Benign Transport of Breast Epithelium Into Axillary Lymph Nodes After Biopsy

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Abstract

The most important prognostic indicator of distant metastasis in breast cancer is histologic documentation of axillary lymph node metastasis. Controversy exists about the importance of micrometastases (<0.2 cm), and current pathology practice includes a careful search for their presence. We describe the histologic findings in a series of axillary lymph node dissections taken approximately 2 weeks after breast biopsy. Each case has limited presence of epithelial cells in the subcapsular sinus of a draining lymph node that we attribute to mechanical transport of tumor and/or normal breast epithelium secondary to the previous surgical or needle manipulation. These cells were accompanied by hemosiderin-laden macrophages and damaged RBCs. While the clinical implication of these findings is unknown, we believe that it will be of no clinical significance and have no untoward prognostic effect.

Incisional and intratumoral biopsy of breast lesions after detection of a clinical or mammographic abnormality is accepted as a safe and reliable diagnostic procedure. Major complications, such as hemorrhage or infection, are rare,[1,2] and less serious complications, such as hematoma formation, are easily prevented. Seeding of needle tracts and disturbance of lesional cells are more worrisome potential complications of biopsies done in women with a diagnosis of breast cancer. This phenomenon commonly is described after biopsy of gastrointestinal[3] and gynecologic[4] malignant neoplasms, and the implications and prognosis are well understood.

Needle tract seeding has been described after stereotactic core needle biopsy of the breast using a 14-gauge biopsy needle.[5] Youngson et al[6] in 1994 described a series of 29 surgical breast specimens in which displaced epithelial fragments were found in stroma or lymphovascular channels in breast lesions removed from women who had undergone a previous needle biopsy procedure. The authors stated that the biologic implications of this finding were unknown. In 1 case, papillary clusters of carcinoma cells, identical to the breast lesion, were seen in the subcapsular sinus of draining axillary lymph nodes on subsequent reexcision. The authors regarded this as metastatic carcinoma with all of its treatment and prognostic implications.[6]

In 1995 Youngson et al[7] again found displaced fragments of carcinomatous elements in 12 of 43 consecutive patients with breast carcinoma who had a surgical procedure after an initial 14-gauge stereotactic core biopsy. Although the authors were certain that the specific histologic features seen in the stroma in their series did not represent true invasive mammary carcinoma, they seemed less certain of the biologic implications of displaced tumor cells in lymphatic spaces.[7]

Brown et al[8] in 1995 demonstrated, using molecular techniques, the presence of circulating malignant cells perioperatively in women with breast cancer undergoing surgical tumor manipulation. Postoperatively, the authors found no circulating tumor cells. No prognostic significance was implied.[8]

Recently in our consultation service, we have seen several post–breast biopsy dissection specimens of axillary lymph nodes with epithelial cells in the subcapsular sinus that we attribute to benign lymphatic transport of these cells as a consequence of the previous surgical manipulation. The clinical significance of these findings is unknown, but we believe that it is important to note that these mechanically micrometastatic lesions are not present in the lymph node because of native metastatic capacity and are unlikely to implicate a risk for widespread disease or true metastasis.

Materials and Methods

The consultative files of the Vanderbilt University Medical Center Breast Consultation Service (Nashville, TN) were reviewed. All cases that had lymph node samples taken after an initial breast biopsy were selected and studied. Fifteen cases were found to have fragments of epithelium in the subcapsular sinus accompanied by hemosiderin-laden macrophages, foreign body–type multinucleated giant cells, physically altered RBCs, and/or lymphocytes. Available microscopic slides were reviewed. The necessary history of previous manipulation was elucidated from available reports and the referring pathologist, clinician, or both. We found no analogous cases by nodal histologic criteria that did not have a recent history of instrumentation of the lesional breast.

