IMMUNOHISTOCHEMICAL PROGNOSTIC PARAMETERS IN BREAST CARCINOMA

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ABSTRACT

The biological behaviour of breast cancer is unpredictable and present prognostic markers do not accurately indicate survival times for individual patients. Recent investigations have focused on a search for intracellular markers which might provide information unattainable by histology. This thesis examines the relationship between traditional pathological prognostic parameters and several new potential prognostic indicators, identified and quantified by immunohistochemical staining, in 115 malignant breast neoplasms.

A modified technique of identifying estrogen receptor (ER) protein in frozen sections and imprints utilizing a new commercial monoclonal anti-ER antibody is reported. Optimal preservation of the ER antigen is observed following fixation in periodate-lysine-paraformaldehyde (PLP) for 10 minutes. An improved, reproducible method of detecting ERs in formalin-fixed paraffin sections using the anti-ER antibody is described.

A recently synthesized monoclonal antibody to proliferating cells, Ki-67, is used to estimate the tumour growth fraction (GF) in all cases and an inverse relationship between GF and ER status is identified. Coexpression of cytokeratin and vimentin intermediate filaments (IFs) is documented, for the first time, in 10.4 per cent of ductal carcinomas. Acquisition of vimentin correlates strongly with a high tumour GF and the role of vimentin as a potential prognostic marker is discussed. Staining of nucleolar organizer regions (NORs) with the silver impregnation technique of

Crocker et al (1986) reveals a correlation between the NOR count and the Ki-67 count. Finally, it is recommended that all lymph nodes in cases of node-negative breast cancer be stained with anti-cytokeratins following the identification of "missed" micrometastases in 22 per cent of 55 cases studied by this technique.

Alpha-lactalbumin, pregnancy-specific ß1-glycoprotein (SP1) and prolactin, three traditional markers for breast carcinoma, are assessed and deemed non-specific and of no prognostic value. Antisera to basement membrane and myoepithelial cell antigens assist in identifying early invasive foci in intraductal carcinomas and in differentiating sclerosing adenosis from well-differentiated carcinoma. Anti-factor VIII and UEA I, employed to detect vascular invasion, provide no advantage over an assessment of haematoxylin and eosin-stained sections.

In conclusion, lymph node status and tumour GF are considered the major prognostic parameters in breast cancer. Minor prognostic markers include ER status, histological type and grade, and tumour size. Expression of vimentin IFs by breast carcinomas and NOR counts may also prove to be of prognostic value.