Report

Tissue mast cells in breast cancer

Department of Pathology, Shadyside Hospital, Pittsburgh (Drs. E. Fisher, Watkins, Johal) and Headquarters National Surgical Adjuvant Breast Project (Drs. E. Fisher, Sass, and B. Fisher), University of Pittsburgh School of Medicine

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Summary

The total number of mast cells and the number of such cells observed within and at the periphery of invasive breast cancers from 424 patients enrolled in protocol 4 of the National Surgical Adjuvant Breast Project were correlated with 38 other pathologic and 6 clinical features. High total mast cell counts as well as those within and at the periphery of the cancers were found to be significantly (p < .05) associated with a patient age less than 50 years and the degree of tumor lymphoid cell reaction. The latter has also been found to be related to young age and other pathologic characteristics related to mast cell content. This suggests that the mast cells may simply represent another cell type of this reactive change. No differences in 10 year disease-free survival were detected in patients without mast cells and those exhibiting varying numbers of such cells. This information indicates that identifiable mast cells do not represent a prognostic pathologic discriminant in patients with breast cancer. However, this does not unequivocally exclude a role of mast cell secretory products, since only intact and not degranulated or disrupted forms of these cells can be counted.

The presence of tissue mast cells in neoplasms has been recognized since the description of this cell type by Ehrlich in 1878 (1). They have also been observed in regional lymph nodes draining tumors regardless of the presence of metastases. Attempts to gain insight into the significance of these findings have been almost exclusively experimental. Some have regarded mast cell reactions to reflect a host defense mechanism. This view has been largely extrapolated from information that heparin, a mast cell moiety, may be antimitotic (2). Further support for this view is offered by the consideration that mast cells might compete with tumor cells for polysaccharide precursors which have been purported to be growth promoters (3). On the other hand, others regard the mast cells in such situations to actually represent growth promoters, while it has also been suggested that these cells exert no singular effect on tumor growth. Results of our own previous experimental studies suggested that the serotonin of mast cells might produce a limited inhibitory effect on experimental tumor growth (4). Although it has long been held that serotonin is lacking in human mast cells this view has recently been disputed (5).

There is little information concerning the possible significance of mast cells encountered in human breast cancer. Hamlin (6), in her pathologic study of possible host influences in breast cancer in 1968, tersely noted the variation in numbers of mast cells

Address for offprints: Dr. Edwin Fisher, Institute of Pathology, Shadyside Hospital, 5230 Centre Ave., Pittsburgh, PA 15232.
at the tumor edges and within regional lymph nodes but did not find any relation between their presence and survival. Hartveit (7) has recently called attention to the inverse relationship between stromal metachromasia and intact mast cells at the infiltrative borders of 50 human breast cancers but did not offer any conclusions concerning the biologic significance of this phenomenon. She (8) also has noted that the mast cells were sparse in regional nodes that exhibited sinus histiocytosis of pure type whereas the converse was evident when the sinus reaction was comprised of both histiocytic and round cell elements. Again the significance of these findings was briefly discussed without conclusion.

The paucity of information concerning the significance of mast cells observed in human breast cancer has prompted us to investigate their possible role in a relatively large number of patients with invasive breast cancer. Unfortunately, few paraffin blocks remained among the pathologic materials from protocol 4 of the National Surgical Adjuvant Breast Project to prepare sections for conventional mast cell stains. However, sections stained by an alcian blue-PAS method were available. Since human (unlike rat) mast cell granules may be vividly colored by the PAS techniques it was considered worthwhile to explore the possible relationship between the frequency of such cells and 38 other histopathologic and 6 clinical characteristics including disease-free survival, which in this particular cohort is now available for the tenth postmastectomy year.

Materials and methods

The materials utilized in this study were derived from 424 patients subjected to radical mastectomy for operable stage I or II invasive breast cancer who were enrolled in protocol 4 of the National Surgical Adjuvant Breast Project (NSABP). Average follow-up of ten years following mastectomy was available for all patients.

Mast cells were identified as stromal cells exhibiting morphological features of mast cells with a diastase resistant, PAS positive, cytoplasmic reaction in sections stained by an alcian blue – PAS sequence after prior treatment with diastase. The numbers of such cells were counted in 10 high power fields within the predominant mass as well as at its periphery or tumor-host interface.

A histogram of the distribution of frequency of number of patients with varying numbers of mast cells within and at the periphery of their cancers as well as total mast cell count was constructed (Fig. 1). Since there appeared to be a division of cases at 4 mast cells, it was decided to perform the determinations according to the categories of 0, 1–4, and 5 or more mast cells per 10 high power fields at these sites.

The relationship between the categories of number of mast cells within, at the periphery, and their combination or total vs. 38 pathologic and 6 clinical characteristics of breast cancer, as described in detail previously (9, 10), was assessed by contingency table analysis (11). Characteristics that demonstrated an association with a P value less than or equal to .05 were considered significant. Life tables of the probability of disease-free survival for 10 years were constructed (12).

Results

Mast cells were detected in 83.5% of cases. A greater number was generally found at the peripheral or host-tumor interface than within or among the principal tumor cell population. However, there was no consistent correlation between the categories of numbers of mast cells at these two sites in individual cases. Table 1 presents the associations between the categories of numbers of mast cells, their location and various pathologic and clinical characteristics including disease-free survival, which in this particular cohort is now available for the tenth postmastectomy year.