Results: Comparing m/c and lat the survival parameters were highly significant in favour of the lateral tumours (p-values: OS 0.0011, DSS 0.009, DFS 0.0001, LC 0.051). Cosmetic results after surgery were 1.65 in lat and 2.15 in m/c (p < 0.005). These values hadn't changed 5 years after RT with 1.69 and 2.13 respectively (p < 0.025).

Conclusion: The medial and central tumour location in the breast is associated with lower survival rates and unfavourable cosmetic results. The reason may lie in the fact that the pathological stage of the internal mammary chain is unknown, while in lateral tumours all patients with positive axillary nodes underwent systemic therapy and (in part) supraclavicular irradiation. The difference in the cosmetic outcome may lie in the fact that the medial part presents with a smaller tissue volume than the lateral half.

300 PUBLICATION

Relationship between insulin-like growth factor 1 (IGF-1), prolactin (PRL), human growth hormone (hGH) and steroid receptors in breast cancer patients

L. Delgado[1], O. Alonso[2], I. Alonso[1], N. Artagaveytia[3], B. Alvarez[2], G. Sabini[1], R. Roca[3], I.M. Musé[1]. [1]Clinical Hospital of the University of Uruguay, Department of Clinical Oncology, Montevideo; [2]Clinical Hospital of the University of Uruguay, Department of Nuclear Medecine, Montevideo; [3]Clinical Hospital of the University of Uruguay, Department of Medicine, Montevideo, Uruguay

IGF-1, PRL and hGH, seem to play an important role in the growth regulation of breast cancer.

The aim of this study was to evaluate if estrogen and progesterone receptors contents (ER, PR) of breast carcinomas were related to serum levels of PRL, hGH, and IGF-1. We studied 90 patients with primary breast cancer. Preoperative serum measurements of PRL, hGH, and IGF-1 were performed by RIA. ER and PR tumor levels were determined by binding assay using radioactive ligands (DCC method). Statistical association was assessed by the Spearman test. We found a significant negative correlation between PRL and ER levels (p = 0.011). Furthermore, a significant negative correlation was also observed between IGF-1 and ER levels (p = 0.002), and with PR levels (p = 0.018). This findings are in favour of the importance of PRL in ER regulation and suggest a possible role for IGF-1 in the regulation of both receptors in breast cancer patients. Therefore, both PRL and IGF-1 serum levels may be factors to be considered when evaluating hormone sensitivity in breast cancer patients.

301 PUBLICATION

Expression of cyclin dependent kinase inhibitor protein p27kip in localized invasive ductal carcinoma of the breast

H. Kourea[1], A. Koutras[1], V. Zolota[1], M. Marangos[1], E. Tzorakoeleutherakis[1], D. Koukouras[1], H. Kalofonos[1]. [1]University of Patras, Medical School, University Hospital, Patras, Greece

Purpose: Expression of p27KIP cyclin-dependent kinase inhibitor, a negative cell cycle regulator, was studied in a series of localized invasive ductal breast carcinoma and correlated with clinicopathological parameters and outcome.

Methods: 103 invasive ductal breast carcinomas, T1 and T2, N0, M0 were reviewed. Formalin-fixed, paraffin-embedded normal (n = 87) and neoplastic (n = 103) tissue samples were studied by immunohistochemistry for p27KIP. Samples were considered positive if >/= of 50% of tumor nuclei showed immunoreactivity. The findings were correlated to standard clinicopathological parameters and outcome.

Results: 43% of cases were T1 and 57% were T2. Disease free survival (DFS) and overall survival (OS) were both 5–144 months (mean 47 and 49 months, respectively), p27KIP expression in tumor and normal tissue was noted in 35% and 62% of cases respectively (P = 0.045). P27KIP expression was positively correlated with estrogen (ER) and progesterone (PR) receptor status (P = 0.0004 and P = 0.05, respectively). Loss of p27KIP was associated with higher tumor grade (p = 0.02). No association with tumor size, DFS and OS was observed.

Conclusions: Localized, early stage invasive ductal carcinomas tend to lose p27KIP expression compared to benign breast epithelium. Although loss of p27KIP is correlated with higher tumor grade and negative ER and PR status in these tumors, loss of p27KIP does not appear to adversely affect their prognosis. This finding is contrary to previously reported series of invasive breast carcinoma of all stages, emphasizing the biological differences among the various tumor stages.

