86

METHEMOGLOBINEMIA DETERMINATION BY HPLC METHOD IN BREAST CANCER

della Rovere F., Granata A., Broccio M, Rando DM. and Broccio G.
Cattedra di Chirurgia d'Urgenza, Università di Messina - Italia

Free radicals (FR) have a primary role in carcinogenesis. They (especially for erythrocyte membrane peroxidation) cause oxyhemoglobin (Hb) to oxidate and denaturate, and consequently they form methemoglobin (metHb), proportionally to the oxidative stress. In previous investigations we observed a close relationship between FR, histamine, erythrocyte membrane permeability and Heinz bodies time of appearance in tumoral disease. Heinz bodies were caused by intoxicating in vitro blood by acetylphenylhydrazine (APH). APH, used as a source of FR, causes Hb denaturation, which increases the amount of metHb. In this work we have compared metHb formation in 30 healthy donors (CTRL), in 30 fibrocystic mastopathy (FM) and in 30 breast cancer (K). Blood has been treated with APH in vitro. The metHb has been dosed, before the treatment and after 90' with HPLC method (Variant, BIO-RAD). The metHb % mean concentration in CTRL was 0.2±0.5, in FM 0.3±0.5 and in K 4.2±2.3. MetHb in K is significantly increased more than in FM and in CTRL (P<0.001). MetHb quantity formed in FM and in CTRL does not show significant difference. MetHb formation induces a percentage decrease in Hb. We think that metHb considerable increasing in K is caused by FR which increase eryhtrocyte membrane permeability and consequently the damaging action of APH (Rfs 106).

87

STANDARD-DOSE CHEMOTHERAPY PLUS G-CSF INDUCES PERIPHERAL BLOOD PROGENITOR CELLS (PBPC) MOBILIZATION IN BREAST CANCER PATIENTS.

Del Mastro L., Venturini M, Garrone O, Sertoli MR, Melioli G, Pasquetti W, Balleari E, Bason C, Ghio R, Rosso R.
Istituto Nazionale per la Ricerca sul cancro e Dipartimento Medicina Interna, Genova, ITALY;

In order to evaluate the ability of a standard-dose chemotherapy (CEF= cyclophosphamide 600 mg/m^2, epirubicin 60 mg/m^2, 5-fluorouracil 600 mg/m^2 IV, q 14 days) plus G-CSF (5 μg/Kg subcoutaneously from day 3 to day 10) to mobilize PBPC, peripheral blood samples were performed in eleven early breast cancer patients undergone to CEF chemotherapy as adjuvant treatment. PBPC were evaluated as number of 14-day CFU-GM/mL and CD34+ cells/μL. Peripheral blood samples were performed on day 0 and from day 3 to day 14 throughout the first 3 cycles of chemotherapy. Mean baseline value (range) was 46 (0-144) CFU-GM and 3 (0-7) CD34+ cells. At the 1st, 2nd and 3rd cycle, mean peak value of CFU-GM was 1146 (5-2683), 897 (28-1850) and 611 (79-1925) , while mean peak of CD34+ cells was 198 (48-951), 142 (15-458) and 119 (9-764) respectively. No substantial mobilization occurred before day 9. The peak values of both CFU-GM and CD34+ cells were observed in all patients at day 10 or day 11. Linear regression analysis showed a positive correlation between CFU-GM and CD34+ cells (r=0.69). Our data demonstrate that PBPC can be mobilized by standard-dose CEF chemotherapy plus G-CSF without any relevant toxicity. Thus, PBPC could be collected by one or more leukaphereses perfomed from day 9 to day 11 in order to support further high-dose chemotherapy.

88

PROGNOSTIC VALUE OF LYMPH NODE INVOLVEMENT >50% AFTER NEOADJU-VANT CHEMOTHERAPY FOR LOCALLY ADVANCED BREAST CANCER

Delva R., Gamelin E., Lortholary A., Maillart P., Pein F., Lorimier G., Alleaume C., Larra F. Centre Paul Papin, Angers, France

The prognostic significance of axillary lymph node involvement after neoadjuvant chemotherapy (NAC) for locally advanced breast cancer was regarded in a retrospective study.

