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REMISSION OF METASTATIC BREAST CANCER AFTER COMBINED SOMATOSTATIN AND ANTIPROLACTIN TREATMENT

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The results of prolactin (PRL) suppresssion as an endocrine monotherapy in human breast cancer have been disappointing. The lactogenic receptor of human breast cancer cells is also stimulated by human growth hormone (GH). Antiprolactin agents suppress only the prolactin secretion without influencing GH levels.As stated previously (HOLTKAMP et al., Onkologie, 11,3,1988), this observation probably explains why antiprolactin agents do not induce regressions in human breast cancer. To investigate the effect of a combined suppression of prolactin and growth hormone, 8 patients with progressive metastatic breast cancer were treated with 7.5 mg Bromocriptine p.o. (2.5/0/5mg) and 2 x 150 mcg (8 am, 10 pm) Somatostatin (SMS 201-995) s.c. for 8 weeks. In all patients a suppression of PRL and GH levels was observed. In one of 8 patients a complete remission of a local recurrence was observed after a treatment period of 8 weeks. This is for our knowledge the first report of a remission of metastatic breast cancer after combined somatostatin and antiprolactin treatment.

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PLASMA PROLACTIN AS A TUMOR MARKER IN ADVANCED BREAST CANCER

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Plasma prolactin (PRL) levels were determined by Radioimmunoassay in 117 breast cancer patients (Pre-menopausal N = 52; Post-menopausal N = 65) and were compared with age matched healthy controls (Pre-menopausal N = 30; Post-menopausal N = 30). Based on the disease status, these patients were grouped into (i) those who developed local or distant metastases, (ii) who had stable disease and (iii) who responded to the various therapeutic modalities at the end of two years. Follow-up examinations showed PRL changes correlating well with the clinical course and even preceded clinical symptoms.
An early rise in PRL is an important finding and may offer a sensitive means to predict the presence of recurrent disease in patients with breast cancer.

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PROGNOSTIC VALUE OF PROLACTIN RECEPTORS IN HUMAN BREAST CANCER.

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The role of prolactin receptors (PRL-R) in human breast cancer (BC) has still now received a little attention and its possible significance as a prognostic factor remains controversial. Overall survival (OS) was considered in 166 women bearing primary BC in a retrospective evaluation from 1978 to 1986, in order to show if the presence of PRL-R and estrogen receptor (ER) in BC samples could be of prognostic relevance. Patients (pts) mean age was 59 years (25-83), premenopausal were 42 (25%), postmenopausal 124 (75%). 105 pts had stage I-II disease at the time of mastectomy, 45 stage III-IV and 16 unknown. Radiometric assay of PRL-R and ER was performed in a single lab and a BC sample was considered PRL-R positive when the specific binding was greater than 0.5%/0.5 mg protein. 10 fmol/mg of cytosol protein was choosen as cut-off for ER positivity. The survival curves were estimated according to the Kaplan-Meier method. Comparison between different curves were made using Log-rank Test. The Cox proportional hazard regression model was used to determine the significance of association between each prognostic factor (PRL-R, ER, menopausal status, stage, nodes involvement) and the OS time.A positive relationship between PRL-R and OS was present in overall pts ($p<0.05$) and particurarly when only stage I-II pts were considered ($p<0.02$). On the contrary, pts bearing ER positive BC did not show a significant survival advantage vs ER negative. The Cox analysis showed that only PRL-R presence had a positive prognostic significance ($P<0.05$) while the stage had a negative one ($p<0.0001$).

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UROKINASE-TYPE PLASMINOGEN ACTIVATOR (uPA) ANTIGEN IS AN INDEPENDENT PROGNOSTIC FACTOR FOR EARLY RELAPSE IN BREAST CANCER PATIENTS

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Cancer cells secrete uPA as an enzymatically inactive proenzyme (pro-uPA) which binds to specific receptors on the tumor cell surface. After binding, pro-uPA is converted by trace amounts of plasmin into the active form (uPA). Receptor-bound uPA converts plasminogen into plasmin which also binds to cell surface receptors. Surface-bound plasmin then degrades proteins of the tumor stroma and the basement membranes. This tumor-associated proteolysis provides the basis for tumor cell invasion and facilitates the release of tumor cells which eventually may lead to metastasis. We measured the total uPA antigen (uPA and pro-uPA) in tissue homogenates (1 % Tx-100) of patients with breast cancer (n = 115) or benign lesions (n = 30) by ELISA and immunohistochemistry. Median values of uPA / mg protein were determined. **Breast cancer: 2.6 ng. Benign lesions: 0.23 ng.** Patients with high uPA content (cut-off **2.6 ng** / mg protein) showed a statistically significant higher incidence of relapse compared to patients with low uPA content (**12.5 months**). Multivariate regression analysis revealed that uPA had the strongest impact on early relapse (**relative risk 21.1**) followed by hormone receptor status (**5.8**) and lymph node involvement (**3.0**). By means of uPA antigen determination high or low risk patients can be selected within the stated risk groups. Lack of correlation between uPA antigen and established prognostic factors thus lends credence to its status as an independent prognosis-associated factor.