel for the Distinction of Hepatocellular Carcinoma and Metastatic Carcinoma

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BACKGROUND

Commonly used markers for diagnosis of hepatocellular carcinoma (HCC) have several limitations:

(1) The sensitivity of Hepatocyte Paraffin 1 (HepPar) and polyclonal CEA (pCEA) is >80% but is low in poorly differentiated cases.

(2) Glypican-3 (GPC) helps in identification of poorly differentiated HCC, but its specificity is not well established.

(3) Adenocarcinoma (AC) markers like MOC31, CK7 and CK19 can be positive in a subset of HCC.

Since limited tissue is available in most cases, it is desirable to determine the combination of markers that will yield the highest sensitivity and specificity.

METHODS

Immunohistochemistry was performed on tissue microarrays generated from 161 HCC, 24 neuroendocrine tumors (NE) and 386 ACs (65 gastroesophageal, 6 pancreatobiliary, 55 lung, 205 breast, 55 colorectal). Three hepatocellular (HepPar, GPC, pCEA) and 6 AC markers (MOC31, CK7, CK19, BerEP4, B72.3, CD15) were evaluated. Positive staining was defined as moderate to strong staining in at least 10% of the tumor.

RESULTS

Hepatocellular markers

HepPar was the most sensitive hepatocellular marker (75%). When combined with GPC, it yielded a sensitivity of >95% for HCC; their combined expression was not seen in any non-HCC case (Table 1). HepPar was expressed by 4% of AC and GPC was expressed by 5% of AC, including gastroesophageal, lung, and breast. One colorectal AC expressed HepPar as did one NE.

pCEA (canalicular pattern) had low sensitivity for HCC (54%) compared to HepPar and GPC. In 24 cases of AC (11% of pCEA+ cases) including pancreatobiliary, breast, and colorectal, the luminal staining pattern was difficult to separate from the canalicular pattern of HCC.

Adenocarcinoma markers

MOC31 was the most sensitive marker for NE and AC (96% and 91%, respectively). In 24 cases of AC (11% of pCEA+ cases) including pancreatobiliary, breast, and colorectal, the luminal staining pattern was difficult to separate from the canalicular pattern of HCC.

Combined use of hepatocellular and AC markers for diagnosis of HCC

The combination of the most sensitive hepatocellular (HepPar) and AC (MOC31) markers revealed the characteristic HepPar+/MOC31+ phenotype in 71% of HCC (Table 3). HCC with the aberrant HepPar+/MOC31+ immunophenotype pose the highest potential for error (Table 4). Majorly HCC with the aberrant HepPar+/MOC31+ immunophenotype express GPC and are negative for CK19 (Table 5). Hence, addition of GPC and CK19 to HepPar and MOC31 yields a powerful 4-stain panel that correctly identifies 97% of all cases of HCC and 92% of aberrant HepPar+/MOC31+ HCC.

REFERENCES


