PROPATH
THE FOCUS
Immunohistochemistry

Traps in Sentinel Lymph Node Biopsies

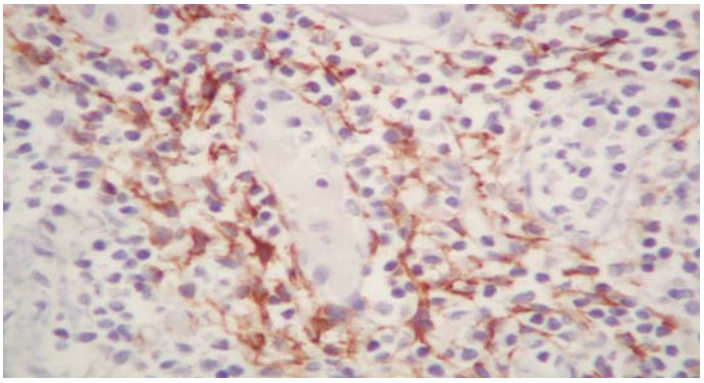
November 2001

by Rodney T. Miller, M.D., Director of Immunohistochemistry

Sentinel lymph node biopsy has entered the mainstream of medical care for patients with breast cancer and melanoma. In most cases, the interpretation of the immunostains on sentinel lymph node biopsies is straightforward, although on occasion difficulties are encountered that can complicate interpretation. Knowledge of potential traps can be of assistance in attempts to render an accurate result. Several of these potential traps are discussed below.

Cytokeratin-positive reticulum cells

Normal lymph nodes contain a population of fibroblastic reticulum cells that normally express low molecular weight cytokeratins (cytokeratins 8 and 18). In some cases, the staining of these cells can be quite prominent, and at first glance might raise the possibility of metastatic carcinoma. These cells are mainly localized in the interfollicular and paracortical areas, as well as in the lymph nodes sinuses. If the clone of cytokeratin antibody used recognizes cytokeratin 8 and 18 (including the low molecular weight cytokeratin antibodies Zym5.2, CAM5.2 and 5D3), these cells will be apparent in nearly every lymph node biopsy. However, they are generally not visible if cytokeratin AE1/AE3 is employed for staining. Cytokeratin-positive fibroblastic reticulum cells have thin elongate cytoplasmic processes (unlike the pattern observed with metastatic carcinoma), and once the pathologist is familiar with the appearance of these cells, they are very easy to recognize and distinguish from metastatic carcinoma. However, there are some authors who feel that antibodies to low molecular weight cytokeratin should be avoided when staining sentinel lymph node biopsies, to avoid misinterpretation of fibroblastic reticulum cells as metastatic carcinoma. We do not have problems distinguishing these cells from carcinoma at ProPath, and feel that this antibody can be a useful reagent in this situation. It can also provide a useful internal positive control, indicating that the tissue antigens are not excessively degraded.

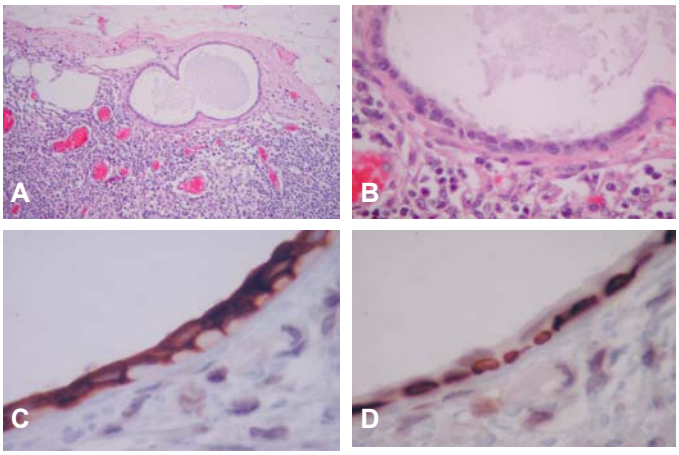


High power photomicrograph of a low molecular weight cytokeratin immunostain on a sentinel lymph node biopsy demonstrates unusually prominent staining of fibroblastic reticulum cells. Not the thin elongate cytoplasmic processes, unlike the appearance of metastatic carcinoma.

