

Four tumor markers in monitoring of patients with breast cancer

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Key Words: Breast cancer, tumor markers, patients monitoring

Abstract — A comparative study of four markers, including 3 enzymes (sialyltransferase, 5-nucleotidase and Zn^{++} dependent nucleoside diphosphatase «CDPase» and sialic acid was performed in 15 women with clinical or subclinical breast cancer under chemotherapy. The levels of the enzymes and sialic acid were measured prior to and during chemotherapy (before each course). The sialic acid and the nucleoside diphosphatase could not be used as markers for the breast cancer because all the measurements were very closed to normal levels. In contrast the activities of sialyltransferase and 5 nucleotidase were at least twice fold than the median of healthy women and could be correlated with the clinical course.

Introduction

Breast cancer is the most common cancer in the western world, including Finland. In women it is the leading cause of death due to cancer (1). The incidence of breast cancer is increasing (2), which implies diagnostic and therapeutic problems in the future. Carcinoembryonic antigen (CEA) is the most commonly used tumor marker today particularly in patients with cancer of colon (12,13) and breast cancer (8,5,9). In this study we used four, well established, tumor markers. Sialyltransferase and UDPase can be used as reliable markers for monitoring the course of ovarian and testicular cancer, especially for the early detection of recurrence after initial response and before any detectable disease localization (10,4). 5'Nucleotidase is also of the same remarkable value in cancer patients monitoring (4). Finally sialic acid is very spread tumor marker (6, 11).

Patients and Methods

Patients: Serum samples were obtained, before starting chemotherapy and at different times during the chemotherapy for up to 12 months from 15 patients admitted to our hospital for advanced breast cancer. Six of them had locoregional disease (T_4N_+ , classified as stage IV) and chemotherapy was their primary treatment. The other nine had recurrent or metastatic disease after modified radical mastectomy in the past. Clinical course was evaluated before each chemotherapy and

the response classified according to the EORT rules. The clinical extend of the disease was the only reference point for the eventual correlation of the markers under investigation and disease.

Chemotherapy: Ten of the patients were under a schedule with Cyclophosphamide, Epirubicin and Fluorouracil (FEC) every 21 days and five women under Cyclophosphamide, Methotrexate and Fluorouracil (CMF) every 21 days too.

Methods: The assay systems for 5'Nucleotidase, Zn^{++} dependent nucleoside diphosphatase are previously described by authors (10,3). Sialyltransferase was measured using the Kessel and Allen method (7) modified by the authors (10). Sialic acid was measured using kit purchased from Boehringer Mannheim.

Results

The values of the four tumor markers, during chemotherapy, are presented in Figures 1-4. The majority of the values of nucleoside diphosphatase and sialic acid (Fig. 1 and Fig. 2) are very closed to normal levels (dotted area). While the levels of sialyltransferase and 5' nucleotidase are at least, in many cases, twice fold than the normal ones. (Fig. 3 and Fig. 4). A clinical correlation of selected values is obvious, in Fig. 3 and in Fig. 4, for bone metastases **I**, locoregional advanced disease **II** and pleural effusion **III**. In contrast there is no clinical correlation **IIII** with selected values of sialic acid and nucleoside diphosphatase (Fig. 1 and Fig. 2).

In one case, after initial response for some months, arise of the sialyltransferase and 5' nucleotidase was ob-

* Correspondence

served before any other biochemical or clinical finding of the forthcoming bone metastase (Fig. 5).

Those two enzymes were also arised, before any

other signal, in a patient with massive recurrence and pleural effusion after a nearly complete response for a couple of months. (Fig. 6).

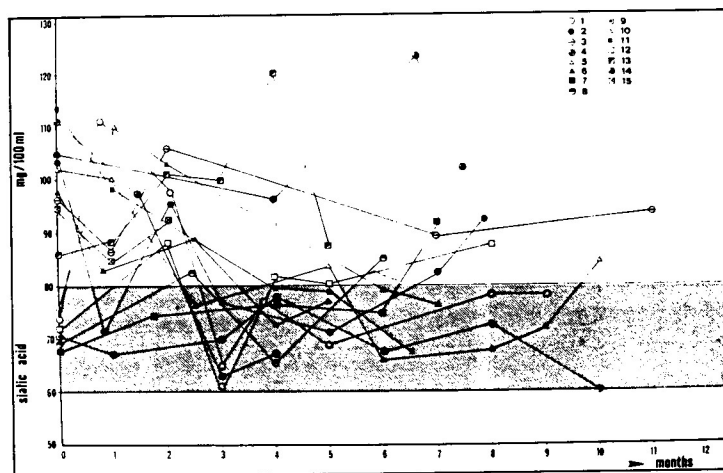


Fig. 1. Sialic acid serum levels during chemotherapy (mg/100 ml). Details for cases 1 and 11 see figures 5 and 6 respectively. The initial high levels in cases 4 and 7 are correlated with the advanced disease. In contrary, there is no clinical correlation between the high levels in cases 13 and 14 to the corresponding disease. (dotted area-normal levels).

