

Conclusion: When BCT performed on DCIS consists of lumpectomy alone, BCT is feasible when the tumor size is 1.1–2.0 cm, without extensive microcalcification on mammography. However, BCT for comedo carcinoma should be approached with caution because of its malignant behavior, although there was no difference in histological extension between comedo and noncomedo carcinoma.

28

POSTER

Apoptosis in ductal carcinoma in situ of the breast: its relationship to prognostic markers

A. Moreno, A. Figueras, B. Lloveras, E. Giera, A. Escobedo. *Ciutat Sanitaria de Bellvitge, Department of Pathology, Feixa LLarga S/N 3-8907 Llobregat, Spain*

Purpose: Programmed cell death (apoptosis) may play a role in tumor development and progression. We evaluated the number of apoptotic cells in subgroups of ductal carcinoma in situ and correlated it with several prognostic markers and expression of genes related to apoptosis regulation.

Methods: In a series of 58 DCIS, immunohistochemical staining was performed for hormone receptors, c-erbB2, p53, bcl-2 and Ki-67 (MIB-1). DNA content was measured by image cytometry. Microvessels were identified by reaction with the Ulex Europaeus I lectin and counted. Apoptosis was detected by the TUNEL (TdT-mediated dUTP-biotin nick end labelling) technique.

Results: High apoptotic index (greater than 3/HPF) is related to high tumor grade, negative hormone receptors, c-erbB2 overexpression, aneuploidy, lack of bcl-2 immunohistochemical stain and angiogenesis. Apoptosis is not related to p53 and high proliferative index expressed by Ki-67 (MIB-1) expression.

Conclusion: Our results agree with previously reported findings in infiltrating breast cancer. The apoptotic index is not influenced by p53 status. A common way for stimulation of both apoptosis and angiogenesis seems to exist.

29

POSTER

Ductal carcinoma in situ: A revision of 43 cases

S. Salicrú, M.D. Sabadell, J.L. Lirola, A. Durán, A. Cabaleiro, A. Pedreira, J. Xercavins. *Hospitals Universitaris Vall d'Hebron, Breast Pathology Unit. Obstetrics and Gynecology, Varsòvia, 114, E-08041 Barcelona, Spain*

Purpose and Methods: We analyse epidemiological variables, clinical behaviour and possible therapeutic implications of DCIS. We have performed a retrospective study using the case-histories of 43 patients with DCIS during the periods 1975–1993 and 1995–1996.

Results: There is a family history of breast neoplasms in 17.5% of cases and digestive cancers in 15%. Three patients have a medical history of breast neoplasm and one patient of endometrial adenocarcinoma; also, three patients have a contralateral breast neoplasm at the same time. The mean age is 55.6 years. We can observe two peaks of incidence: the maximum between 41 and 50 years and the other at the seventh decade of life. Neither the menarche was premature (13.11 yr.) nor the menopause was late (47.17 yr.). 60% of patients are in menopause. 16.7% had no gestation. Breastfeeding occurred in 70.6% of patients. Women consult us because of a mammographic finding in 47.6% of cases. 65% have non-palpable lesions. 53.8% of lesions are localised in the left breast. The main distribution in the breast is in the upper outer quadrant area (63.8%). Microcalcifications are the most frequent mammographic finding (53.7%). In 19% there are not any findings in the mammography or they are benign. Initial treatment has always been surgical. When we have performed axillary lymph node dissection we have not obtained any positive node results. In recent years we have drastically decreased the realisation of axillary lymphadenectomies. Recurrences have been 6.98% of total.

Conclusions: The fifth decade of life is the age of major incidence. Incidence of bilateral breast neoplasm in our cases is 14%, emphasising that nobody had taken tamoxifen as coadjuvant treatment of their preceding neoplasm. The main distribution of DCIS is the same as in invasive ductal carcinoma. Microcalcifications found in a screening mammography are one of the most important factors in the diagnosis of DCIS. In none of the cases where we have done an axillary lymphadenectomy there were positive nodes; this supports a less aggressive surgical procedure than in the invasive carcinoma. All our recurrences occurred after a breast-conserving surgery.

30

POSTER

Local recurrence in women with ductal carcinoma in situ (DCIS) according to the treatment

G. Limite, U. Pace, C. Pizzi, A. Riccardi, M. Imbriaco, M. Di Maio, G. Petrella, G. Pettinato, A. Sodano, A. Contegiacomo, P. Forestieri. *Cattedra Oncologia Chirurgica, Chirurgia Generale ed Oncologia, Via Pansini 5, I-80131 Naples, Italy*

There is still much controversy regarding the most appropriate therapy for patients with ductal carcinoma in situ (DCIS) of the breast. This study was undertaken to evaluate the clinical outcome in 38 patients with DCIS treated at the University "Federico II" of Naples, Italy between 1989 and 1998. The age of the patients ranged from 29 to 74 years. Pathologic evaluation included the size or extent of the lesions and the margin width. Tumor size was <15 mm, 16–40 mm and >40 mm in 9, 9 and 4 cases respectively. In 16 cases the tumor size was not available. Widely clear tumor margins were detected in 35/38 (92%) of the cases, while infiltrated margins were detected in 3/38 (8%) of the cases. Breast conserving therapy (BCT) including excisional biopsy and quadrantectomy was performed in 18 of the 38 patients (47%), of which 9 patients received postoperative radiotherapy (RT). The remaining 20 patients were treated with mastectomy on the basis of the presence of multifocal DCIS at the excisional biopsy. After a median follow up of 46 months (range: 3–104), three (8%) local recurrences were observed: in 2 cases the patients were treated by BCT with or without RT, in the remaining case mastectomy was performed.