302 PUBLICATION

Circulating antibodies against a breast tumor antigen

R. Pasquinelli[1], I. Capasso[2], M. D'Aiuto[2], P. Barba[3], A.M. Anzisi[1], G. D'Aiuto[2], J. Guardiola[3]. [1]INT – Oncologia E; [2]INT – Chirurgia A, Senologia; [3]CNR, Istituto Internazionale di Genetica e Biofisica, Napoli, Italy

Purpose: Determination of circulating antibodies against tumor neoantigens is important for the development of preventive or therapeutic vaccines. We report here the finding of antibodies against the breast tumor antigen, GCDFP-15gp 17.

Methods: An ELISA assay in which GCDFP-15/gp17 was used as a substrate was developped. Sera from three groups of patients were then examined (Group A including 73 breast carcinoma patients; Group B including 38 patients carrying benign breast conditions and Group C including 16 controls.

Results: Patients were considered positive when the amount of anti-GCDFP-15gp17 circulating Ab present was above the average value observed for control group C + 3x standard deviation. 5.5% of patients with breast carcinoma and 2% of patients with benign diseases expressed these antibodies. The specificity of circulating Ab was determined by competition with an anti-GCDFP-15gp17 mAb and their IgG and IgM isotypes were also assessed.

Conclusions: Patients with breast carcinoma or benign lesions secreting GCDFP-15gp17 exhibit a humoral immune reaction against the tumor antigen. The presence of IgM and IgG isotypes indicates that this response is mediated by T helper cells and suggests an approach to breast tumor vaccination.

303 PUBLICATION

Correlation between proliferating cell nuclear antigen (PCNA) and p53 protein expression in breast carcinomas. Can they have a prognostic value?

L. Lazar[1], Ioana Berindan[2], O. Balacescu[2], Rodica Risca[2], E. Neagoe[1], G. Lazar[1]. [1]Surgical Department – Oncological Institute, Cluj-Napoca; [2]Tumor Biology Department-Oncological Institute, Cluj-Napoca, Romania

Purpose: The correlation between overexpression of PCNA and p53 protein in different stages of breast carcinomas together with histopathological parameters were studied, for establishing a prognostic value.

Methods: 93 patients with in situ and invasive breast carcinomas were studied for both PCNA and p53 overexpression. Correlation with tumor size, histological and malignancy grade and the lymph node status was done. The study was made on paraffin-embedded tissues; (MoAb DO-7 from Dako, for p53 and MoAb PC10 for PCNA) from Boehringen-Mannheim,. The scale of positive PCNA tumor cells was between 0–3.

Results: a number of 52/93 (55.9%) revealed in different grades positive reaction for PCNA, and 80/93 (86%) revealed overexpression of p53 protein. Positive reaction for PCNA was associated with invasive tumor size, lymph-node metastasis and high malignancy grade. 54% from invasive carcinomas were p53 positive. We had 20% from positive PCNA cases marked on scale 1 (SI: weak) 18% on scale 2 (SI: moderate) and 12% on scale 3 (SI: strong).

Conclusion: our results reveal that high PCNA immunoreactivity and overexpression of p53 can be associated with poor prognosis (PCNA and p53 distributed in invasion areas). This study demonstrate that both PCNA and p53 protein have no independent prognostic significance but if they are correlated with histological parameters, they can become of great interest in the prognosis.

304 PUBLICATION

Increased E-cadherin and keratin 18 expression is associated with better prognosis in patients with human breast cancer

Y. Glienke, I. Fuchs[1], H. Bühler, A. Lorenz, F. Opri, H. Voss[2], G. Schaller. [2]Dep. of Gyn. and Inst. of Pathology of the Medical Center, Free University Berlin and Dep. of Gyn.; [1]Charité Humboldt University Berlin, Germany

Purpose: Besides classical prognostic factors in Human Breast Cancer i.e. lymph node status, tumor size/grading and estrogen (ER) and progesterone (PE) status, the value of adhesion and cytoskeletal proteins as inhibitors of metastasis are largely underestimated. Therefore an immunohistochemical examination for E-cadherin (E-cad) and keratin 18 (K18) was performed to

evaluate the prognostic value in addition to clinicopathological parameters and patient survival.

