PP-9-10 The Prognostic Significance of Protein Tyrosin Kinase, ER, PR, and the Mitotic Activity Index in 86 Primary Breast Cancer Patients

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In 86 primary breast cancer patients, we evaluated the prognostic significance of PTK (n = 81), ER (n = 83), PR (n = 83), and the mitotic activity index (n = 60). We compared the prognostic significance of these variables with classical prognosticators like; menopausal status, T-stage, N-stage, and histological grading according to Bloom and Richardson.

Protein tyrosin kinases (PTK) are enzymes which phosforylate proteins on tyrosine. These enzymes form an important part of signal tranduction pathways leading to cell proliferation. PTK activities were assayed in cytosolic extracts according to a non-radioactive dot blot method. Estrogen (ER) and Progesterone receptor (PR) levels were measured by enzyme immuno assay in cytosolic fractions. The mitotic activity index (MAI) was defined as the number of mitotic figures per 10 high power fields (HPF). The median follow up period was 30 months (range: 4–50).

After univariate analysis, disease free survival (DFS) was found to be correlated significantly ($p < 0.05$) to: T-stage, N-stage, histological grading, and ER (cut off point: 100 fmol/mg). After multivariate analysis, T-stage, N-stage, and ER (cut off point: 100 fmol/mg) appeared to be independent prognostic factors ($p < 0.05$). According to these preliminary results we demonstrated that PTK, PR and MAI, in contrast to ER, have no additional prognostic significance, with regard to DFS. We will continue this study with a longer follow up and a greater (approximately 500) number of patients.

PP-9-11 Oncogene Evaluation (c-int2, c-erb B2, c-myc) in 265 Breast Carcinoma pT1–T2, pN0–N1, M0

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Current prognostic factors in breast cancer concern tumoral size (pT), axillary node status (pN), Scarff-Bloom grading and hormonal receptor status. This study was undertaken to evaluate metastatic power of oncogenic parameters as c-int2, c-erbB2, c-myc which are often amplificated in breast cancer.

For the assay, DNA extraction was followed by slot-blot (erbB2, int2) or southern-blot (myc) hybridization method. Semi quantitative evaluation was made by densitometry. Results differ from 0 (no amplification) to amplification level 2–3 (+), 4–5 (++), > 6 (+++).

From 1987 to 1989, 265 invasif breast carcinomas were included in this study: 61.9% of patients were menopaused, 50.2% were axillary nodes noted as pN0, 78.1% were RE+, 34% of patients were Scarff-Bloom grade I, 38.1% grade II and 23.8% grade III. With a median follow-up of 57 months (0–89), 59 relapses were registered. In this study, patients with worse pronostic (pN1b, Scarff-Bloom III, RE-) received medical adjuvant treatment.

Amplification rate to int-2, erbB2, myc was respectively 9.4%, 14.3%, 21%. In univariate survival analysis, erbB2 and myc showed significant association ($p = 0.0009$ and $p = 0.0055$ respectively) when we consider amplification results as four classes (0/+/++/+++).

In contrast the Cox regression model with conventionnal disease parameters do not show significant association whatever the oncogene. Only pN, RE, pT have significative value.

PP-9-12 Breast Cancer Oestrogen-Receptor Negative Tumors, PS_2 Expression and DFI

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PS_2 protein expression has been reported to have prognostic significance in human breast carcinomas and to correlate with estrogen receptor positivity.

We have examined PS_2 expression in 183 primary NØER+ breast cancer and in 119 NØER− breast cancer and related PS_2 expression to disease behaviour-Cut off point for PS_2 to discriminate between positive and negative was 12 ng/mg protein. Follow up — 5 years.

In group NØER+ 112/183 (66.6%) were PS_2+ ($PS_2 > 12$ ng/mg protein). In group NØER − 18/119 (15.1%) were PS_2+ PS_2+ was associated with good prognosis in the group NØER+ were only 13/112 (11.6%) had recurrence of their disease. In group NØER − 11/18 (61.1%) (NØER − $PS_2 > 12$ ng/mg protein) had recurrence compared with 36/101 (45.6%) (NØER − $PS_2 < 12$ ng/mg protein).

In patient with oestrogen-receptor negative tumors, PS_2 expression predicted a shorter DFI.

PP-9-13 High Positive Rate of PS2 Expression in Forefront Intraductal Cancerous Area in Breast Cancer

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Multiple sections of 40 consecutive cases with invasive ductal carcinoma of the breast, all of which had wide intraductal cancerous extension, were examined by immunohistochemical analysis for evaluation of hormone dependency in several areas of breast cancer tissues. In this study, we examined the expression of pS2 protein in the central invasive area (CIV), central intraductal cancerous area (CDC) and forefront intraductal cancerous area (FDC). pS2 staining was positive in 52.5% (21/40) of CIV and a significant correlation was found between pS2 expression in CIV and the estrogen receptor status (ER). pS2 staining was positive in 77.5% of CDC and 85.0% of FDC, respectively. A majority (68.4%) of the cases that were negative pS2 in CIV were positive for pS2 in FDC. Moreover, the cases with noncomedo intraductal carcinoma in premenopausal status showed a higher positivity of pS2 expression in FDC than the cases with comedo-carcinoma, though the number of cases of comedo-carcinoma was limited. These findings suggest that endocrine therapy may be useful after breast conserving treatment regardless of the ER status of the primary tumor.

PP-9-14 Clinical Significance of Pyrimidine Nucleoside Phosphorylase Staining in Breast Cancer

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Pyrimidine Nucleoside Phosphorylase (PyNPase) is a synthetic enzyme of converted nuclear acid. Some clinicians found that high PyNPase activity in malignant tumors led to metastasis and cachexia. In a previous study we measured the PyNPase activity of breast cancer tissues and investigated its correlation with other prognostic factors. We found that the lymph-node metastases cases and the lymphatic vessel invasion positive cases were higher than the negative cases ($P = 0.00766$, $P = 0.00095$). So, it is clear that PyNPase activity has a clinical significance as a promising prognostic factor in breast cancer. This enzyme is heterogeneous and present in tumorous tissues.

Therefore, it is important to investigate PyNPase activity correlation with PyNPase staining. We found that the group with higher PyNPase activities had shown more highly stained tissues. From these results, we feel that PyNPase staining is a more useful, simple, and speedy method than measuring of PyNPase activity.

PP-9-15 Analysis of Angiogenesis, PCNA, c-*er b* B-2, and p53 Associated with Long-Term Survival in Japanese Women with Breast Cancer

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To evaluate the clinicopathological significance of angiogenesis, we immunohistochemically stained one representative section of the breast tumor with factor VIII-related antigen staining. There were 109 patients with breast cancer from 1971 to 1979. We examined the relationship between microvessel count (MVC) and PCNA, c-*er b* B-2, p53, and other conventional factors. There was no relationship between MVC and PCNA, c-*er b* B.2, p53, age, menopause, clinical tumor size (T), histological classification, nuclear grade, node metastasis, histological grade, mitosis index, necrosis, and lymphatic invasion. However, there was a relationship between MVC and blood vessel invasion ($p < 0.02$). MVC, PCNA, c-*er b* B-2, and p53 were compared with the overall survival rate at 20 years by logrank analysis. A 20-year cumulative survival rate in the two groups of MVC, PCNA, and p53 were statistically significant, while the rate of c-*er b* B-2 was not significant. Cox's multivariate analysis was also performed. T ($p = 0.0187$),