Wednesday, 30 September 1998

16:00-18:00

PARALLEL SESSION

Locally advanced and locally recurrent breast cancer

31

INVITED

Locally advanced and metastatic breast cancer

R.D. Rubens. *Guy's Hospital, London, UK*

In locally advanced breast cancer, the high incidence of subsequent distant metastases and poor survival has led to the use of systemic treatment as part of management, both as an adjunct to radiotherapy and as primary systemic treatment. High response frequencies to chemotherapy are achieved, although complete pathological response is infrequent emphasising the importance of adequate locoregional treatment. Survival advantages from this approach remain to be demonstrated.

In metastatic disease the development of new agents continues to provide increasing treatment options. Of particular current interest are new aromatase inhibitors for endocrine treatment and taxoids for chemotherapy. New immunological approaches entail antibody administration and vaccines (active specific immunotherapy).

Recognition that osteolytic bone destruction in the skeleton is mediated by osteoclasts stimulated by tumour-derived cytokines has led to the therapeutic use of bisphosphonates. These agents have become the treatment of choice for hypercalcaemia; they also reduce pain and the incidence of pathological fracture.

32

ORAL

^{99m}Tc-MIBI scintigraphy evaluates response to neoadjuvant chemotherapy in locally advanced breast cancer

A. Festa¹, A. Tofani¹, R. Sciuto¹, A. Semperebene¹, R. Cucchi¹, S. Rea¹, C. Botti², M. Mottolese³, M. Benevolo³, C.L. Maini¹. ¹Dpts of Nuclear Medicine; ²Surgery; ³Pathology, "Regina Elena" Cancer Institute, Rome

Purpose: This study evaluates ^{99m}Tc-MIBI scintigraphy for the assessment of breast tumor response to neoadjuvant chemotherapy in locally advanced breast cancer (LABC).

Methods: ^{99m}Tc-MIBI scintigraphy, clinical and mammo-graphic evaluations were performed in 29 patients with LABC before and after neoadjuvant chemotherapy. Scintigraphic studies were obtained in supine and prone lateral views after 740 MBq ^{99m}Tc-MIBI (Cardiolite, Dupont) i.v. injection.

Surgery was planned 15 days after chemotherapy; pathological status and immunohistochemical studies were obtained in all patients.

Results: Sensitivities for a correct prediction of tumor presence after chemotherapy were 65% for scintigraphy, 34% for clinical evaluation and 69% for mammography. Specificities for a correct prediction of tumor absence after chemotherapy were 100% for scintigraphy, 33% for clinical evaluation and 33% for mammography. 99mTc-MIBI in this series did not correlate with p-170 expression, proliferating nuclear antigen, Her-2/neu oncogene protein, anti-human endothelial cell CD31 antigen, estrogenic and progesterone receptor status.

Conclusions: 99mTc-MIBI is effective in monitoring the response to presurgical neoadjuvant chemotherapy in LABC patients. Its diagnostic yield is clearly superior to clinical evaluation alone and to mammography in patients with complete response. Subcellular metabolic correlates of MIBI uptake need further evaluation in larger series.

33

ORAL

Flap recurrence following mastectomy for breast cancer: local failure or systemic disease

G.J. Byrne, C.S. Bronder, R. Swindell, A. Howell, N.J. Bundred. *South Manchester University Hospital, Department of Surgery, Withington Hospital, Nell Lane, Manchester M20 8LR, UK*

Purpose: Treatment of Flap Recurrence (FR) after mastectomy for breast cancer remains controversial. We attempted to identify histopathological and clinical characteristics of FR which predicted for poor survival.

Methods: Between 1976 and 1991, 2755 mastectomies without radiotherapy were performed for breast cancer in our unit, an overall FR rate of 10.3% was observed (mean follow up = 12.2 yrs range 5–20 yrs). 256 FR's following mastectomy for T1-T3 tumours were identified and examined for factors predicting survival.

Results: Nodal status at presentation ($P < 0.05$), time to recurrence and presence of concurrent systemic disease (CSD) influenced survival. Five year survival for those women with CSD at the time of FR ($n = 45\%$) was poor when compared to survival in women without CSD (55%) ($p = 0.0001$). Early recurrence (< 2 yrs following mastectomy) correlated with poor survival ($p < 0.0001$) even allowing for CSD ($p < 0.001$). The type of recurrence (single spot, multiple spot or field change) did not influence survival. The site of first systemic recurrence (FSR) following FR (bone = 19%, visceral = 64%, both = 17%) contrasted with the FSR in women who did not have FR (bone = 63%, visceral = 21%, both = 16%) ($p < 0.001$).

