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Letter to the Editor

Detection of Virus Antigen in Male Breast Cancer

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IN RECENT years a tumor antigen has been identified in human breast cancer by the indirect immunoperoxidase method. This antigen cross-reacted immunologically with a glycoprotein of the mouse mammary tumor virus (gp 52, with a molecular weight of 52,000) [1]. The specificity of this reaction has been established by absorption experiments [2]. Positive responses were detected only in breast carcinoma, being absent in benign breast lesion as well as in malignancies other than breast [2]. Recently, Keydar *et al.* [3] have suggested a correlation between the severity of the disease and the presence of gp 52 cross-reacting antigen. We studied the detectability of gp 52 antigen in male breast cancer and its possible role as a prognostic factor.

Paraffin-embedded tissues of nine cases of male breast cancer were available. Brief clinical details are given in Table 1. In eight cases a radical modified mastectomy was performed. In one case a simple mastectomy was performed, since lung metastases were already present (Case 4). Sections from the paraffin-embedded tissues were stained according to the indirect immunoperoxidase method for detection of gp 52 cross-reacting antigen in the laboratory of the Department of Microbiology, Tel Aviv University, as described by Keydar *et al.* [4]. Five cases were found to be gp 52 Cross-reacting antigen-positive (Figs 1–3), and in four cases the antigen could not be detected. The five cases which stained positively were in an advanced stage of the disease at the time of mastectomy according to the tumor diameter and/or the presence of axillary lymph node or distant metastases. Follow-up data revealed that three of them died from metastatic disease. On the other hand, in three out of the four cases in which there was no evidence of metastatic or recurrent disease the gp 52 antigen reaction was negative (Table 1).

The mouse mammary tumor virus (MMTV) was discovered about 40 yr ago and identified as a B-type RNA virus [5]. Injection of the virus results in development of mammary tumor in the mouse but not in other laboratory animals. Particles resembling murine B-type and C-type viruses were identified by ultrastructural studies in human breast cancer tissues, as well as in human milk [6]. The subsequent isolation and biochemical and biophysical analyses of these particles revealed further similarities, principally the presence of RNA-dependent DNA polymerase (reverse transcriptase) complexed to a 70S RNA molecule, features characteristic of oncornaviruses [7]. In addition, molecular hybridization studies have demonstrated a partial homology between RNA molecules found in human breast tumors and the RNA genome of the MMTV. Ritzi *et al.* [8] developed a radioimmune assay and established that the circulating blood contains levels of gp 52 of MMTV which clearly identify tumor-bearing animals. It was shown that metastatic and primary tumors in mice have been detected with complete certainty by increased plasma cell levels of gp 52 and that surgical excision of the tumor is followed by a sharp (10–100-fold) decrease of the plasma gp 52 levels [9]. Tumor regrowth was characterized by increased gp 52 levels and some recurrences were diagnosed before they were palpable. Animals that remained tumor-free maintained gp 52 levels at or below 15 mg/ml. Unfortunately the detection of such an antigen in human plasma seemed to be beyond the present sensitivity of radioimmunoassay. Therefore, in the search for mammary tumor virus antigens in

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Table 1. Clinical data and immunoperoxidase staining in nine cases of male breast carcinoma

Case	Age (yr)	Histological type	Axillary lymph node metast.	Tumor dia. (cm)	Follow up	GP 52 antigen
1	45	inf. duct. ca.	+	1.0	died	pos.
2	78	inf. duct. ca.	+	2.0	died	pos.
3	51	inf. duct. ca.	-	5.0	died	pos.
4	89	inf. duct. ca.	*not available	4.0	alive — 2 yr	pos.
5	68	intraduct. ca	-	2.0	alive — 10 yr	pos.
6	49	intraduct. ca.	-	2.0	alive — 10 yr	neg.
7	69	inf. duct. ca.	-	1.0	alive — 4 yr	neg.
8	76	inf. duct. ca.	+	3.5	alive — 3 yr	neg.
9	84	inf. duct. ca.	-	2.0	alive — 2 yr	neg.

*Lung metastases, alive with metastases after 2 yr.

human breast carcinoma the immunohistochemical method was adopted. With the indirect immunoperoxidase technique, detection of such an antigen cross-reacting with gp 52 of MMTV is possible in routinely processed paraffin-embedded tissues of human breast tumors [2]. Approximately 50% of human female breast carcinoma is found to be gp 52 cross-reacting antigen-positive. A significantly high percentage (64.5%) of positive cases occurs in the mixed intraductal and invasive histopathologic group [10].

