Intraductal Carcinoma Arising in Intraductal Papilloma in an Axillary Lymph Node

Review of the Literature and Proposed Theories of Evolution

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- We report a case of an axillary lymph node containing benign glandular lesions, intraductal papilloma with florid and atypical duct hyperplasia, and ductal carcinoma in situ. We propose 2 theories for the development of the intraductal papilloma: from adjacent benign glandular inclusions, or from displaced epithelial cells from a previous intraductal papilloma in the ipsilateral breast. This case identifies yet another etiology for false-positive sentinel lymph nodes morphologically and by immunohistochemistry.

(Top) Arch Pathol Lab Med. 2008;132:1940–1942

The presence of intraductal papilloma in an axillary lymph node is a rarely recognized phenomenon, described in both recent¹ and past²–⁴ literature. In one of these cases, ductal carcinoma in situ (DCIS) has been described as arising in a background of intraductal papilloma in an axillary lymph node.¹ Still others have described DCIS adjacent to benign epithelial inclusions in an axillary lymph node.⁵ We describe yet another case of intraductal carcinoma arising in a background of intraductal papilloma with atypical duct hyperplasia and adjacent benign glandular inclusions. We concur with the theory that the intraductal carcinoma probably arose from the benign glandular inclusions. Additionally, we propose that the phenomenon of displacement, particularly of an intraductal papilloma in the ipsilateral breast, could contribute to the development of intraductal carcinoma in this context.

REPORT OF A CASE

The patient was a 55-year-old woman with a medical history significant for lumpectomy in the left breast 10 years earlier. She presented with a nodule that was initially core biopsied to reveal intraductal papilloma. Follow-up excision showed residual intraductal papilloma with atypical duct hyperplasia focally at the level of DCIS. The DCIS was a low to intermediate grade, cribriform type with calcifications (Figure 3). Previous biopsy-site changes were present. In addition, associated reactive changes, such as squamous metaplasia (Figure 4) and cystification, were present (Figures 1 and 2). Also noted were adjacent benign glandular inclusions (Figure 5). There was no evidence of invasive or metastatic carcinoma. Immunohistochemistry using p63 showed staining of myoepithelial cells in the benign glandular inclusions, areas of benign intraductal papilloma, and squamous metaplasia. The areas of DCIS containing a uniform population of atypical cells did not stain with either p63 (Figure 6) or smooth muscle actin (Figure 7). Rereview of the previous lumpectomy slides from 10 years before showed the previous DCIS to be identical to that in the current specimen. In addition, a single area of iatrogenically displaced tumor cells was identified in the granulation tissue of the core biopsy site (Figure 8).

COMMENT

Malignancies arising from benign glandular inclusions in lymph nodes have rarely been described in pelvic lymph nodes containing müllerian carcinomas,⁶,⁷ thyroid,⁸ salivary glands,⁹ and the axilla.¹⁰–¹⁵ In the axilla, benign heterotopic glands are hypothesized to arise from breast or skin appendage glands by theories of implantation, metaplasia, or embryonal rests.¹⁰ The coexistence of benign glandular inclusions and intraductal carcinoma in axillary lymph nodes lends support to the theory that the former led to the latter. The morphology of these benign glands can range from benign ducts to squamous-lined cysts, apocrine-lined cysts, or fibrocystic changes, such as sclerosing adenosis or florid duct hyperplasia. If it is possible for benign glandular inclusions to undergo proliferative changes, then the potential for neoplastic change is also possible. In our case, in addition to benign glandular inclusions, there was also intraductal papilloma with florid duct hyperplasia. A p63 immunohistochemical stain identified the benign glands by highlighting the basal myoepithelial cells of the bilayered glands. There was a spectrum of changes within the intraductal papilloma ranging from florid to atypical duct hyperplasia, culminating in intraductal carcinoma, further supporting an origin from benign glands (Figure 3). There was no staining of the ductal cells in the DCIS by either p63 or smooth muscle actin (Figures 6 and 7).

Another recognized etiology of glandular epithelium occurring in axillary lymph nodes is displacement, that is, benign lymphatic transport of epithelial cells from the breast to lymph nodes.¹¹,¹² These epithelial cells may be transported passively because of a physiologic response after the trauma of a core biopsy.¹³ We have seen this phenomenon almost exclusively with papillary lesions because of their inherent fragile nature.¹⁴,¹⁵ As a result of a
Figure 1. Core biopsy showing axillary lymph node containing intraductal papilloma and squamous metaplasia (hematoxylin-eosin, original magnification ×40).

Figure 2. Whole mount of excision specimen showing axillary lymph node containing intraductal papilloma with focal cystification (hematoxylin-eosin, original magnification ×10).

Figure 3. High-power field of Figure 2, showing atypical ductal hyperplasia focally at the level of ductal carcinoma in situ as shown by the population of uniform cells (hematoxylin-eosin, original magnification ×100).

Figure 4. High-power field showing focal squamous metaplasia (hematoxylin-eosin, original magnification ×100).

Figure 5. Subcapsule of lymph node showing benign glandular inclusions (hematoxylin-eosin, original magnification ×40).

Figure 6. p63 stain shows negative staining in areas of ductal carcinoma in situ containing uniform cells (original magnification ×40).
core biopsy, the delicate arborizing stalks of an intraductal papilloma may fragment, leaving remnants in the needle tract to be eventually drained into the axillary lymph node. This mechanism of cell transport from the axillary lymph nodes may also be facilitated by intraoperative massage, sometimes performed to help localize the sentinel lymph node. In our case, there was evidence of displacement of epithelial cells from a previous lumpectomy specimen containing an intraductal papilloma with atypical duct hyperplasia and DCIS (Figure 8). In lymph nodes, these displaced cells usually have a micro-vascular architecture admixed with damaged erythrocytes and histiocytes. These features were lacking in our case most likely because of the lengthy time frame (10 years) from initial needle localization.

In the modern era of sentinel lymph node biopsy, the pathologist is obligated to perform a detailed and sensitive histopathologic examination for metastatic carcinoma. Consequently, there has been an overrecognition of artifacts and mimics in sentinel lymph nodes, such as heterotopic glands. The presence of these inclusions has no adverse effects, except for their misinterpretation and possible overtreatment as metastatic carcinoma.

This case emphasizes that sentinel lymph nodes may harbor heterotopic benign inclusions and displaced benign and malignant cells. Thus, the finding of epithelial cells in sentinel lymph nodes should not automatically be equated with metastatic carcinoma, particularly in cases of DCIS. This case also highlights the danger of performing polymerase chain reaction as a diagnostic test in the evaluation of sentinel lymph nodes because benign inclusions and displaced cells can serve as false-positive pitfalls.

The biological significance, that is, the metastatic capability, of displaced cells in axillary lymph nodes has always been questioned. Currently, no evidence exists, to our knowledge, to support the notion that epithelial cells transported by mechanical means have malignant potential. Similar to the untoward effect of single tumor cells in the peripheral blood, displaced cells in lymph node probably lack metastatic capability. This may be due to the incorrect biochemical makeup of the cells and inappropriate milieu for establishing metastasis. However, it is hypothesized that, given sufficient time, displaced cells may mutate to survive and proliferate in the new environment, a possibility that may have occurred in our case given the long time span. Thus in our case, although we favor an origin for the intraductal carcinoma from the adjacent benign glandular inclusions, we cannot exclude the possibility of displacement and benign transport as an etiology.

References