Lipid associated sialic acid in plasma (LASA-P), plasma DM/70K, tumor epidermal growth factor and tumor DNA index in women with ovarian cancer

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Abstract. We studied two plasma biomarkers in 67 patients with ovarian cancer who had surgery between 1990 and 1992. Lipid associated sialic acid in plasma (LASA-P) was assayed by biochemical extraction and partition. DM/70K was detected with the monoclonal antibody NB12123. We found a highly significant correlation between these two markers ($p < 0.0001$). Neither marker was associated with age or tumor stage or grade. We also studied two tumor markers, Epidermal Growth Factor Receptor (EGFR) and DNA Index (DI). EGFR and DI were also not related to age of patient, tumor stage, or tumor grade, nor were they related to LASA-P or DM/70K. However, EGFR and DI were positively correlated with each other ($p = 0.04$), suggesting that tumor EGFR may be associated with poor survival.

Introduction

There have been numerous reports of the existence and potential clinical value of human tumor markers (1). But many markers do not have the sensitivity or specificity needed for a cancer diagnostic screening test. Also, many markers are elevated in several malignancies and benign conditions. In ovarian cancer, the circulating plasma markers CA 125, Lipid Associated Sialic Acid in Plasma (LASA-P), CA 19-9, and CEA have been studied (2). After second look surgery, the finding of two elevated markers, one month or more apart in patients clinically free of disease, was strongly suggestive of recurrence. Another circulating plasma marker, DM/70K, is elevated in 70% of patients with ovarian cancer (3). High levels of DM/70K are also associated with other gynecologic malignancies, as well as carcinoma of the lung and breast. Markers in the tumors themselves are of interest in ovarian cancer. DNA index (DI) (4) and Epidermal Growth Factor Receptor (EGFR) (5) have both been evaluated. We report here on our study of LASA-P, DM/70K, DI and EGFR in ovarian cancer patients.

Patients and methods

We studied 67 patients with ovarian cancer who had surgery between 1990 and 1992. All tumors were epithelial ovarian carcinomas except for one involving the fallopian tube. Plasma specimens to be assayed for LASA-P and DM/70K were collected in tubes containing ethylenediamine tetra acetic acid (EDTA) and frozen until tested. LASA-P was assayed by biochemical extraction and partition (6). DM/70K was detected with the monoclonal antibody NB12123 (3).

Fresh frozen tumor specimens were analyzed by flow cytometry to assess DI (4). EGFR was measured in the same specimens by radioimmunoassay (7). Dianon Systems, Stratford, Connecticut, performed all assays.

Results

We could find no relationship between LASA-P or DM/70K and tumor stage, tumor grade or age of the patient. However, we did find a highly significant correlation between DM/70K and LASA-P levels (Fig. 1). Tumor EGFR and tumor DI were also not related to age of patient, tumor stage, or tumor grade, nor were they related to LASA-P or DM/70K. However, EGFR and DI were positively correlated with each other (Fig. 2).

Discussion

Tumor DI is a useful prognostic factor in ovarian cancer. Patients with diploid or near diploid tumors (DI < 1.25) survived significantly longer than those with aneuploid tumor (DI > 1.25) (4).

Tumor EGFR is associated with poor prognosis in breast cancer (7). In ovarian cancer, the role of EGFR is less certain. One study associated EGFR with improved response to chemotherapy and increased overall survival (8); another investigation linked EGFR in advanced ovarian cancer with

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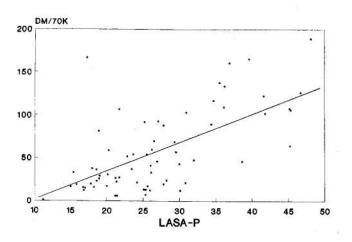
Figure 1. Plasma levels of DM/70K (arbitrary units/ml) and LASA-P (mg/dl) in 67 women with ovarian cancer. There is a significant correlation of these two assays (r = 0.67, p < 0.0001).
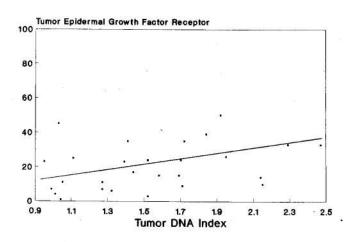

Figure 2. Tumor Epidermal Growth Factor Receptor (fmol/mg) and tumor DNA Index (1 = diploid). These two measurements are significantly correlated (n = 28, r = 0.383, p = 0.04).

found in the lipid fraction of plasma. LASA-P is elevated in most patients with disseminated ovarian carcinoma and normal in almost all patients with benign ovarian tumors. LASA-P measurements correlate well with serum CA-125. Moreover, the sensitivity of LASA-P and CA-125, when used together, is higher than when either assay is used alone (2). Our finding of a strong correlation between LASA-P and DM/70K measurements suggests that the combination of the two assays might be more sensitive than either one alone. This sensitivity might be increased even further with the addition of CA-125. Although more evaluation is necessary, the use of all three assays could be of more value in early detection and post treatment follow-up of ovarian cancer than the use of one or even two assays in tandem.

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poor prognosis (9). Our finding of a positive correlation of EGFR with DI suggests that tumor EGFR should be associated with poor prognosis. Further studies are needed to clarify this finding. DM/70K is one of the more promising new circulating tumor markers for ovarian epithelial carcinoma. Unlike CA-125, which is only rarely elevated in mucinous ovarian malignancies, DM/70K seems to be a marker for all types of epithelial ovarian carcinomas, regardless of histologic type or degree of differentiation. In addition, circulating DM/70K levels are high in patients with all stages of ovarian cancer, including more than half of those with early stage disease. Thus, DM/70K might be useful for early detection of ovarian cancer, as well as for monitoring patients with the disease (1). However, DM/70K is still designated as being for investigational use only. LASA-P is a biomarker useful in a wide range of malignancies. It reflects alteration in the surface membrane of malignant cells. The assay for LASA-P measures gangliosides and glycoproteins