AN ASSESSMENT OF THE CLINICAL USEFULNESS OF TWO SERUM MARKERS, CA 15 3 AND HMFG 2 IN LOCALIZED AND METASTATIC BREAST CANCER

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SUMMARY

CA 15 3 is a circulating glycoprotein defined by two monoclonal antibodies (115 D 8 and DF 3) with good specificity for breast cancer. Tumour-associated antigens have been detected by the monoclonal antibody HMFG 2 using a low pH ELISA method. We compare the values obtained using these two assays in patients with localized and metastatic breast cancer.

CA 15 3 and HMFG 2 levels were measured in 61 patients, 24 localized and 37 metastatic, evaluated by standard biochemical and radiological testing. Of the patients with metastatic disease 78.4% had an elevated CA 15 3 level whereas only 8.3% of patients with localized disease had an elevated level ($\chi^2 = 28.2, p = 0.001$); 29.8% of patients with metastatic disease had elevated HMFG 2 levels while among those with localized disease 16.7% had elevated levels ($\chi^2 = 0.57, p = NS$). We conclude that only CA 15 3 is a useful marker in advanced disease.

KEY WORDS Breast cancer Monoclonal antibodies CA 15 3 HMFG 2

INTRODUCTION

Mammary carcinomas have been found to secrete mucin-like glycoproteins. CA 15 3 is a circulating antigen expressed by human breast tissue and is defined by two antibodies, 115 D 8 against antigens of human milk fat globulin (Hilkens et al., 1984) and DF 3 directed against a membrane fraction of human breast cancer (Kufe et al., 1984).

CA 15 3 has been found to be a useful marker for monitoring of patients with breast cancer (Hayes et al., 1986). The use of the monoclonal antibody HMFG 2 raised against a delipidated preparation of the human milk fat globulin has been advocated for the serological detection and monitoring of breast cancer (Dhokia et al., 1986). In this study we have compared these two assays on the sera of patients with localized and metastatic breast cancer.

PATIENTS AND METHODS

Serum samples were obtained from patients attending The Edinburgh Breast Unit during 1989. The patients were staged according to UICC criteria at the time of

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Table 1. Distribution of CA 15 3 and HMFG 2 levels in patients with breast cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>CA 15 3 U ml(^{-1})</th>
<th>HMFG 2 U ml(^{-1})</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;35</td>
<td>&gt;35</td>
<td>&lt;40</td>
</tr>
<tr>
<td>Localized</td>
<td>22</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Metastatic</td>
<td>8</td>
<td>29</td>
<td>26</td>
</tr>
</tbody>
</table>

\(\chi^2 = 28.5, p < 0.001; \chi^2 = 0.57, p = \text{NS.}\)

Samples from 61 patients were analysed: 24 patients had localized disease and 37 metastatic. The average age was 54.8, range 40–78.

CA 15 3 immunoradiometric assay was measured using the CIS International kit according to the manufacturer's instructions. HMFG 2 was analysed using a sandwich ELISA method. The upper limit of normal for the CA 15 3 assay was set at 35 U ml\(^{-1}\) based on sera from healthy blood donors. This value is in the range quoted by other authors (Colomer \textit{et al.}, 1989; Pons-Anicet \textit{et al.}, 1987).

The upper limit of normal for HMFG 2 was set at 40 U ml\(^{-1}\) based on sera from Edinburgh B.T.S.

RESULTS

Using the CA 15 3 assay in patients with localized disease the median value was 12.4 U ml\(^{-1}\), the mean was 15.2 U ml\(^{-1}\) (range 5.9–48.2 U ml\(^{-1}\)). Results for metastatic disease with CA 15 3 gave a median of 81.7 U ml\(^{-1}\), mean 384.6 U ml\(^{-1}\) range 11.5–3530 U ml\(^{-1}\).

The HMFG 2 values in localized disease resulted in a median of 10 U ml\(^{-1}\) and a mean of 29 U ml\(^{-1}\) (range 0–200 U ml\(^{-1}\)). Results for metastatic disease with HMFG 2 gave a median of 23.3 U ml\(^{-1}\), mean 69.8 U ml\(^{-1}\) (range 0–500 U ml\(^{-1}\)). Using the normal values for both assays obtained from healthy blood donors no significant difference was seen between the distribution of values obtained with HMFG 2 between localized and metastatic disease. However there was a significant difference between values for localized and metastatic disease using the CA 15 3 assay (see Table 1).

DISCUSSION

Polymorphic epithelial mucin-based (PEM) tumour markers have been extensively studied as a discriminator between benign and malignant disease, because of the low positivity rate in early malignant disease these markers have no role in this situation (Bon \textit{et al.}, 1990). However, they can discriminate early from advanced breast cancer (Bon \textit{et al.}, 1990).
Studies have found the CA 15 3 assay to be a useful marker for metastatic breast cancer. Various authors have used a range of normal values for CA 15 3, but taking an upper limit of 35 U ml\(^{-1}\) 55–91 per cent of metastatic patients were found to have elevated levels (Hayes et al., 1986; Colomer et al., 1989; Pons-Auicet et al., 1987). Ten per cent of localized patients were found to have CA 15 3 levels greater than 35 U/ml (Hayes et al., 1986). HMFG 2 levels have been found to be elevated in 72 per cent of patients with metastatic breast cancer (Dhokia et al., 1986). The mucin-like cancer associated antigen (MCA) has shown concordance with the changes in clinical status in 64 per cent of locally recurrent breast cancer patients, and in 84 per cent of patients with metastatic disease (Laurence et al., 1991).

During the follow-up of 285 patients with early breast cancer 27 developed distant metastases, tissue polypeptide antigen (TPA) was found to be elevated in 63 per cent of these and to mirror clinical signs more accurately than CA 15·3 or CEA assayed at the same time. The closest association was with the combination of all three markers when 87 per cent of metastatic patients were found to have elevated levels. However 83 per cent had elevated levels of the CA 15·3 and TPA combination (Nicolini et al., 1991).

In this study CA 15·3 levels correlated well with the stage of disease. We found significantly elevated levels in 78·4 per cent of patients with metastatic breast cancer, compared with 8·4 per cent of patients with localized disease. However we did not find the HMFG 2 assay correlated with the stage of disease; 29·8 per cent of patients with metastatic disease had elevated levels, and 16·7 per cent of patients with localized disease had raised levels.

We feel that CA 15·3 is a useful marker for monitoring metastatic breast cancer but would agree with previous authors that it is not sensitive enough to detect early breast cancer (Bon et al., 1990). HMFG 2 did not prove to be a useful marker in breast cancer.

REFERENCES


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