Epithelial inclusions or other benign epithelial cells in lymph nodes

Incidental benign epithelial inclusions are probably most commonly encountered in lymph node biopsies from female patients with gynecologic malignancies (endosalpingiosis), although on occasion they are also observed in lymph nodes from other sites, including axillary lymph nodes. Frequently, they are readily distinguished from metastatic carcinoma if the tumor is morphologically different. However, if these structures are found in the sentinel lymph nodes from patients that have well differentiated ductal carcinoma, interpretation can be problematic. Interestingly, we have found that in the cases of axillary lymph node epithelial inclusions that we have observed at ProPath, smooth muscle myosin immunostains can be very useful, as they have highlighted an associated myoepithelial layer in several cases of this problem. (At the time of this writing, we have not been able to evaluate the use of myosin for this problem in

non-axillary sites, although it would be worthy of consideration). There are also reports of "benign transport" of breast epithelium (benign breast epithelium or breast cancer epithelium) into axillary lymph nodes occurring after biopsy (reference 2 below), and these cases may be much more difficult to distinguish from true cases of metastatic tumor. The authors of this study noted that these deposits are associated with hemosiderin laden macrophages, foreign body type giant cells, lymphocytes, and physically altered red blood cells. This phenomenon will hopefully be studied by other investigators, since it is difficult to completely disprove the possibility of micrometastatic disease in these cases. Other authors have described benign mesothelial cells occurring within lymph nodes, usually in nodes draining areas of serosal effusions with reactive mesothelial hyperplasia. We have not yet observed this at ProPath and are not aware of this finding in axillary lymph nodes, which would seem to be quite unlikely. However, if sentinel lymph node biopsy becomes a common procedure for other types of non-breast carcinoma, it would be prudent to keep these studies in mind when interpreting sentinel lymph node biopsies from those patients.



H&E sections (A&B) of an axillary sentinel lymph node biopsy on a women with well differentiated (grade 1) ductal breast carcinoma, demonstrating an epithelial structure. The low molecular weight cytokeratin immunostain highlighted the inner epithelial cells (C) and a smooth muscle myosin immunostain (D) documented an underlying associated myoepithelial cell layer, confirming the benign nature of the lesion.. The epithelial cells were also positive for ER and PR.

Nevus cells of the lymph node

In patients with melanoma, identification of cells expressing melanoma-related markers (such as S100 protein, MART-1, HMB-45, or tyrosinase) in sentinel lymph node biopsies is often a reflection of metastatic melanoma. However, nevus cells (an incidental benign finding unrelated to metastatic melanoma) also express these markers, and this can result in difficulties in interpretation. Nevus cells have been reported to be present in up to 6% of cases. It is important to keep in mind that the nevus cells are localized to the lymph node capsule or connective tissue framework (trabeculae) of the lymph node (rather than in the subcapsular sinus or substance of the lymph node). Therefore, it is important to make certain that immunoreactive cells are not restricted to the capsule or trabecular connective tissue framework before interpreting immunoreactive cells as a reflection of metastatic melanoma.

REFERENCES:

1. Xu X et al: Undesirable Cytokeratin Immunoreactivity of Native Non-epithelial Cells in Sentinel Lymph Node from Patients with Breast Carcinoma. Archives of Pathology and Laboratory Medicine 124:1310-1313, 2000.
2. Carter BA et al.: Benign Transport of Breast Epithelium into Axillary Lymph Nodes after Biopsy. American Journal of Clinical Pathology 113 259-265, 2000.
3. Bautista NC et al; Benign Melanocytic Nevus Cells in Axillary Lymph Nodes. A Prospective Incidence and Immunohistochemical Study with Literature Review. American Journal of Clinical Pathology 102: 102-108, 1994.
4. Carson KF et al: Nodal Nevi and Cutaneous Melanomas. American Journal of Surgical Pathology 20 (7): 834-840, 1996.
5. Edlow DW et al: Heterotopic Epithelium in Axillary Lymph Nodes: Report of a Case and Review of the Literature. American Journal of Clinical Pathology 59:666-673, 1973.
6. Argani P et al: Hyperplastic Mesothelial Cells in Lymph Nodes: Report of Six Cases of a Benign Process That Can Simulate Metastatic Involvement by Mesothelioma or Carcinoma. Human Pathology 29: 339-346, 1998.
7. Parkash V et al: Benign Mesothelial Cells in Mediastinal Lymph Nodes. American Journal of Surgical Pathology 23 (10): 1264-1269, 1999.
8. Isotalo PA et al: Hyperplastic Mesothelial Cells in Mediastinal Lymph Nodes Sinuses with Extranodal Lymphatic Involvement. Archives of Pathology and Laboratory Medicine 124:609-613, 2000.
9. Weeks DA et al: Benign Nodal Lesions Mimicking Metastases from Pediatric Renal Neoplasms: A Report to the National Wilms Tumor Study Pathology Center. Human Pathology 21 (12):1239-1244, 1990.

Rodney T. Miller, M.D.
Director of Immunohistochemistry
(214) 237-1631
Fax: (214) 237-1770
rmiller@propathlab.com

Prior editions are available on our website.

PROPATH
8267 Elmbrook Drive, Suite 100 • Dallas, Texas 75247-4009
(214) 638-2000 • Fax: (214) 905-3457
www.propathlab.com