SEMINARS IN BREAST DISEASE

# Regional Metastases, Artifacts, and Mimics in Axillary Lymph Nodes

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**Axillary lymph node status is an important prognostic factor in breast cancer. In most patients, sentinel lymph node biopsy has replaced axillary dissection because it decreases morbidity and permits accurate staging and local control. The increased histologic scrutiny of sentinel lymph nodes and consideration of drainage phenomena has led to a heightened awareness and detection of previously described but rare findings. These include false-positive findings such as benign heterotopic glands, transported epithelial cells, nevus cell aggregates, megakaryocytes, multinucleated giant cells, silicone lymphadenopathy, and histiocytes, all of which may mimic metastatic carcinoma. Conversely, degenerated or treated cancer cells can appear artifactually negative, mimicking histiocytes. In addition, many artifactual changes in lymph nodes are due to the use of immunohistochemistry. Overlapping staining with dendritic cells, histiocytes, and plasma cells can be misinterpreted as positive. Most of these issues can be resolved by comparing the lymph node findings with the primary tumor.**


**KEYWORDS** axillary lymph nodes, mimics, artifacts, false positive, false negative, heterotopic glands, benign transport, cytokeratin

In patients with breast cancer, axillary lymph node status remains the most powerful prognostic factor for predicting recurrence and survival.[1] Pathologic evaluation of axillary lymph nodes is necessary for proper staging, prognostic assessment, and to further define adjuvant therapy strategies. Given the morbidity associated with standard axillary lymph node dissection, the alternative of sentinel lymph node sampling has been widely accepted because it not only permits accurate axillary staging but also provides good local control. Despite the technique's introduction more than 10 years ago, there is still no consensus regarding routine histologic examination of sentinel lymph nodes, specifically the number of levels performed, utility of immunohistochemical stains (cytokeratin), intraoperative sectioning and/or touch imprints, and the use of molecular studies. Regardless of the methodology employed, for most pathologists it entails a more detailed and sensitive histopathologic search for tumor in the selected node(s). Not surprisingly, this has led to an increased detection of micrometastases (<2 mm), the clinical significance of which is currently unknown as reflected in the revised staging for breast cancer.[2]

Theoretically, the sentinel lymph node is the first lymph node draining the axilla, and thus receives any and all material draining from the breast either passively (by drainage) or actively (by metastasis) (Fig. 1). In our experience, we have seen foreign body giant cells, dye laden histiocytes, hemosiderin laden macrophages, calcifications, pigment, mucin, and dense secretory material almost exclusively in sentinel lymph nodes. In addition, perhaps due both to past drainage phenomena and the intense histologic scrutiny often performed in sentinel lymph node slides, there has been a heightened awareness, recognition, and detection of previously described rare findings such as benign heterotopic glands and capsular nevus cells. Thus, in this era of sentinel lymph node biopsy, the pathologist needs to be vigilant for not only micrometastases (true positives), but also confounding factors in the form of histologic mimics and artifacts (false positives and false negatives) both on H&E and immunohistochemistry, the subject of the remainder of this paper. It is important to be aware of these findings because of the prognostic implications of falsely understaging or incorrectly upstaging patients. We recommend routinely comparing the lymph node findings with those of the primary tumor to aid in resolving such issues.

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## Histologic Mimics and Artifacts

### Benign Glands (Fig. 2A)

Heterotopic glands have been described in lymph nodes adjacent to the thyroid, salivary glands, and breast, specifically


