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Diagnostic Pitfalls in Axillary Sentinel Lymph Node Evaluation

*Emmanuel Agosto-Arroyo and Marilin Rosa**

Department of Anatomic Pathology, Moffitt Cancer Center, USA

Introduction

Surgical excision of axillary lymph node(s) is standard practice in the management of invasive breast cancer. Whether sentinel or axillary lymph node excisions are performed, typically the histopathological distinction of metastatic carcinoma is straightforward. However, there are rare, though, important pathological entities that may pose a diagnostic challenge in the evaluation of axillary sentinel lymph nodes, including heterotopic epithelial inclusion and nevus cell aggregates.

Heterotopic Epithelial Inclusions

In the axilla, heterotopic inclusions can be found within the lymph node capsule and/or parenchyma [1-4]. The morphologic features of these inclusions are varied. Heterotopic mammary-type glands can be present in the axillary lymph node and resemble benign mammary epithelium, as well as, undergo fibrocystic changes, epithelial hyperplasia, apocrine metaplasia, cysts and sclerosing adenosis [5]. Mammary-type glands are the most common heterotopic inclusion in the axillary lymph nodes [6]. Other types of inclusions include: squamous epithelium and mixed squamous and glandular components. Glandular elements with müllerian-like features can also be seen in a minority of axillary lymph nodes heterotopic inclusions, typically identified by the presence of microvilli [1].

The presence of heterotopic epithelial inclusions in the axillary lymph node is rare and the origin is unknown, but displaced epithelium during prior procedure [5] and embryologic maldevelopment [6] have been hypothesized as possible histogenesis.

The differential diagnosis of heterotopic epithelial inclusions includes metastatic carcinoma to the lymph node. The presence of glandular elements within the nodal capsule and intraparencymal, rather than the lymph node sinusoids, is suggestive of heterotopic epithelial inclusions. Most of the heterotopic glandular elements of mammary-type show evidence of myoepithelial cells by Hematoxylin and Eosin (H&E) and with myoepithelial cell markers on immunohistochemistry. This fact does not hold true for inclusions with squamous and müllerian-like features, both of which lack evidence of myoepithelial cell markers. Inclusions of müllerian-like origin are immunoreactive for WT-1 and PAX-8 [7].

Nevus Cell Aggregates

Melanocytic nevus presenting as intracapsular and intratrabecular cell aggregates is a well-known diagnostic entity in various anatomic locations. The cells forming the nevus aggregates resemble intradermal nevi, ranging from oval, or spindle cell, to epithelioid cells. Some aggregates may lack or contain minimal pigment, others may show substantial pigment content, resembling blue nevi. Their location is commonly intracapsular, however, intratrabecular and intraparenchymal nevus cell aggregates can arise within the lymph node.

Nevus cell aggregates occur more frequently in the axilla than in other anatomic locations and have been found in 0.54% of examined axillary lymph nodes [8]. The histogenesis of nevus cell aggregates is unknown. A possible etiology is that the cells are derived from perithelial cells around the nodal vasculature [9]. Another possible etiology is the development of the nevus cell aggregates from embryologic remnants.

Metastatic carcinoma can easily be ruled out from the differential diagnosis of nevus cell aggregates by lack of immunohistochemical staining with pancytokeratin. Metastatic melanoma and nevus cell aggregates are both positive to S100, MART-1 and Melan-A. HMB45 is positive in metastatic melanoma and negative in nevus cell aggregates [10]. Another useful marker is Ki-67,

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Correspondence:
Marilin Rosa, Department of Anatomic Pathology, Comprehensive Breast Program, Moffitt Cancer Center, 12902 Magnolia Drive, Tampa, FL 33612, USA, Tel: 813.745.2846; Fax: 813.745.1708;
E-mail: Marilin.Rosa@moffitt.org

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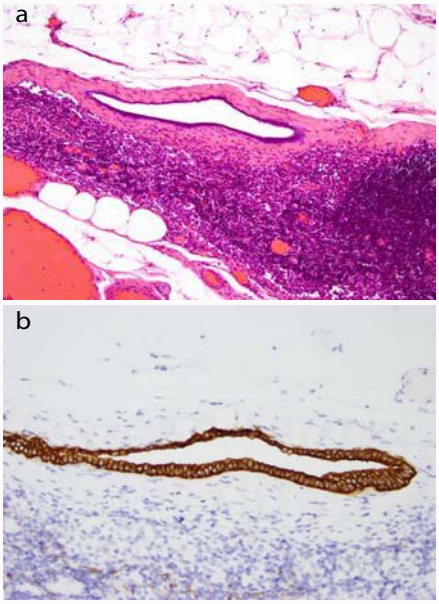

Figure 1: Intracapsular heterotopic epithelial inclusion with a lining of single cells with focal pseudostratification (a, H&E 100X), showing positivity to cytokeratin AE1/AE3 immunohistochemical stain (b, IHC 200X).

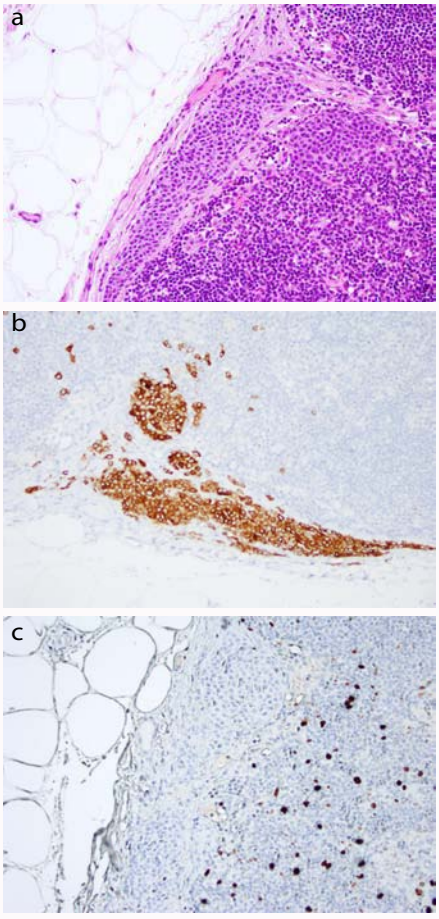

Figure 2: Subcapsular nevus cell aggregate (a, H&E 200X), with infiltration of the cells into the lymph node parenchyma as seen by the immunohistochemical stain with Melan-A (b, IHC 200X). The nevus cell aggregates are negative to Ki-67 proliferation index (c, IHC 200X).

which has been reported to be less than 1% in nevus cell aggregates [10] and highly positive in metastatic carcinoma.

Conclusion

The presence of metastatic carcinoma within the lymph node is a marker of loco-regional disease and an independent prognostic factor. Accomplishing the correct pathological diagnosis is of utmost importance management of patients with invasive breast cancer. Awareness of rare, but benign, lesions within the axillary lymph node helps the pathologist to avoid misinterpretation with metastatic neoplasms.

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