CAN IMMUNOHISTOCHEMISTRY DISTINGUISH BETWEEN PRIMARY AND METASTATIC HEPATIC CARCINOMA?

(Fucich LF, Cheles MK, Thung SN, Gerber MA and Marrogi AJ. Primary vs Metastatic Hepatic Carcinoma : An immunohistochemical study of 34 cases. Arch Pathol Lab Med 1994; 118 : 927-30)

SUMMARY

Objective : To determine if immunohistochemistry is useful to distinguish between primary and metastatic hepatic carcinoma.

Study Design : Cases of hepatocellular and adenocarcinoma of liver from surgical and autopsy pathology files as diagnosed on routine histopathology with the help of haematoxylin-eosin stain.

Patients : Thirty four patients with hepatic space - occupying lesions (a single lesion in 6 patients, multiple lesions in 5 patients and unspecified in remaining 23 patients). The histopathology diagnosis included 14 hepatocellular carcinoma (HC), 10 cholangiocarcinoma (CC), 7 metastatic carcinoma (MC) (colonic : n=4, pancreatic : n=2, mammary : n=1) and three cases were unclassified.

Intervention : The paraffin embedded blocks of biopsy and autopsy cases were taken out and sections of 4 µm thickness were cut. The immunohistochemistry staining was carried out by using a panel of 7 monoclonal antibodies. The monoclonal antibodies which were used were as follows - α fetoprotein (AFP), α 1 antitrypsin (AAT), monoclonal carcinoembryonic antigen (MCEA), myelomonocytic antigen (Leu-M1), tumour associated glycoprotein (B72-3), A-subunit coagulation Factor XIII (Factor XIIIa) and blood group substance (Le^x).

Main Outcome Measures : Sections were defined as immunohistochemically 'positive' if definitive crisp labelling was seen in atleast 10% of tumour cells by two observers. The positive staining was classified as either predominantly cytoplasmic or membranous or both. The presence or absence of nuclear staining was also noted.

Main Results : The typical immunoreactivity of HCs included positivity for AAT, AFP and factor XIIIa and no staining for B72-3 and Leu-M1. Of 14 patients who were originally diagnosed as having HC, AAT was expressed in 86% and AFP was

expressed in cytoplasm in half of the patients. Factor XIIIa displayed cytoplasmic reactivity in 71% cases of HC. Le^x was present focally in 3 cases of HC, as was monoclonal CEA. These 3 cases showed features of hepatocholangiocarcinoma. In all 10 cases of CC there was staining for both Leu-M1 and Le^x. The pattern of reactivity was cytoplasmic for Leu-M1 and it was both cytoplasmic and membranous for Le^x. In 6 cases there was expression of B72-3 and monoclonal CEA in cytoplasm. None of the cases of CC showed staining for AFP and AAT only one case showed staining for AAT and factor XIIIa. As far as MC is concerned, there was expression of both Leu-M1, and Le^x in a cytoplasmic distribution in all the seven cases. The membranous accentuation of Le^x seen in all cases of CC was not present in the cases of MC. Four of the 7 cases of MC showed reactivity for B72-3 as well and the staining pattern of Leu-M1, and B72-3 was predominantly both cytoplasmic and membranous. In 3 of the 7 cases of MC, there was expression of monoclonal CEA, in 1 case there was expression of AAT and in 2 cases there was expression of factor XIIIa.

Conclusions : Histologic differentiation of HC from CC and MC can be greatly aided by immunohistochemical studies. Using a panel of 7 antibodies, cases of HC displayed cytoplasmic reactivity for AAT, AFP and factor XIIIa. Cases of CC showed membranous and cytoplasmic reactivity for Le^x but only cytoplasmic reactivity for Leu-M1, and B72-3. On the other hand cases of MC showed only cytoplasmic staining but not membranous accentuation for Le^x but Leu-M1, and B72-3 showed membranous as well as cytoplasmic staining. The antibody MCEA showed variable results and hence was considered not useful. Therefore the results strongly suggest that a panel of 6 monoclonal antibodies (except MCEA) will greatly help in differentiating between primary and metastatic carcinoma.

Comments

The differential diagnosis of primary vs metastatic hepatic carcinoma can be a difficult problem on routine histology especially so when clinical history does not indicate a primary lesion else-

where. Several studies have suggested the use of immunohistochemical markers, such as polyclonal CEA or various keratins with variable success to distinguish HC from CC. The issue of differentiating CC from MC has also been addressed recently in the literature.

The authors decided to use all the new as well as previously available monoclonal antibodies as a retrospective study in form of a panel of 7 antibodies. They demonstrated that immunohisto-

chemistry is useful to distinguish between primary and metastatic hepatic carcinoma and recommended a panel of 6 monoclonal antibodies to achieve the aim.

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