PATIENTS AND TREATMENTS : Between 01/1988 and 02/1992, 66 patients were treated by NAC for : stades IIa(2 pts), IIb(9), IIIa(16), IIIb(39). All were treated by standard chemotherapy with 5Fluorouracile, Cyclophosphamide and Doxorubicine : FAC (20 cases), Epiadriamycine :FEC 50 (15) and FEC 75 (12), Mitoxantrone:FNC(17), Pirarubicine: FTC(2) for 4 to 6 courses. Afterwards all patients underwent surgery: mastectomy (50) or tumorectomy (16) and axillary lymph node dissection for all but one. Then, patients were treated by chemotherapy (the same protocol or another) an/or tamoxifen, and finally by radiotherapy.

RESULTS : after NAC it was observed : Clinical Complete Response (CCR) : 22 pts and non CCR : 43 ; Pathological Complete Response (PCR) : 9 and non PCR : 56 ; N- : 18 and N+ 46 ; N+< 3 : 29 ; N+ >= 3:35 ; N+< 50% of taken nodes 37 and N+>=50% : 27.

EVOLUTION : 65 patients are eligible for evolution because of one condition : minimum 6 months follow-up without any event (local recurrence, metastasis, death). Average follow-up is 28 months. It was observed : event 27 - metastasis : 22 - local recurrence : 12 - death : 17. Actuarial method was used for statistical analysis. There is no statistical difference between PCR and non PCR for any event. N+ is of predictive value only for death p<0.01. N+> 3 only for local recurrence. On the contrary there is a great difference according N+if <or>=50% : event : 7/37 (19%) vs19/27(70%) p<0,001 – metastasis : 5/37 (13,5%) vs 16/27 (59%) p <0,001 – death : 3/37 (8%) vs 13/27 (48%) p<0,001 –local recurrence : 3/37 (8%) vs 9/27 (33%) p<0,01. Events occured within less than one year after the end of treatment except for three patients (26,31,38 months). A change or not a change in treatment after surgery does not provide a significant enough difference for an event.

CONCLUSION : the level of 50 % positive pathologic lymph node on axillary dissection after NAC appears in this study as a major pathologic prognostic factor for respectively metastasis, local recurrence and death, whatever the type of regimen chosen after surgery, even if modified. It is stronger than the pathological response on breast and on the classical level of 3 invaded nodes. This allows us to distinguish a group of patients with a worse prognosis who would need an adapted, probably intensified treatment.

89

DETECTION OF PR AND KI-67 IN PARAFFIN-EMBEDDED TISSUE: A COMPARISON WITH FRESH TISSUE RESULTS

De Marco L., Scotti R., Negro R., Migaldi M., Zunarelli E., Botticelli L., Criscuolo M.
Institute of Pathological Anatomy, University of Modena, Modena Italy

There is general agreement about the fact that presence of hormonal receptors (HR) and low proliferative activity (PA) in breast cancer are correlated with a better prognosis. So far, HR and PA have been investigated on fresh tissue, but, being nowadays available new commercial HR - and Ki-67-antibodies for immunohistochemical detection on formalin-fixed, paraffin-embedded tissue, we aimed, with the present study, to evaluated whether progesteron (PR) and Ki-67 expression on fresh tissue does correlate with that observed on paraffin-embedded tissue. Our series includes 35 frozen primitive breast carcinomas on which PR (Abbot) and Ki-67 (Dako) were immunohistochemically detected; later on, the same staining was repeated on paraffin-embedded samples (PR, Dako; Ki-67, Dako). ER-ICA test was not performed because of the large amount of reports showing the reliability of this technique on both tissues. PR-ICA and Ki-67 have been counted, both on frozen and paraffin-embedded samples, by means of a semiautomatic system made up by a monitor grid linked to a Leitz microscope. Linear regression analysis, performed to work out any possible correlation between scores drawn from both methods, pointed out a significant one for both PR-ICA (r=0.787, p,0.002) and Ki-67 (r=0.885, p,0.0001). In conclusion, this study shows that PR and Ki-67 immunohistochemical staining on formalin-fixed, paraffin-embedded tissue can be successfully performed with results which overlap those recorded on fresh material. Morover, this technique makes much easier to perform retrospective studies on stored paraffin embedded tissue.

