ADVANCES IN ONCOLOGY

Current Developments in the Management of Solid Tumor Malignancies

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IN FOCUS: Breast Cancer

The Evolving Role of Axillary Dissection

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H&O What has been the traditional use of axillary dissection?

MM The traditional use of axillary lymph node dissection (ALND) has been to provide prognostic information and to maintain local control in the axilla. Axillary lymph node status has long been the most important prognostic factor in breast cancer. Traditional ALND removes nodes in levels I and II of the axilla (below the lower edge and underneath the pectoralis minor muscle), which usually results in the removal of 15–25 lymph nodes, and was standard practice in women with invasive cancer. Axillary dissection was necessary in order to identify or exclude the presence of nodal metastases, as there were no other reliable techniques available for staging in the past—laboratory testing, imaging, and predictive models were not able to identify subsets of women with very low risks of axillary node metastases. It is an excellent method of local control, and only 2–3% of women with positive nodes who undergo ALND will end up having an axillary first failure.

H&O Why has there been a shift away from axillary dissections?

MM Over time, surgical treatment of breast cancer has switched from mastectomy to breast conserving therapy. Because women no longer had to cope with the loss of the breast and the numbness of the chest wall, the morbidity of ALND became increasingly more apparent. Symptoms of ALND such as discomfort, change in sensation, and a lifetime risk of lymphedema, became a more obvious problem. Concurrently, more women were being diagnosed through screening mammographies, which enabled tumor detection at a much smaller size and, therefore, the risk of having axillary node disease was lower. More and more women were undergoing a surgery that was of no therapeutic benefit, simply to determine if they were node-negative. In addition, the use of adjuvant systemic therapy expanded from node-positive women only to node-negative women as well; thus, the findings of ALND were no longer being used to determine therapy.

H&O What is the role of sentinel node biopsy in breast cancer?

MM Sentinel lymph node biopsy (SLNB) is a technique to identify the first node or nodes that a cancer would spread to if it were to metastasize. SLNB has the advantage of reliably identifying node-negative women by removing just a few lymph nodes as opposed to the majority of nodes in the axilla. The morbidity of SLNB, both short- and long-term is much lower than that of axillary dissection, as documented in randomized trials comparing the 2 procedures. Both the American College of Surgeons Z11 trial and the Almanac trial in the United Kingdom found a much lower incidence of paresthesias, decreased arm mobility, and lymphedema with SLNB biopsy. This technique has become the staging procedure of choice for women who have clinically negative axillary nodes. As clinicians learn more about SLNB biopsy, it has become apparent that there are relatively few contraindications to the procedure. One contraindication is inflammatory breast cancer or other T4 breast cancers, where limited data

suggest that SLNB is not an accurate technique of staging. At present, the role of ALND is for women who are found to have metastases in their sentinel node. ALND remains the standard management for these women because there is no way to predict whether or not additional positive nodes are present. The need for ALND in women with micrometastases, very small tumor deposits in the sentinel node, is the subject of controversy. For women who present with positive nodes that are evident on clinical exam or on imaging studies, SLNB is not recommended; it is more cost effective to confirm that the nodes are positive by doing a preoperative fine needle aspiration and then performing an ALND.

Early on, researchers were concerned about recurrence with SLNB, but there is an accumulating body of data that states that the likelihood of having a recurrence in the axilla after undergoing SLNB which is negative for cancer is extremely low—less than 1% at 4 years' follow-up.

H&O What clinical trials are being conducted with sentinel node biopsy?

MM Because SLNB removes only a few lymph nodes, unlike ALND, pathologists can perform a much more detailed examination of these sentinel nodes. This has led to the increasingly frequent identification of micrometastases. The prognostic significance of these micrometastases is not yet understood and there is a lot of ongoing research trying to address this question. All of the studies that have been published to date have been retrospective and have varying results. Some researchers claim that micrometastases are important in prognosis, whereas others argue that they are not. The real answer to this question will be determined by 2 ongoing prospective trials, one that is conducted by The American College of Surgeons Oncology Group (ACOSOG) and the other, which is done by the National Surgical Adjuvant Breast and Bowel Project (NSABP). Both of these studies address the issues of morbidity, efficacy, safety, and the significance of low-volume disease. Investigators for the NSABP trial (NSABP B-32) performed SLNB. Node-negative patients were randomized to standard level I and II ALND or no further surgery. Study endpoints include overall survival, disease-free survival, and morbidity. Centrally performed immunohistochemistry (IHC) was used to detect micrometastases and will allow issues of local recurrence and prognosis to be addressed in this subset. Investigators for the ACOSOG trial (ACOSOG Z0010) performed a single-arm study of women undergoing breast-conserving therapy who underwent SLNB. If the nodes were negative by routine processing, no further axillary surgery was carried out. As in the NSABP study, central IHC was used to identify micrometastases. Overall and disease-free survival, local regional control, and morbidity are the endpoints in this study. Both trials have finished recruiting patients, but have not yet reported outcomes.

Suggested Readings

Morrow M. Axillary surgery in DCIS: Is less more? *Ann Surg Oncol*. 2008;15:2709-2719.

White RL Jr, Wilke LG. Update on the NSABP and ACOSOG breast cancer sentinel node trials. *Am Surg*. 2004;70:420-424.