Thursday, 17 April 2008 12:30–14:30

POSTER SESSION

Pathology

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Prognostic significance of lymphovascular invasion in node-positive patients with primary operable breast cancer

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Background. Lymphovascular invasion (LVI) is a major and significant predictor of distant recurrence for node-negative breast cancers. The aim of this study is to assess its prognostic impact for distant recurrence in node-positive patients with primary operable breast cancer.

Methods. The study group consisted of 374 node-positive breast cancer patients operated on between January 1989 and December 1992 at the Bergonié Institute (median follow-up: 126 months). For each case, LVI was determined on three haematoxylin and eosin-stained (HE) sections. Only unequivocal emboli located at distance from the tumour were considered.

Results. LVI was identified in 46% of tumours and was significantly associated with age $\leqslant$40 ($p = 0.02$), histological mSBR grade III ($p = 0.01$), negative estrogen receptor ($p = 0.032$). No significant correlation was found with pathological tumour size, number of involved axillary lymph node or HER-2 over-expression. After performing multivariate analyses, HE LVI appeared to be a significant predictor of distant recurrence not only in the whole group (HR: 1.70 – 95% CI: 1.21−2.40 – $p = 0.002$), but also in the subgroups of non HER2-overexpressing tumours ($n = 324$) (HR: 1.82 – 95% CI: 1.24−2.67 – $p = 0.002$) and non HER2-overexpressing endocrine sensitive tumours ($n = 282$) (HR: 1.71 – 95% CI: 1.12−2.62 – $p = 0.013$).

Conclusion. In our study, LVI was found to be statistically correlated with age, histological grade and estrogen receptor status, but not with pathological tumour size and number of axillary lymph node involved, suggesting that LVI is an integral part of the tumour genotype rather than an event during evolution of the tumour. In addition, LVI appeared to be an independent significant prognostic factor for distant recurrence in the studied N+ tumours.

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Morphological and molecular analysis of Circulating Tumor Cells (CTCs) in breast cancer: a real possibility

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Background: Detection and characterization of CTCs in peripheral blood may have some clinical utilities to choose targeted therapy and monitor treatment response and disease recurrence. The first main step to reach this aim consists in employing reproducible systems to isolate and typify CTCs.

Materials and Methods: 20 ml blood samples were collected from 84 patients with breast cancer in different stages of desease. CTCs were isolated and counted with CellSearch System® (Immunicon Co.) by means of immunomagnetic separation, using ferrofluid nanoparticles binding anti-epithelial cell adhesion molecules (EpCAM), and fluorescently stained with Epithelial Cell Kit®. CTCs were defined as nucleated epithelial cells, positive for DAPI, CK 8, 18, 19 and negative for CD45. A case was defined as CTCs positive if more than 1 cell was identified. Concomitantly, we also used Tumor Phenotyping Reagent® to investigate HER-2/neu and EGFr expression. Moreover, using Profile Kit® CTCs were isolated to performe morphological and molecular analysis: slides were set up and investigated by Papanicolaou staining, Fluorescence in situ hybridization (FISH) to investigate HER2/neu and Immunocytochemestry (ICC) to investigate CK, ER, PGR, Ki67, C-erbB2.

Results: 54 patients were CTCs positive, with a median value of 12/7.5 ml. HER-2/neu and EGFr expression were investigated in 48 cases (48% positive, 52% negative) and 12 cases (17% positive, 83% negative) respectively. Morphological analysis by Papanicolaou staining showed a clear evidence: CTCs differ from original neoplastic tissue's cells presenting a rounded shape probably modified by the liquid medium, blood, in which they circulate. However, in our experience, two cellular kinds generally appear: the most representative one characterized by small size, round cells with large nucleus (high nucleus/cytoplasmic ratio), both isolated (similar to blood cells) or in clusters; the other group characterized by larger and sometimes elongated cells.

Conclusions: Counting, biocharacterisation and morphological analysis of CTCs are possible using a good, simple, automated and standardized method to isolate and better investigate them in order to give useful informations about patient's care and probably, in the future, individual therapies.

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Decrease of expression of androgen receptor in triple negative breast cancer

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Background: The role of ER, PR and HER2/neu as prognostic and predictive factors in human breast cancer is well established. Triple negative breast cancer is characterized by lack of expression of estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu. Previous studies have showed that breast cancer tumors are expressing androgen receptor (AR) in 40−70% of the cases. However, the functional role and clinical value of AR expression in breast cancer have still not been clearly defined. This study was set up to investigate the expression profile of AR in relation to ER alpha/beta, PR and HER2/neu in tumors of patients with breast cancer.

Methods: We developed a retrospective study in 76 patients with confirmed diagnostic of invasive ductal carcinoma. We assessed by immunoblotting and IHC (using specific monoclonal antibodies) the distinct expression pattern of ER alpha/beta, PR, HER2 and AR. Chi-square and log rank tests were used to determine differences between proportions of each marker and mortality and survival distributions respectively (P value $\leqslant$0.05 was considered significant).

Results: The 76 patients were women. The median follow-up was 58 months (1–346). The median age of the patients was 48 years (22−81 ys). The number of patients and percent with positive tumors for ER alpha/beta, PR, HER2/neu and AR are showed in the table.

	ER		PR	HER2/neu	Triple negative	AR
	alpha	beta				
No. of patients	34	28	27	16	18	32
%	45%	42%	35%	21%	24%	42%

N = 76 patients

Only three patients (4 %) with triple-negative tumors were positive for AR expression. This relationship was significant ($P = 0.01$) in comparison with the 58 (76%) patients with non-triple negative tumors where we found 31 (41%) of the patients were positive for the expression of AR. In triple negative cases, we did not found correlation with the overall survival.

Conclusion: Our findings suggest loss of AR expression may be involved in tumor progression in breast cancer patients. We need further studies to demonstrate clinical significance of AR in these patients.

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Cancer of the stomach in breast cancer patients is often metastatic disease

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Background: In patients with breast cancer, the differential diagnosis between metastatic disease or primary cancer of the stomach can be challenging in a gastric biopsy and these diagnoses have completely different clinical implications. Since the incidence of primary gastric cancer in western countries is low compared to the incidence of breast cancer, we hypothesized that cancer of the stomach in a breast cancer patient is often metastatic disease.

Materials and Methods: Patients with breast cancer and cancer of the stomach in the years 1988 until 2005 were retrieved from our files. In our laboratory approximately 300 new patients with breast cancer are diagnosed each year. Patients with gastric cancer preceding the diagnosis of breast cancer were excluded. Age at the time of the breast cancer diagnosis and interval-time until the diagnosis of cancer of the