90

INFLAMMATORY BREAST CANCER:COMBINED THERAPY WITH CHEMO-THERAPY PLUS LONIDAMINE,SURGERY AND RADIOTHERAPY.

de Matteis A.,D'Aiuto G.,Longo C.,Capasso I.,Botti G., Falco I.,Facchini G.,Labonia V.,Landi G.,Marone A.
Istituto Nazionale dei Tumori,Naples,Italy.

Inflammatory breast cancer occurs with an incidence of 1 to 4% among all breast cancers.These patients have a poor prognosis:most women experience metastatic dissemination in the first two years.Patients with IBC are treated at our institution with Chemotherapy (FEC regimen:5-FU 500 mg/sqm i.v. d 1,Farmorubicin 100 mg/sqm iv d 1,CTX 500 mg/sqm i.v. d 1 every 3 weeks)x4 cycles + Lonidamine 450 mg/os/die. After 4 cycles responsive patients (CR+PR) are operated on radical mastectomy followed by a further 4 cycles of FEC+Lonidamine and Radiotherapy.Stable and progressive patients are treated with primary Radiotherapy and Salvage Chemotherapy (Mitomycin 15 mg/sqm i.v. every 6 weeks+Mitoxantrone 10 mg/sqm i.v. every 3 weeks x 4 cycles).27 patients entered in the study.We obtained CR+PR in 22 patients (81%),a minimal response in 3 patients,NC in 2 patients.At present time 20 patients are free of disease.

91

BREAST CANCER: INFLUENCE OF AGE ON TREATMENT CHOICE OF SURGEON AND RADIATION ONCOLOGIST.

De Winter K., Van den Weyngaert D., Becquart D., Scalliet P.
Dep. of Radiation Oncology, AZ Middelheim, B-2020 Antwerp.

Conservative surgery with radiotherapy or mastectomy offer equal chances for local control and survival of breast cancer, but may have a different impact on quality of life. The few available data indicate that breast conservative surgery is less often proposed to elderly patients, an attitude based on the premises that breast conservation is of less concern to older women. The aim of this retrospective study was to investigate the influence of age on treatment choice between conservative and radical surgery, and on prescription of irradiation schemes.

From Jan. 1983 to Dec. 1988, 492 patients with T1-2-3, N0-1, M0 histologically proven carcinoma of the breast were treated in the department, and were followed for a mean time of 64 months. Mean age was 54.1 years (range 24-81), with 98 patients older than 65 and considered as elderly. Conservative surgery was performed in 40 % of patients, mastectomy in 60 %; 93 % had an axillary sampling. The policy in the department was to irradiate thoracic wall or breast upto 47 Gy, followed by a boost of 20 Gy after conservative surgery. Lymph node areas were irradiated in case of axillary node invasion or when no axillary sampling was performed.

There was a significant trend toward more advanced T-stage with increasing age (p=0.03), but there was no correlation between N-stage and age. Multivariate analysis revealed that even after correction for tumorstage, there was an obvious trend to treat older patients with more radical surgery (p<0.001), which may have a negative influence on quality of life. Elderly patients less frequently underwent axillary lymph node sampling (p<0.001); therefore they were likely to be understaged. Since they also less frequently received axillary irradiation (p=0.047), there was no compensation for this and they also may be undertreated. The total irradiation dose delivered on the initial tumorsite was smaller in elderly patients, because they were less often boosted (p<0.001). In this group of patients there were no significant differences in local control and survival between younger and older patients. In comparison to younger patients, elderly breast cancer patients were understaged and albeit more radical in some ways, undertreated, despite the lack of guidelines to do so on a scientific base.