Neural Cell Adhesion Molecule in Breast, Colon and Lung Carcinomas

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Abstract. Neural cell adhesion molecules (NCAM) play an important role in embryogenesis and in some tumors, especially of neuroectodermal origin. In this study, 18 cases of invasive breast carcinoma, 7 cases of sigmoid colon carcinomas and 17 cases of the non-small-cell lung carcinoma were immunostained for NCAM. NCAM expression, usually focal, was observed in some cases only. NCAM was expressed in the membranes, in a fine granular pattern. In 3 cases of breast cancer cytoplasmic localisation of NCAM was also observed, which may suggest its cytoplasmic formation. Furthermore, in 3 cases expression of NCAM in histologically normal ductal lobular units adjacent to invasive breast cancers without the presence of this antigen in cancer tissue was observed. The immunostaining was weak or absent in sigmoid colon carcinomas. In this study we confirm the observation of some authors that NCAM expression occurs in some cases of non-small-cell lung carcinomas.

Key words: CD56 (NCAM); breast cancer; sigmoid colon carcinomas; squamous cell lung carcinomas.

Introduction

Our previous data6, 9 suggested that some stromal cells of cancers may form thin-walled vascular channels and that from their perivascular mesenchyme arise myoid-like cells. These cells have stained with antibody to smooth muscle actin, rarely to desmin and sarcomeric actin, as well as to synaptophysin (Syn) and/or chromogranin A (ChgA). We suggested that these cells belong to the stem cells from which cancer cells may arise. The fact that some cancer cells express Syn and/or ChgA as well as sarcomeric actin suggests that the progenitor stem cells are of myogenic origin and share some properties with the neuron. The known facts that the nerve growth factor (NGF) is a strong stimulator of breast cancer cell proliferation8 and that the neural cell adhesion molecules (NCAM) are present in some cases of non-small cell lung carcinomas2 support this view.

To check this hypothesis we examined the presence of NCAM in the breast, lung and colon cancers using immunohistochemical methods.

Materials and Methods

Tissues from 18 primary tumors of invasive breast carcinomas, 7 cases of sigmoid colon carcinomas and...
17 cases of non-small cell lung carcinomas were investigated. The control groups were dysplastic breast lesions, tissue sections from sigmoid colon taken for diagnostic purpose, as well as lung with tuberculosis, hamartoma and bronchectases (Table 1). Sections from each case were selected for immunostaining using antibody to NCAM (Novocastra, monoclonal NCL-CD56-1B6, microwave oven). Bound antibody was detected using a commercial kit (Dako, LSA B2 Peroxidase K675). As a negative control, sections were treated with mouse nonimmune sera. As a positive control, sections of medulloblastoma were used.

### Results

In all the kinds of carcinomas only some cases expressed NCAM. In the breast carcinomas, 3 cases expressed NCAM as fine granular patterns in the cytoplasm of the majority of the tumor cells (Fig. 1). In 5 breast cases only singular groups of carcinoma cells expressed fine granular NCAM on the surface membrane (Fig. 2). The presence of membranous NCAM in histologically normal epithelium of the ductal lobular units adjacent to invasive breast carcinoma, while the tumor tissue was completely negative, was observed in 3 cases (Fig. 3).

The immunostaining of sigmoid colon carcinomas was scanty. In three cases neoplastic cells expressed NCAM focally, on the surface membrane.

In non-small cell lung carcinomas, only four of the cases expressed NCAM. Positive staining was usually found in some basal cancer cells (Fig. 4). Also, the mesenchymal bands of stromal tissue, always connected with part of the thin-walled channels and situated between the cancer foci or near their subbasal part, expressed NCAM. Along those mesenchymal bands, NCAM expression was observed in linear joined beady arrangements of cancer cells (Fig. 5). The control groups of benign breast lesions, sigmoid colon and lung without tumors were negative with antibody to NCAM, while the control sections of medulloblastoma expressed NCAM in all neoplastic cells (Fig. 6).

### Discussion

The neural cell adhesion molecules are thought to play a role in embryogenesis, development and contact-mediated interactions between neural cells. Expression of NCAM has been shown in small-cell lung carcinoma\(^2\) and in other neuroendocrine lung tumors, but not in squamous cell carcinoma and adenocarcinoma\(^1,6\). In archival material of 889 patients with non-small-cell lung cancer, the expression of NCAM has been found, but the tumor histology or stage did not correlate with positive reactivity\(^7\). There was no information about breast and colon carcinomas.

In some breast cancers observed in this study, NCAM appeared inside the cytoplasm of majority tumor cells. This may suggest their cytoplasmic formation. Expression of NCAM on the epithelial cell membrane in histologically normal ductal lobular units adjacent to invasive breast carcinoma without the presence of this antigen in cancer tissue is analogous to some other observations. It has been shown that the expression of NCAM was most pronounced in hyperactive thyroid, while it was scarce, focal or absent in colloid goiter, Hashimoto struma or thyroid carcinoma\(^2\).

We have shown that in cases in which hyperplastic ducts nodules were on the periphery of breast cancer tissue, Syn and/or ChgA was always seen in their epi-
Figs. 1. Positive staining for neural cell adhesion molecule in breast cancer. Fine granular patterns in the cytoplasm of the majority of tumor cells. × 400; 2. Carcinoma cells of breast, fine granular NCAM on the surface membrane. × 800; 3. Membranous NCAM in histologically normal epithelium of the ductal lobular units adjacent to invasive breast carcinoma. × 400; 4. Membranous NCAM in some basal cells of lung carcinoma. × 400; 5. Mesenchymal stromal bands connected with thin-walled channels express NCAM. Along these mesenchymal bands were cancer cells joined linearly in a beady arrangement. × 400; 6. Medulloblastoma with expression of NCAM. × 400
thelial cells independent on the presence or absence of these neuroendocrine markers in cancer cells. Also, NCAM expression was in morphological normal ductal lobular units adjacent to cancer foci. The fact that NCAM appears in embryogenesis and in preneoplastic dysplastic changes suggests that the mammary ducts, as maternal structures in the development of the breast, may express the first changes during activation of genes with aberrant differentiation of progenitor cells. This would be in agreement with the observation of some authors about the loss of heterozygosity in histologically normal tissue adjacent to breast carcinomas.

Our results confirm observations of some authors⁵ that the expression of NCAM was present not only in small-cell lung carcinomas. The expression of NCAM in lung tumors is analogous to previous observations concerning expression of synaptophysin and sarcomeric actin⁶. Their presence in the basal cell layer of cancer foci and in perivascular mesenchymal tissue, from which cancer cells may arise, indicates that the NCAM appears in the earliest stages of carcinogenesis.

References


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