Fig. 2. Nucleoside diphosphatase (CDP ase) serum levels during chemotherapy (nMols/h/ml) details for cases 1 and 11 see figures 5 and 6 respectively. The high level of CDPase seen in case 2 (4th month) was incongruent with some Kind of clinical deterioration. The repeated high levels of CDPase in case 4 were correlated with the active disease. In the vast majority of the other cases the levels were within the normal limits (dotted area-normal levels).

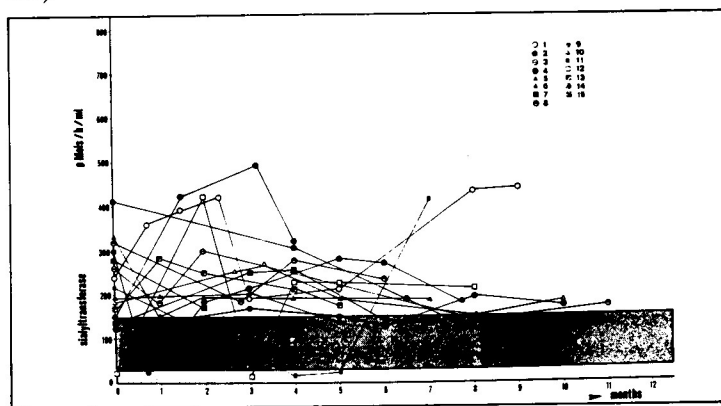
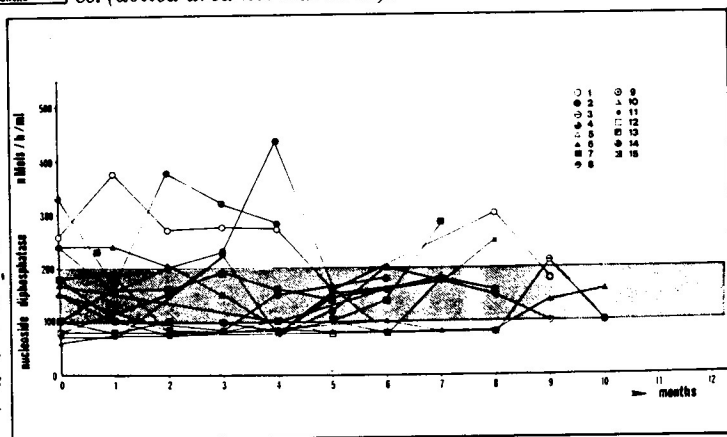
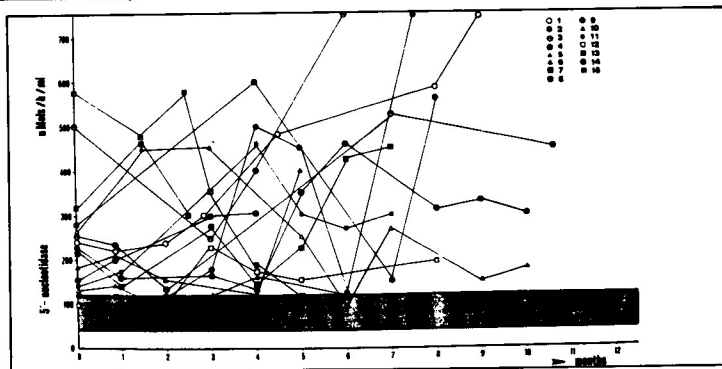


Fig. 3. Sialyltransferase serum levels during chemotherapy (pMols/h/ml). Details for cases 1 and 11 see figures 5 and 6 respectively. The extremely high levels in case 4 are correlated with the locoregional advanced disease. The descending levels in case 14 are correlated with the clinical remission and, in contrary, the increasing levels in case 7 are correlated with the local recurrence and bone metastases in this case. (dotted area-normal levels).

Fig. 4. 5'-nucleotidase serum levels during chemotherapy (nMols/h/ml). Details for cases 1 and 11 see figures 5 and 6 respectively. With the exception in case 2, all other high levels are correlated with advanced disease, especially liver involvement (for example case 8), or additional disease dissemination. (dotted area normal levels).