Methods: In this retrospective study formalin fixed and paraffin embedded tissue specimen of 75 patients with breast cancer were immunohistochemically stained. Specific anti-E-cad monoclonal antibody, HECD-1, and anti-K18-antibody, CK2, were used. The staining intensity was compared with clinico-pathological values and follow-up datas spanning 80 months.

Results: A definitive positive staining was observed in 21 (28%) specimens for E-cad and 15 (20%) specimens for K18. The survival rate in the E-cad-positive group (81%) and in the K18-positive group (93%) was much higher than in the E-cad-negative or K18-negative groups (both 48%). E-cad and K18 were independent from each other and independent from lymph node status, tumor size/grading and estrogen status. The relative risk to die due to breast cancer within 80 months was decreased in groups positive for K18 (0.08), E-cad (0.28), and ER (0.49). A positive lymph node status increased the relative risk (3.66).

Conclusion: These results suggest that E-cad and K18-expression can serve as independent prognostic indicators for the invasive potential of breast cancer.

305   PUBLICATION

Immunohistochemical studies on oncogene products (C-erbB-2) and p53 protein in human breast cancer: Is it significant for tumor evolution?

L. Lazǎr[1], Ioana Berindan[2], O. Bǎlǎcescu[2], E. Neagoe[1], Rodica Rişcǎ[2], G. Lazǎr[1]. [1]Surgical Department, Oncological Institute, Cluj-Napoca; [2]Tumor Biology Department, Oncological Institute, Cluj-Napoca, Romania

Purpose: The prognostic value of membranal C-erbB-2 oncoprotein and p53 protein was determined in a study of 93 cases of breast tumors surgically removed. For a correct evaluation the relationship beetwen these markers and tumor size, histological and malignancy grade and limph node metastases was done.

Methods: 93 patients with different stages and types of breast carcinomas were analysed immunohistochemically with specific antibodies on paraffin-embedded material, for both c-erbB-2 and p53 proteins on serial sections of 4 μm. C-erbB-2 staining was rated by counting the number of positive cells and the intensity of the reaction. The markage with MoAb for p53 overexpression was established by numbering the stained nuclei. We used MoAb Do-7 Dako, Denmark for p53 and anti c-erb B-2 oncogene protein from Boehringer-Mannheim.

Results: C-erbB-2 oncoprotein was overexpressed in 74 cases and p53 protein in 80 cases. C-erbB-2 is more specifically as an early factor for poor prognosis while p53 proteins owerexpression is a long term factor poor prognosis.

Conclusions: The simultaneous determination of c-erbB-2 oncoprotein and overexpression of p53 protein seems to have a prognostic significance for breast cancer patients. We consider that is of much interest to focus the studies for small-size tumors and the axillary lymph node status. The membrane c-erbB-2 level seems to be an important independent prediction for the prognosis.

306   PUBLICATION

Possible causes of breast cancer in women working at coke-chemical factory (CCF)

V.A. Gurieva, T.L. Gonopolskaya, E.G. Ivanov. Department of Obstetrics and Gynecology, Altay State Medical University, Barnaul, Russian Federation

Purpose: Unfavorable influence on reproductive system of factors associated with coke-chemical manufacture is well known. We studied risk factors for breast cancer in women working at CCF.

Methods: Mammologic and general examination of 1379 women working at CCF with age range from 20 to 54 years was performed. Women with breast cancer and women from conrol group underwent extended examination including assesment of hormonal and immune status.

Results: Breast cancer was revealed in 3 cases. Women with breast cancer were found to have significantly more risk factors compared with control (15.9 + 10.6 versus 14.8 + 6.1, p < 0.05) according to WHO's 56 criteria of breast cancer risk, proposed in 1984. These women had worked in principal workshops for 10–15 years and had reproductive age. Most important factors were a high fat diet and vitamine deficient diet, somatic pathology – obesity, hypertension, hepatocholecystitis and neuro-endocrine syndroms. No one had first degree relatives with cancer. Two women had A (II) blood group. One woman had hyperprolactinemia (785 mM/l) with

relative hyperestrogenemia. All women with breast cancer had decreased amount of T-cells (CD3+) – 61.10 + 0.51 versus 72.10 + 4.40 (p < 0.01) and IgA antibodies – 2.68 + 0.24 versus 4.62 + 0.90 (p < 0.05).

