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### Histiocytoid breast carcinoma: Histopathological study and a proposal of the diagnostic criteria

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**Purpose:** Histiocytoid breast carcinoma (HBC) is a rare variant of breast carcinoma; only about 30 cases have been reported. Some authors give emphasis to its diagnostic difficulty because of the histologic similarities to some types of breast cancer and benign lesions. The precise incidence of this tumor is not known, partly because of lack of definite criteria for its histological diagnosis and also lack of wide recognition of this tumor. The purposes of this study are to establish its histodiagnostic criteria and to clarify the origin.

**Methods:** We reviewed histological specimens from 1,010 breast cancer patients treated at our hospital between 1972 and 1996 and found 3 cases of pure HBC and 3 cases of combined HBC (two with pleomorphic lobular carcinoma and one with apocrine ductal carcinoma). These 6 cases were examined histopathologically, as well as cytologically and ultrastructurally in some cases.

**Results:** Two of the 3 pure HBC cases contained foci of in situ lobular carcinoma. Targetoid and Indian file invasive patterns, the features characteristic of lobular carcinoma, were present in all 3 pure HBC cases and 2 combined HBC with pleomorphic lobular carcinoma. Diastase-resistant periodic acid-Schiff (PAS) positive granules and granular immunoreactivities for gross cystic disease fluid protein-15 (GCDPF-15) were characteristic of the histiocytoid tumor cells in both the pure and combined HBC.

**Conclusions:** We would like to propose the histodiagnostic criteria as follows; 1) histiocytoid appearance of the tumor cells with invasive pattern similar to invasive lobular carcinoma, 2) diastase resistant granular PAS positivity in the tumor cytoplasm, and 3) Diffuse granular cytoplasmic positivity for GCDPF-15. The majority of HBC are of lobular origin, though the apocrine ductal origin is also possible in a small number of HBC. The prognosis of HBC appears to be dependent on the stage of the disease and may be not always poor.

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### Analysis of 47 breast lesions screen detected treated by surgical biopsy: Surgical margin status and presence of residual tumor at the surgical reexcision

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**Purpose:** The meaning of surgical margin status in breast cancer biopsies is unclear. The aim of this work is to evaluate the presence of residual tumor during surgical reexcision of biopsies with margin status involved by tumor component.

**Methods:** We analysed 47 cases of screen-detected breast lesion from 1991 to 1997 which underwent reexcision for surgical status margin involved by or close to a tumor component. The surgical margin status was classified as positive (when tumor, in situ or invasive, was transecting the inked specimen margin); close ( $\leq 2$  mm the margin); negative ( $> 2$  mm from margin). We also analysed the histological type of the tumor, the multifocality, and the presence of extensive intraductal component (EIC).

**Results:** When margin specimen was close to an in situ tumor we found 43% (3/7) of residual neoplastic tissue at surgical reexcision; when the margin status was close to an invasive tumor without multifocality we found no cases of residual tumor; when margin status was involved by invasive carcinoma we found 100% (5/5) of residual tumor at reexcision; and 60% (16/27) when it was involved by in situ component. The presence of residual tumor at reexcision increased when primary tumor was multicentric or with extensive intraductal component (45% vs 89%).

**Conclusion:** According to the literature, adequate surgical excision is important in minimising the risk of local recurrence in breast conserving treatment. In our opinion reexcision should be made in case of involved margins with invasive component, presence of EIC or multicentric in situ lesions.

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### Expression of S100- $\alpha$ and S100- $\beta$ in atypical papilloma, atypical papillomatosis and atypical intraductal hyperplasia of the breast

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**Purpose:** We have found S100 subunits immunohistochemistry is a powerful tool in the diagnosis of actin-negative areas of intraductal epithelial proliferation of the breast. In brief, usual intraductal papilloma, papillomatosis and intraductal hyperplasia expresses both S100- $\alpha$  and S100- $\beta$  in a heterogeneous pattern but ductal carcinoma in situ (DCIS) can express only S100- $\alpha$  in a monotonous pattern (Histopathology 1997, 30, 533-541). A further question is whether it can help better categorizing borderline intraductal proliferation.