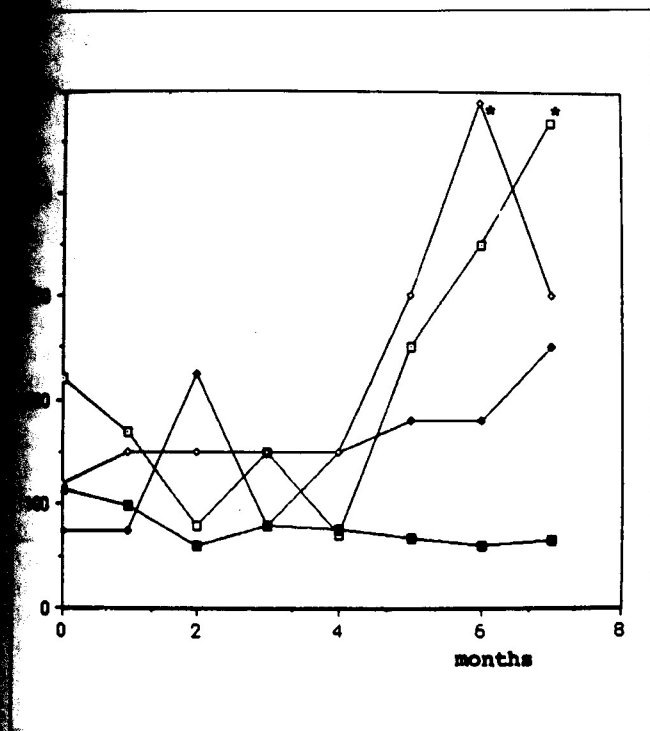


Fig. 5. Levels of the four tumor markers during chemotherapy, —□— STF, —◇— CDP, —■— Sialic acid and —○— 5' nucleotidase in a patient of age 60 T₄N₃MO disease. Primary chemotherapy modified CMF and TAM.

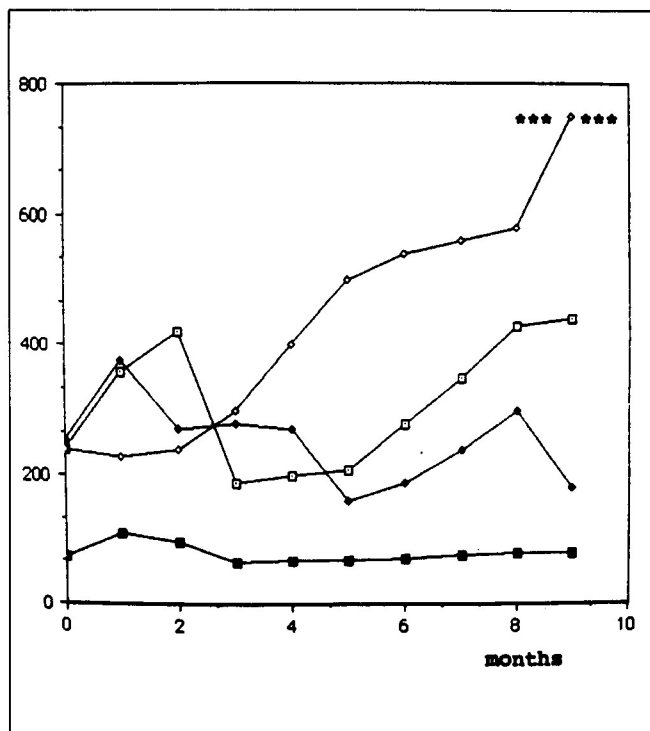


Fig. 6. Levels of the four tumor markers during chemotherapy, —□— STF, —◇— CDP, —■— sialic acid and —○— 5' nucleotidase, in a patient of age 52, T₄ N₁ MO disease. She had also ER 38 fmols/mg protein. Primary chemotherapy FEC and TAM.

Discussion

It has been our experience that the contemporary measurement of many tumor markers is of remarkable value. It has been also our experience that the combination of clinical and laboratory data, when simultaneously analyzed, produces the most accurate assessment of patient monitoring. Although two of the four parameters, sialic acid and nucleoside diphosphatase, could not be used as markers in breast cancer, the aim of this work was carried out and the results of sialyltransferase and 5' nucleotidase confirmed their usefulness as markers for monitoring of patients with breast cancer, during chemotherapy. Maybe the combination of these two markers with CEA or other antigens would be of greater interest.

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