Nanometastases May Be Tied to Ca Recurrence

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San Antonio — The presence of isolated tumor cells in a sentinel lymph node boosts a breast cancer patient's risk of recurrence or other adverse events 2.5-fold, Dr. Saverio Alberti said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

This finding from the largest-ever long-term study of the prognostic significance of isolated tumor cells is at odds with other studies, which have concluded these cells have no significant impact on recurrence, metastasis, or mortality risks.

However, all the negative studies were underpowered and/or included too little follow-up, according to Dr. Alberti of the University of Chieti (Italy). "More than 50% of breast cancer recurrences happen more than 5 years after surgery. So 3- to 4-year studies simply won't do," he added.

Dr. Alberti presented a single-institution study of 702 consecutive patients with early-stage breast cancer followed for a median of 8.2 years after axillary lymph node dissection. The 377 women with histologically negative sentinel lymph nodes by standard sectioning and hematoxylin and eosin staining had further pathologic analysis. Each of 6,676 lymph nodes removed from patients in this subgroup had 250 sections taken, with each section subjected to both anticytokeratin immunohistochemistry and hematoxylin and eosin staining.

Of the 377 patients, 13% had nodes containing isolated tumor cells not more than 0.2 mm in diameter, which Dr. Alberti calls nanometastases. The risk of local recurrence, contralateral breast cancer, or distant metastasis at 8 years in patients with nanometastases was 2.5-fold greater than in patients who were truly node negative. Event rates were closely similar in the two groups until 36 months, at which point they diverged sharply, he said.

The risk associated with nanometastases was similar to that with micrometastases 0.2-2.0 mm in size in the Italian study. American Society of Clinical Oncology guidelines recommend routine axillary node dissection for patients with micrometastases on sentinel node biopsy.

Dr. Alberti foresees that the best use of nanometastases as a prognostic indicator would be to incorporate them as one of the factors employed in the nomogram developed at Memorial Sloan-Kettering in New York for use in assessing which sentinel node–positive patients should receive a complete axillary dissection. The nomogram, based on eight characteristics of the primary tumor and sentinel node lesion, is gaining use in clinical decision making (Ann. Surg. Oncol. 2003;10:1140-51).

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DR. ALBERTI

In a separate presentation, Dr. Emiel Rutgers of the Netherlands Cancer Institute, Amsterdam, argued that at present the finding of nanometastases in a sentinel node has no clinical relevance and affected patients should be classified as node negative.

He cited a Dutch retrospective study involving 2,150 patients with early breast cancer who underwent sentinel lymph node biopsy. The prevalence of nanometastases in the sentinel node was 4.9%. Fewer than 8% of patients who were sentinel node positive for nanometastases had additional metastases in other nodes. The result was upstaging of 4% of the patients, with no recommended change in anyone's treatment. Therefore, the benefits of doing an intensive search for isolated tumor cells are questionable, Dr. Rutgers said.

He added that recent evidence indicates not all immunohistochemistry-positive cells in the sentinel node are viable isolated tumor cells. Some are iatrogenically displaced normal epithelial cells (J. Clin. Oncol. 2006;24:2013-8).

The goal of research involving nano- and micrometastases is to develop a means of identifying the 15% of patients with early-stage breast cancer who will relapse. This would enable the other 85% to be spared unnecessary adjuvant systemic therapy. In Dr. Rutgers' view, a more promising approach than the labor-intensive search for nanometastases of as-yet unproven prognostic value involves predictive gene array tests. ■