Conclusion: Flap recurrence occurring in the first year following mastectomy for breast cancer predicts poor survival. All FR is likely to be a manifestation of systemic visceral metastasis and therefore all require systemic therapy.

34

ORAL

Determinants of prognosis after first isolated locoregional recurrence of breast cancer

C. Schmoor¹, W. Sauerbrei¹, G. Basten², H. Rauschecker³, M. Schumacher¹. *For the German Breast Cancer Study Group (GBSG); ¹Institute of Medical Biometry and Medical Informatics, University of Freiburg; ²Department of Gynecology, University of Heidelberg; ³GBSG Coordinating Center, Germany*

Purpose: Prognosis of breast cancer patients after occurrence of first isolated locoregional recurrence is evaluated in the data of four prospective studies of the GBSG.

Methods: From 1984 to 1989, 2746 patients have been recruited into the studies. During follow-up (median = 8 years), 337 patients developed an isolated locoregional recurrence as first event. Progression-free (PFS) and overall survival (OS) after locoregional recurrence was determined (median follow-up = 4.5 years) and analyzed by means of a multivariate Cox regression model.

Results: 185 patients developed a second event of whom 150 patients died. PFS and OS rates at 3 years are 0.45 and 0.62, respectively. Significant and independent prognostic impact was due to nodal status, tumor grade and estrogen receptor of the primary tumor and to the length of the disease-free interval (DFI) after primary treatment. Sufficient separation of resulting risk strata have been achieved by a simple classification scheme solely based on nodal status and DFI.

Conclusion: Determinants of prognosis after first isolated locoregional recurrence have to be taken into account for designing risk adapted, future clinical studies in these patients. Risk strata can be defined by means of a simple classification scheme.

35

ORAL

Identification of recurrent breast cancer with radiolabelled isonitriles

J.R. Buscombe¹, J.B. Cwikla¹, S.P. Parbhoo², S. Gehani², A.L. Jones³, J. Hinton⁴, A. Deery⁵, J. Crow⁵, A.J.W. Hilson¹. *¹Departments of Nuclear Medicine; ²Breast Surgery; ³Oncology; ⁴Radiology; ⁵Histopathology, Royal Free Hospital and School of Medicine, London, UK*

Purpose: The radiolabelled isonitrile, Tc-99m MIBI, is known to have a high level of accuracy in identifying primary breast cancer. However, it may be of more use in suspected recurrent breast cancer when previous surgery and radiotherapy changes the radiological appearance of the breast. The aim of this project was to assess the accuracy of Tc-99m MIBI in suspected recurrent breast cancer.

Methods: 54 patients (mean age 60 years) with clinical or mammographic suspicion of recurrence were studied 1–23 years (mean 6 years) after initial diagnosis and treatment. 24 patients had undergone mastectomy so a total of 84 breasts were studied. All patients underwent breast and local tissue imaging with Tc-99m MIBI and 80 breasts also had x-ray mammograms. The results of imaging were correlated with cytological or histological examination, correlative imaging and 6 months clinical follow-up.

Results: 31 patients had recurrent cancer within the breast tissue, 13 were identified by mammography (sensitivity 41%), and 21 by Tc-99m MIBI (sensitivity 70%). The specificity of 2 methods were similar (Tc-99m MIBI-83% vs mammography-91%). In addition 19 sites of cancer were confirmed outside the breasts, 15 (79%) were identified on the Tc-99m MIBI scan.

Conclusion: Tc-99m MIBI imaging is able to identify recurrent breast cancer both within the breast and surrounding loco-regional tissues and may provide unique and complementary information to mammography.

36

ORAL

Isolated local-regional recurrence of breast cancer: Impact of radiotherapy on dissemination and survival

C. Kamby¹, L. Sengeløv². *¹Department of Oncology, Centre, Finsen; ²Department of Oncology, University Hospital Herlev, Denmark*

Purpose: To evaluate the impact of local-regional control on dissemination and survival of patients with isolated local-regional recurrence treated with curative radiotherapy only.

Methods: From 1983–85, 83 mastectomised patients with histologically verified isolated local-regional recurrence of breast cancer participated in a prospective study investigating the frequency of metastases. The rate of second local failure, time to dissemination and survival were related to 31 potential prognostic factors using uni- and multivariate survival analyses.

Results: Median follow-up (range) was 122 months (111–144). 30 patients had local-regional failure. The actuarial failure rate was 48% after 10 years. 51 patients developed metastases; median time to distant disease was 51 months. Median survival was 84 months and survival rate was 36% after 10 years. Node status at primary diagnosis and haemoglobin level at recurrence were significant independent prognostic factors for both survival and dissemination. 10-year survival of node negative patients with normal haemoglobin was 50% compared to 2% for patients with positive nodes and low haemoglobin levels. Local-regional failure after radiotherapy for isolated local-regional recurrence had neither influence on the risk of dissemination nor the duration of survival.

Conclusion: One third of the patients has local-regional confined disease which can be controlled by radiotherapy only; achievement of local-regional control had no influence on risk of distant disease and death. Poor prognosis patients can be selected by simple methods and should be considered for future adjuvant systemic therapy.