**Method:** We reviewed atypical papilloma (5 cases), atypical papillomatosis (6 cases) and atypical intraductal hyperplasia (9 cases) from our consultation cases.

**Results:** Epithelial cells of atypical papilloma and papillomatosis lacked immunoreactive S100- $\beta$ ; S100- $\alpha$  was weakly and diffusely expressed in 2 cases of atypical papilloma and 3 cases of atypical papillomatosis and negative in the remaining cases. All atypical intraductal hyperplasia contained focal DCIS defined by S100 subunits immunoreactivity.

**Conclusion:** S100 subunits immunostain is valuable in making a more reproducible classification of borderline intraductal proliferation.

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### Biologic markers in small cancers of the breast and breast preneoplastic lesions

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**Materials and Methods:** We collected breast lesions detected by mammography. Altogether 95 lesions were obtained. Of these 35 were considered totally benign histologically: 12 papillomas, 13 atypical ductal hyperplasia, 4 lobular cancer in situ and 2 adenosis, 27 were in situ ductal cancers: 9 high grade and 18 low grade and 32 infiltrating cancers: 11 lobular and 21 ductal, of which 7 were of grade 1, 8 of grade 2 and 6 of grade 3. Paraffin sections were stained immunohistochemically for oncoproteins p-53, p21, bcl-2, c-neu, proliferation marker Ki-67 (MIB1), apoptosis related protein apo-fas and adhesion molecule CD-44.

**Results:** The staining results were very variable, it seems clear however, that the greater the chance of a lesion is to becoming overtly malignant, the more heterogeneous the cell population becomes, and the more the staining results diverge from the staining patterns of morphologically normal epithelium. Benign lesions were not p-53 positive, and small cell DCIS was rarely positive (mean  $3\% \pm 1$ ). Interesting features were the differences between lobular and ductal cancers: Ductal cancers were more often p-53 and CD44 positive and had lower proliferative activity, whereas lobular cancer was more positive for p-21, bcl-2 and c-neu. Apo-fas stained a little more than a third of both benign and malignant epithelium. Only papillomas had a somewhat low staining percentage (mean  $26\% \pm 21$ ), table 1.

table 1: The means and standard deviations of the percent of positive cells in each type lesions stained with the 7 antibodies used.

Lesion name	No. of cases	p-53	p-21	bcl-2	c-neu	MIB	CD44	apo-fas
adh	22	$2 \pm 1^*$	$48 \pm 27$	$49 \pm 38$	$7 \pm 16^*$	$1 \pm 3$	$41 \pm 32$	$36 \pm 25$
papillom	12	$0.4 \pm 1^{**}$	$43 \pm 32$	$71 \pm 33$	$15 \pm 32$	$0.8 \pm 2$	$53 \pm 40$	$26 \pm 21$
DCIS1	18	$3 \pm 12$	$37 \pm 34$	$56 \pm 41$	$33 \pm 41^*$	$4 \pm 6$	$43 \pm 35$	$48 \pm 31$
DCIS2	9	$30 \pm 35^{**}$	$35 \pm 36$	$34 \pm 47$	$38 \pm 36^*$	$4 \pm 3^*$	$34 \pm 33$	$37 \pm 35$
duct. ca.	20	$17 \pm 32^*$	$45 \pm 34$	$59 \pm 37$	$14 \pm 32$	$9 \pm 18$	$38 \pm 30$	$38 \pm 31$
lob. ca.	12	$3 \pm 9$	$59 \pm 34$	$70 \pm 36$	$26 \pm 40$	$3 \pm 6$	$16 \pm 29$	$37 \pm 37$

<sup>\*\*</sup>, \* P < 0.05

**Discussion:** Preneoplastic lesions of the breast are mostly recognised histologically, but it would be helpful to know more about a lesion to be able to give advice on follow up of patients.

**Conclusion:** The biologically relevant immunohistochemical patterns for prognostication of premalignant breast lesions must still be sought for.