Conclusion: For development of breast cancer were found to be important length of service at CCF and background disturbances of health most prominent in hormonal and immune systems.

307   PUBLICATION

Determination of fibrin D-dimers in patients with breast cancer after cytotoxic chemotherapy

C. Koufos, N. Tsavaris, C. Kosmas, A. Travlou. Department of Pathophysiology and First Department of Medicine, Laikon General Hospital, Athens University School of Medicine, Athens, Greece

Purpose: The biologic behaviour of cancer cells relates to tumor burden, tumor invasiveness as well as some factors of the fibrinolytic pathway.

Methods: The aim of the present study was to monitor changes in the serum levels of fibrin D-dimers in patients with breast cancer undergoing cytotoxic chemotherapy separated into two groups; group A: patients receiving adjuvant chemotherapy and group B: patients undergoing chemotherapy with advanced/metastatic disease. D-dimers were determined with the Latex method (Diagnostica Stago); normal values: <0.5 μg/ml.

Results: Elevated D-dimer values were found in 4/20 (20%) patients in group A (range: 5–36 μg/ml) and in 14/20 (70%) patients in group B (range: 11–102 μg/ml) (P < 0.01) before the initiation of chemotherapy. The study is ongoing and further patient accrual is in progress and data will be presented regarding changes in D-dimer serum levels during or after cytotoxic chemotherapy. In particular, interest should be given to patients receiving adjuvant chemotherapy and show elevation of D-dimer levels.

Conclusion: Serum D-dimer levels may prove to constitute an important prognostic factor in patients with breast cancer receiving chemotherapy in the adjuvant setting or for advanced/metastatic disease.

308   PUBLICATION

Prognostic value of cathepsin D in breast cancer (BC) patients

E. Adrover, M.L. Maestro[1], T. Sanz-Casla[1], V. Del Barco[1], R. Valor[1]. "Virgen de la Luz" Hospital, Medical oncology, Cuenca; [1]University Hospital, Laboratory, Madrid, Spain

Purpose: to assess the prognostic value of cathepsin D quantification on yumour cytosols as a biological marker in BC patients.

Pts and Methods: 147 pts with primary BC were selected for study; median follow-up was 5 yrs. Mean age 59 yrs (range 25–88); postmenopausal 72%; T1: 32%; T2: 44%; T3–T4: 24%. N0: 45%; N1–3: 26%; N > 4: 29%. Histologic type: ductal Ca: 88%; Lobullar Ca: 8%; histologic grade SBR1: 7%; SBR2: 59%; SBR3: 34%. Cathepsin D was quantified on tumour cytosols by CIS radioimmunoassay. Results were compared according to pt and tumour characteristics.

Results: Mean cathepsin D value was 70 pmol/mg cytosolic prot. (range 0–706). With regard to pt and tumour characteristics, cathepsin D mean level was higher in premenopausal women (p = 0.007). Tumour size, nodal invasion and hormone-receptor status were the main prognostic factors for disease free (DFS) and overall surviva (OS) 1.5-year OS was 70% and DFS was 58%. In multivariate analyses, DFS and OS were shorter for cathepsin D levels >30 pmol/mg prot (p = 0.01) and (p = 0.04) respectively.

Conclusion: in our series, cathepsin D levels >30 pmol/mg prot is and independent factor for DFS and OS in breast cancer patients.

309   PUBLICATION

Influence of prognostic factors on overall and disease free survival in male patients with primary carcinoma of the breast

H. Stranzl[1], U. Prettenhofer[1], R. Mayer[1], F. Quehenberger[2], P. Willfurth[1], H. Guss[1], A. Hackl[1]. [1]Department of Radiotherapy, [2]Department of Informatics, Statistics and Documentation, University Medical School of Graz, Austria

Purpose: To determine the value of prognostic factors (age, stage of disease, extent of lymph node involvement, histological grading and hormone receptor status) in male patients.

Patients and Methods: In 31 male patients (mean age 65.7 years, SD ± 11.5) with breast cancer therapy regimen included postoperative