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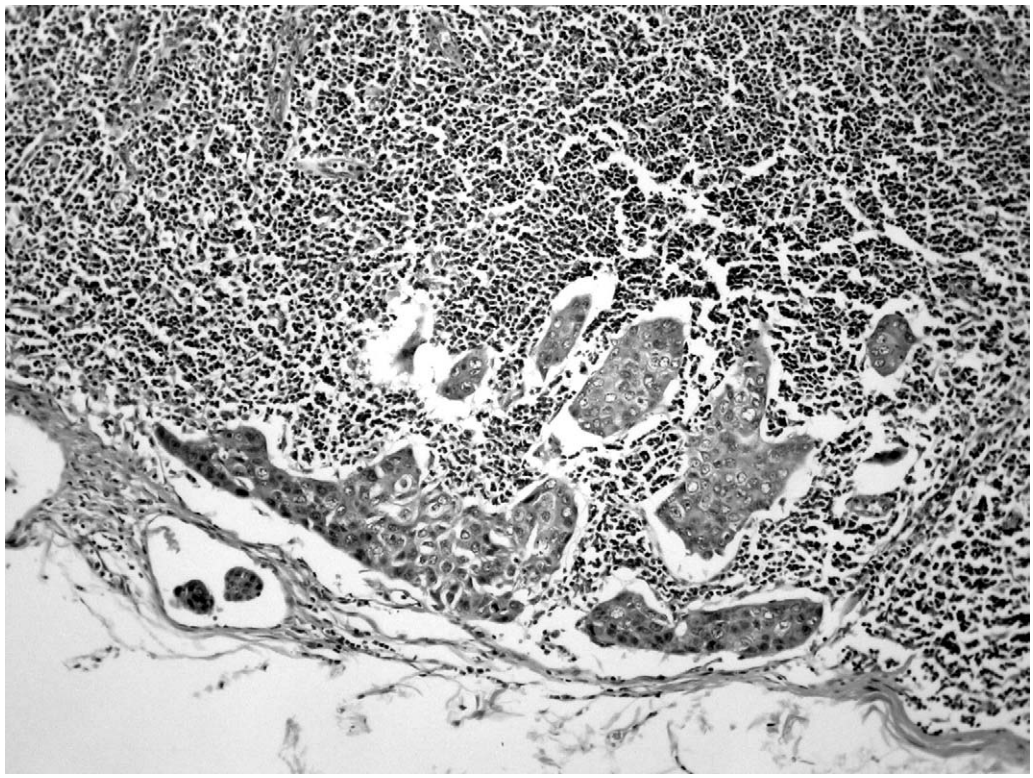

**Figure 1** Metastatic carcinoma present in subcapsular spaces and lymphatics of a lymph node.

in axillary lymph nodes. In the latter, they are thought to originate from breast or skin appendage glands, explained by theories of implantation, metaplasia, or embryonal rests. Glandular morphology ranges from benign ducts, to squamous lined cysts, apocrine-lined cysts, and/or fibrocystic changes such as sclerosing adenosis or florid duct hyperplasia. They can be capsular, subcapsular, and/or occasionally parenchymal and may be surrounded by fibrosis. The signif-

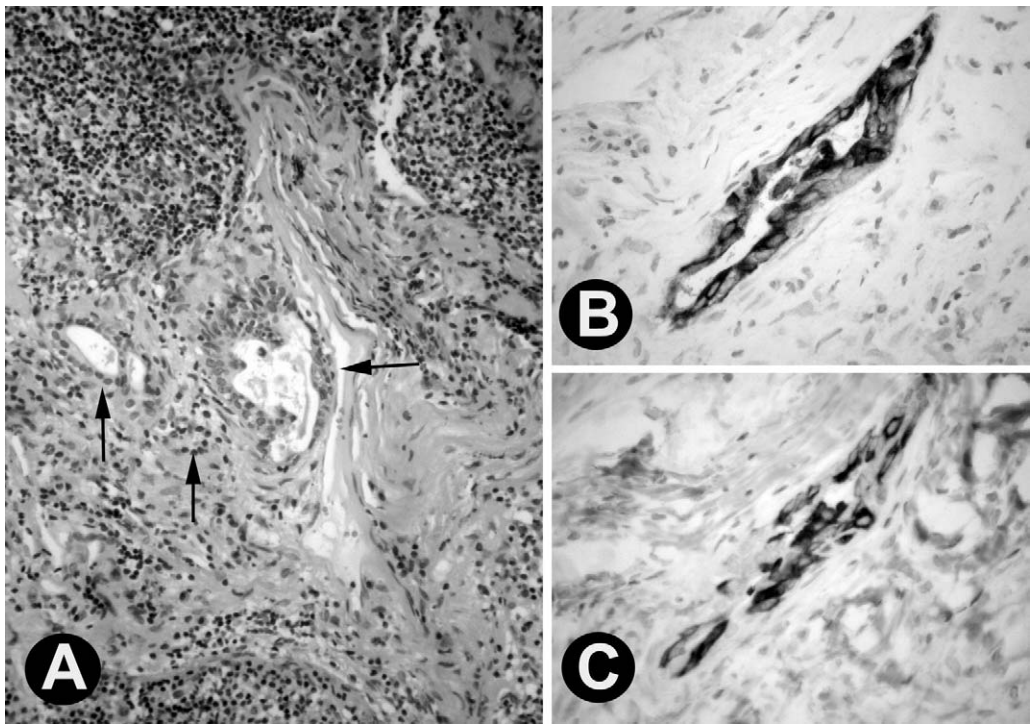


**Figure 2** (A) Benign glands in lymph nodes mimicking metastatic ductal carcinoma. (B) Immunohistochemical stain for cytokeratin stains the luminal epithelial cells, (C) whereas the p63 stain marks the myoepithelial cell layer.