

Significance of Axillary Macrometastases and Micrometastases in Mammary Cancer

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SOPHISTICATED studies from several centers have correlated prognosis with the presence or absence of axillary lymph node metastases in patients with carcinoma of the breast.^{1, 5, 6, 7, 10, 11, 12, 13, 15} Division of the lymph nodes into three levels, from base to apex of the axilla, provides more precise prognostic data.^{2, 3, 8, 9, 14} The present study was done to determine whether an additional simple refinement would be useful. Lymph node metastases at the lowest and highest axillary levels were categorized as either macrometastases or micrometastases. This determination is simple and can be done on slides prepared from the routine examination of radical mastectomy specimens.

Material and Methods

The data have been compiled from the records of 227 patients with primary operable infiltrating carcinoma of the breast treated by the Halsted type of radical mastectomy in the year 1960, at the Memorial and James Ewing Hospitals, New York City. An 8-year follow-up period is available for each patient. The surgically removed specimens were originally studied by a standardized pathologic procedure which included histologic examination of the primary carcinoma, selected samples of each quadrant of the breast, the nipple, and the grossly visible lymph nodes. The axillary lymph nodes were separated into three groups: lowest, mid, and highest. The

divisions were made according to relationships to the pectoralis minor muscle: Level I (lowest): lymph nodes lateral and inferior to the pectoralis minor muscle; Level II (midaxillary): those behind the pectoralis minor muscle; Level III (highest axillary nodes): those medial and superior to this muscle.³

The 227 records were obtained by searching the pathology files starting with January 1, 1960. Records of patients were selected in which reports indicated that treatment was by radical mastectomy for a primary operable carcinoma and there were: (1) no metastases in any axillary lymph nodes, or (2) metastases to lymph nodes at Level I only (Levels II and III were negative for tumor), or (3) metastases to Levels I, II and III. Two hundred twenty-seven records were considered sufficient to provide numbers in each group from these 1960 accessions to allow valid comparisons. Groups (2) and (3) were further divided into subgroups with (a) macrometastases, and (b) micrometastases.

The histologic slides from each case were reviewed and then photocopied. The extent of metastases was evaluated microscopically and then a mark in red ink was made on the lymph node image of the corresponding photocopy. This produced a permanent visual record for measurement and comparison. A metastasis measuring 2 mm. or more was rated a *macrometastasis*, while any smaller than 2 mm. was rated a *micrometastasis*. We now had three major groups of patients. Group I: no axillary metastases; Group II: metastases to only the lowest axillary lymph nodes (Level I); Group III: metastases to all axillary lymph node levels (Levels I, II, III).

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Groups II and III were further divided as to whether the metastases were macrometastases (over 2 mm.) or micrometastases (under 2 mm.). We then compared survival data of each group and subgroup.

Results

Patients with no axillary metastases fared best with a survival of 82% (51/62). Patients with metastases in only the lowest axilla (Level I) had a survival rate of 71% (45/63); while those with metastases to the apex of the axilla had a 55% survival rate (66/102).

Of the 63 patients with metastases to lymph nodes at Level I, 18 had micrometastases and 45 had macrometastases. Although the survival rate of this entire group was 75% (45/63), those with micrometastases had a survival rate of 94% (17/18), those with macrometastases had a survival rate of 62% (28/45).

The survival of all patients with metastases to Level III was 55% (66/102). Those with only micrometastases had a survival rate of 59% (13/22); whereas, those with macrometastases had a survival rate of 29% (23/80).

When groups are compared it is evident that the survival of patients with metastases limited to Level I (71%) was not very different from those with no detected axillary metastases (82%).

There was a real difference in survival within the group with metastases only to Level I when those with micrometastases (94% survival) are compared to those with macrometastases (62% survival). Patients with micrometastases have essentially the same survival rate as the patients with no detected metastases.

Patients with macrometastases at Level I are prognostically comparable to patients with micrometastases at Level III since the survival of the former was 62% while that of the latter was 59%. Actually patients with only micrometastases at Level III are prognostically more closely related to the patients with macrometastases Level

I than to patients with macrometastases in their own group. The survival rate for patients with macrometastases at Level III (29%) was only half that of patients with micrometastases (59%).

Discussion

The results of this review demonstrate the value of indicating not only which lymph node levels are involved with metastatic carcinoma, but also whether the metastases are *micro* or *macro*. If we consider volume of tumor rather than cross-section measurement of a metastasis, a macrometastasis would have a volume 100 to 100,000 times that of a micrometastasis.

Prognostically there is greater heterogeneity within groups (Level I and Level III) than there is between groups, when each is subdivided according to macro and micrometastases. We have been optimistic about patients with metastases to Level I only. This review further supports such optimism; and we now have reason to be more optimistic about those patients who have only micrometastases. However, we must also recognize that patients who have macrometastases at Level I do not justify the same general optimism we formerly accorded the entire group. Indeed, these patients are similar to those with micrometastases at Level III.

Conversely, we were generally pessimistic when Level III lymph nodes were involved. There is now reason to be less pessimistic when these lymph nodes contain only micrometastases. Unfortunately, the full measure of pessimism must be directed to patients with macrometastases in lymph nodes at Level III.

This study was done partly to develop information relating to the need to clear lymph node specimens. Clearing lymph nodes of an occasional mastectomy specimen is no problem. However, in an institution with an active breast service, clearing lymph nodes from mastectomy (and other types of specimens with lymph nodes) could create a major burden in time con-

sumed, as well as in demands for space and personnel. Nevertheless, if the value of the information obtained justified this burden, the procedure should be done. We cannot now evaluate the procedure since we have not done it in this study. Nevertheless, some interesting related considerations are pertinent.

Since the survival of patients with only microscopic metastases to Level I (94%) was not very different from those with no detected metastases (82%), we suggest that having cleared the former axillae to find additional 2 mm. lymph nodes, or more micrometastases would have added nothing to prognostic data. Conversely, this statement can be challenged by supposing that if lymph nodes were cleared in the specimens from patients with no detected metastases, some metastases may have been found. If this were the case, one could plead that a significant separation between those with no metastases and those with Level I metastases may have been obtained. Nevertheless, if the metastases found were 2 mm. or smaller, no significant information would have been added. We are not yet convinced that the demand on space, time, personnel, and cost required to handle the load required to clear all specimens would produce commensurately significant prognostic data to justify the procedure. We believe that there is value in indicating whether metastases to each level are micrometastases or macrometastases. This can be done with no additional burden to the present system.

There may be some value to adding a photocopy of the lymph nodes to the pathology report to visually convey the extent of metastatic involvement.

Summary

The significance of axillary lymph node levels in 227 patients with carcinoma of the breast has been evaluated. It was found that survival rate of patients with microscopically positive lymph nodes at Level I is within the range of patients with negative lymph nodes at all axillary levels, but

is significantly different in patients with grossly involved Level I axillary lymph nodes. It was also found that survival rate of patients with microscopic metastases at Level III is about the same as in grossly involved Level I lymph nodes; while the survival rate is significantly worse in patients who had grossly involved Level III lymph nodes compared to microscopically involved Level III lymph nodes.

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