CORRELATIONS

Althrough, not number one female cancer cause in India, breast cancer ranks second. At the Gujarat Cancer and Research Institute, we have been studying the role of steriod receptors and steriod and peptide hormones as well as tumor markers in breast cancer patients for last seven years.

The ER and PR are now recognised as important determinants of breast cancer biology. Steriod receptors in the different stages was the strongest predictor of overall and relapse free survival. Nonuniform distribution was observed between these receptors and nodal positivity/negativity, histologic grade and survival. Necrosis of the tumor may be an independant prognosticator. The presence or absence of lymphocytic infiltration offered some degree of prognostication. Lymphocytic infiltration in combination with progesterone receptor conferred some prognostic power in relapse free survival.

A number of epidemiologic and endocrinologic investigations have suggested an association between hormones and breast cancer. In the present study 84/111 (75.6%) patients had advanced breast cancer and 92.7% patients had abnormal ovarian function which might be due to advanced breast cancer or hyperprolactinaemia. We have observed a decreased

trend of FSH and E_2, no change in LH and an increase in PRL and markers as stage advanced.

Moreover, it was observed that peptide hormones and markers were low, whereas steroid hormones were higher in node negative and grade I tumours as compared with node positive and grade II + III tumors. These findings collectively announce node negative patients as relatively less aggressive while advanced tumors more aggressive. This was further validated by the observed low steriod receptor negativity of the node negative patients as compared with the node positive patients.

Chemo- and endocrine therapy resulted into a significant rise in gonadotropins with concomitant low E_2 leading to ovarian failure in pre-menopausal patients. This resulted into amenorrhea which was documented by decreased ratio of eastradiol : gonadotrpins. These results indicate that drug induced amenorrhea in pre-menopausal patients was not responsible for the improvement of disease free survival observed in these patients because majority of our patients developed recurrences immediately after completion of adjuvant therapy.

Interestingly, we have observed in few patients only, that prior to death there was a significant drop in the FSH and

LH with concomitant rise in PRL. On the other hand, in patients who were in remission, the gonadotropins remained elevated with low PRL levels. This finding needs confirmation by analysing some more samples.

Plasma Prl levels were consistent with low E_2 and Pg alongwith elevated FSH and LH. Hyperprolactinaemia (>3Ø ng/ml) was noted in 41.4% patients. Although, to our knowledge this study for the first time demonstrates the relative significance of PRL as an index of tumor aggressiveness and that its levels significantly increased with progression. The high prolactin levels were significantly reduced to almost normal levels amongst the patients who remained in remission. This suggests that elevated prolactin has to do with metabolic processes of the metastatic tumor. It might be possible that prolactogenic hormones like estrogens stimulate prolactin dependent tumor cells via prolactin release. Thus, prolactin probably modulates the effect of other hormones on tumor growth in advanced breast carcinoma.

An early rise in prolactin in advanced breast carcinoma is an important finding and may offer a sensitive means to predict the presence of occult disease which is often difficult to evaluate. This view of prolactin being an

indicator of progressive disease is supported by the fact that in case of non-responders a rise in prolactin preceded clinical symptomss.

The prolactin estimations have demonstrated a sensitivity 93.54% , specifictiy 95.23%, predictive values for positive and negative tests of 96.66% and 90.90% respectively and diagnostic efficency 94.23% in breast carcinoma monitoring. Thus, serial prolactin estimations may be a more sensitvie indicator for assessing a response to treatment. Serial estimations of rising prlactin levels are useful in early diagnonsis of recurrence in progressive disease.

Steroid receptors have long been acknowledged as important determinants of breast cancer biology. We therfore, correlated prolactin levels with steroid receptors. No corelations were observeed between prolactin and the ER or PR status.

The present findings indicate that determinations of CEA, TPA and CA 15-3 were not useful for stage II breast carcinoma pateints when compared with controls. This might be due to the low sensitivity on one hand and the absences of organ or tumor specifictiy on the other. Node negative and grade I tumors had low concentrations of these markers as compared to node positive and grade II + III tumors. CEA

determination appear especially valuable in monitoring patients with metastatic disease in bone, a condition oftern difficult to follow by other means. Furthermore, lower expression of CEA with soft tissue metastasis was explained by the fact that the soft tissue metastasis were diagnosed more readily due to their localization.

When monitering breast cancer patients by these markers, the observation of each patients's individual antigen plasma profile is the most important criterion in surveillance. The retrospective serial marker measurements made during the follow-up of breast cancer patients who relapsed, indicated that CA 15-3 determination could announce the onset of dissemination before it was detectable by the usal clinical criteria. The levels of CEA, CA 15-3 and TPA in the present study demonstrated a rise with disease progression. Moreover, the marker levels of preceding samlpe were also elevated reflecting into a lead time of 2-5 months before the progression was validated by other established criteria. The elevations of CEA were statistically non significant, limiting its application only to small group of patients. All these data alongwith that obtained in the present study point towards a limited scope for CEA estimations in monitoring pre-menopausal breast carcinoma patients.

TPA levels exhibited a statistically non-significant rise

amongst responders. The high false positive/negative rate, seriously limits the use of TPA in pre-menopausal breast carcinoma monitoring.

The effectivness of cytotoxic treatments was not accuately indicated by TPA and CA 15-3. It was observed that a small fraction of breast cancer patients did not have elevated CA 15-3 levels at any time during clinical course. The high false positive/negative rate of TPA and low sensitivity, specificity and predictive value of CEA and CA 15-3 prevents their use as an indicator of disease status.

We have obtained best correlations between steroid receptors, steriod hormones, peptide hormones and markers with the various clinico-pathologic variables in pre-menopausal breast carcinoma patients.

The PRL estimations have demonstrated a sensitivity 93.54%, specificity 95.23%, predictive values for positive and negative tests of 96.66% and 90.90% respectively and diagnostic efficiancy 94.23% in breast carcinoma monitoring. Thus, serial prolactin estimation may be a more sensitive indicator for assessing a response to treatment. Serial estimations of rising prolactin levels are useful in early diagnosis of recurrence in progressive disease. At present, we are monitoring our breast carcinoma patients with plasma prolactin.