DIFFERENTIAL EXPRESSION OF DF3 ANTIGEN BETWEEN PAPILLARY CARCINOMAS AND BENIGN PAPILLARY LESIONS OF THE BREAST

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ABSTRACT

Murine monoclonal antibody (MAb) DF3, prepared against a membrane-enriched fraction of breast carcinoma metastasis, has previously shown differential reactivity to breast carcinoma cells and normal or benign breast epithelial cells. Using the avidin-biotin peroxidase complex immunohistochemical method, we have examined cytoplasmic DF3 antigen expression in breast papillary lesions to define whether the MAb DF3 distinguishes papillary carcinomas from benign papillary lesions. MAb DF3 reacted with antigen in the cytoplasm in 17 of 19 papillary carcinomas, 12 (63%) of which demonstrated significant levels of cytoplasmic DF3 expression (>20% of carcinoma cells reactive). In contrast, none of the benign lesions examined demonstrated more than 10% of epithelial cells reactive in the cytoplasm. Specimens containing a spectrum of lesions from benign papilloma through atypical hyperplasia to carcinoma showed a corresponding general increase in DF3 antigen expression in the cytoplasm with the transition of papilloma to carcinoma. These results suggest that papillary carcinomas express DF3 antigen in the cytoplasm, and this may help to distinguish them from benign papillary lesions on the basis of cytoplasmic reactivity.

INTRODUCTION

Surgical treatment for papillary lesions of the breast, including papillary carcinoma, papilloma, or papillomatosis (epitheliosis), should be performed on the basis of precise histopathological diagnosis and biological behavior of given lesions. The relationship of benign papillary lesions to carcinoma has been described using follow-up studies¹,² and a three-dimensional reconstruction study.³ The histopathological differentiation of papillary carcinoma from benign papillary lesions has been described.⁴⁻⁷ It is still difficult, however, to diagnose papillary

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cancer when no foci of invasive carcinoma cells are detected or the given tumor cells lack the complete criteria for the diagnosis of carcinoma in situ. In our study, we were able to help differentiate papillary carcinoma from benign papillary lesions based on the expression of breast carcinoma-associated antigen.

The identification of human breast carcinoma-associated antigens and the development of monoclonal antibodies (MAbs) directed against these antigens have been the subject of much investigation. Among them, MAb DF3, generated by using a membrane-enriched fraction of a human metastatic breast carcinoma as immunogen, recognized high molecular weight determinants (330,000 to 450,000) found in secretory breast epithelial cells and breast carcinomas. The antigen reactive with this MAb was found on the surface of live mammary carcinoma cell lines (MCF-7 and BT-20) but was not found on the surface of colon carcinoma cell lines by using solid-phase radioimmunoassays. Elevated levels of DF3 antigen have been found in the circulation of patients with breast carcinomas. Furthermore, using a radioimmunometric method, Gion et al. have recently demonstrated higher levels of DF3 antigen (CA15/3) in the cytosol of breast carcinoma than in normal breast tissues.

MAb DF3 has shown a strong differential reactivity to cytoplasmic antigen in breast carcinomas versus reactivity to antigen concentrated on apical borders of benign lesions and normal mammary epithelial cells by using immunohistochemical assays. We have recently demonstrated elevated levels of cytoplasmic DF3 antigen expression in atypical hyperplasia as well as carcinoma in situ of the breast, compared with hyperplasia without atypia and nonproliferative disease. This study was initiated to define if a difference exists on the basis of level of expression of tumor-associated antigen between malignant and benign papillary lesions of the breast.

MATERIALS AND METHODS

Monoclonal Antibodies

Murine IgG1 MAb DF3 was generated by an immunization of BALB/c mice with a partially purified membrane-enriched fraction of a human breast carcinoma metastasis to the liver. The characterization of MAb DF3 has been described in detail elsewhere. An isotype identical control MAb MOPC-21 (murine IgG1, Litton Bionetics, Charleston, SC) was used as a negative control for all tissue samples.

Tissues

Formalin-fixed, paraffin-embedded tissue specimens were obtained from 19 patients with papillary carcinoma and 16 patients with benign papillary lesions of the breast from the Department of Pathology, Yale University School of Medicine, New Haven, CT. The serial sections of each specimen were cut 5 μm thick and mounted on gelatin-coated glass slides. One section from each specimen was stained with hematoxylin and eosin (H&E) for histopathological diagnosis.

Histopathological Diagnosis

The differential diagnosis of papillary lesions was basically made using the criteria proposed by Kraus and Neubecker and Azzopardi. The criteria, including cellular atypia as well as structural atypia to differentiate intraductal carcinoma from benign papillary lesions, were described in detail elsewhere. Benign papillary lesions were classified