Keydar *et al.* [3] found a correlation between the stage of the disease and the frequency of detectability. Moreover, in the group of patients of the same stage of disease, the prognosis was better in those which were antigen-negative. In our series of male breast carcinoma the detectability of gp 52 cross-reacting antigen was five out of nine cases (55.5%). Although our series is too small for statistical evaluation, the results supported the concept for a correlation between the detectability of gp 52 cross-reacting antigen and the stage of disease and prognosis in male breast cancer. Furthermore, the ability to detect the gp 52 cross-reacting antigen may be used to determine a primary breast tumor origin in lymph node metastasis in cases of occult breast carcinoma.

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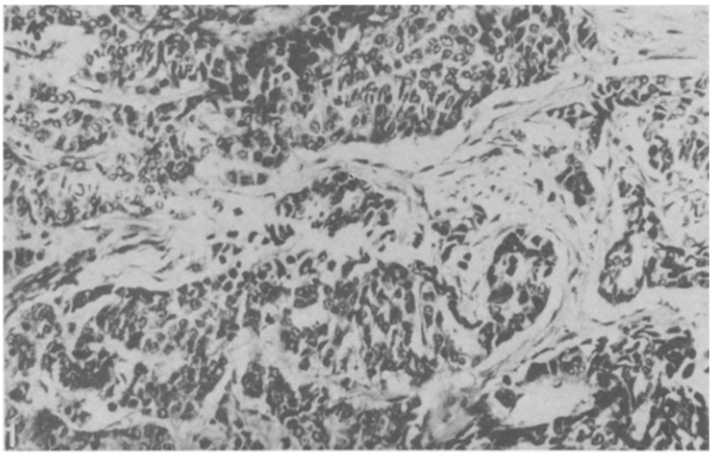

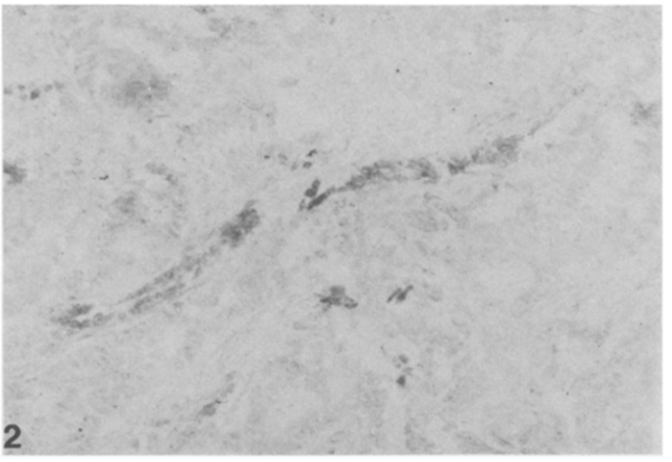

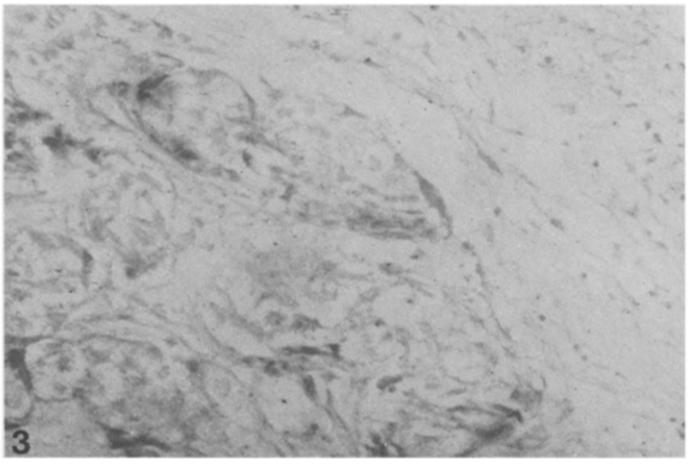

Fig. 1. Invasive male breast carcinoma. HE, ×250.
Fig. 2. Immunoperoxidase stain of an invasive breast carcinoma. ×160.
Fig. 3. Immunoperoxidase stain of another invasive breast carcinoma. ×250.