Results

Clinicopathologic Features

Patient age ranged from 39 to 78 years. Three patients underwent a needle core biopsy, and the remainder underwent an excisional biopsy. A diagnosis of ductal carcinoma in situ was given in 7 cases, and invasive carcinoma was the diagnosis for the other 8 cases. All of the women underwent a second procedure that included axillary lymph node sampling. These procedures took place within 22.6 days, on average, of the initial biopsy. There was 1 outlier at 4 months, but most operations took place within 2 weeks.

On final diagnosis of the definitive specimen, 7 cases were ductal carcinoma in situ, 4 cases showed invasive mammary carcinoma, 1 had pleomorphic lobular carcinoma, and 3 had no evidence of residual cancer. Four women had benign epithelium (3 with micropapilloma), 5 had epithelium identical to the ductal carcinoma in situ seen in the breast lesion, and 6 cases had cells identical to the invasive carcinoma in the subcapsular sinus of the draining axillary lymph node **Table 1**.

In the breast excision specimen, evidence of previous surgical manipulation was present in the form of recent needle track formation or biopsy site within or immediately adjacent to the lesion of interest **Image 1**.

In each case, the subcapsular sinus of at least 1 lymph node, usually an identified sentinel node, contained clusters of cells derived from the breast **Image 2**. Small clusters of epithelial cells, always smaller than 1 mm and usually 100 to 200 µm, were accompanied by hemosiderin-laden macrophages, foreign body–type multinucleated giant cells, physically altered RBCs, and lymphocytes **Image 3**. In 11 cases, the epithelial clusters were from the carcinoma. However, in 4 cases, the epithelium noted in the subcapsular sinus was not derived from the cancerous breast lesion. Three cases showed papillary fragments **Image 4**, and 1 showed benign breast glands **Image 5**. Our only case of invasive lobular carcinoma showed individual cancer cells, not clusters, scattered in the lymph node sinus **Image 6**. In 3 cases, displaced cellular fragments also were noted lodged in lymphovascular spaces next to the needle track in the main reexcision specimen **Image 7**.

Discussion

The presence of these tiny groups of epithelial cells in the lymph node subcapsular sinus could be interpreted in a number of ways: (1) They may represent metastases with implications for distant disease. (2) They may represent regional metastases with less obvious implications for distant disease and disease-free survival. (3) They may represent epithelial inclusions of embryologic or embolic histogenesis. (4) They may represent, as we believe, a forced habitation due to tumor disruption and displacement into nearby lymphatic vessels.

Small clusters of breast cancer epithelium in axillary lymph nodes usually are interpreted as local micrometastatic disease. Although the issue still is under discussion, the presence of micrometastatic disease may well portend a poorer long-term and disease-free survival for patients with a diagnosis of invasive mammary carcinoma. The American Joint Committee on Cancer, however, states that the prognosis for patients with pn1a micrometastatic (<0.2 cm) disease is similar to that for patients with pn0 disease.[9]

The results of studies in this area are conflicting and should be interpreted with caution. Rosen et al[10] studied sufficient numbers of patients with micrometastatic disease

Table 1
Clinicopathologic Features

Case. No	Age (y)	Biopsy Type	Biopsy Diagnosis	Interval	Surgery Type	Breast Final Diagnosis	Lymph Node Diagnosis
1	66	Excisional	Invasive mammary carcinoma	15 d	Lumpectomy, axillary dissection	Invasive mammary carcinoma	Invasive mammary carcinoma
2	41	Needle	Invasive mammary carcinoma	21 d	Modified mastectomy, sentinel node biopsy	Invasive mammary carcinoma	Invasive mammary carcinoma
3	39	Excisional	Invasive mammary carcinoma	14 d	Modified mastectomy, axillary dissection	Invasive mammary carcinoma	Invasive mammary carcinoma
4	50	Excisional	Invasive mammary carcinoma	14 d	Modified mastectomy, axillary dissection	Atypical lobular hyperplasia	Invasive mammary carcinoma
5	69	Needle	Invasive mammary carcinoma	15 d	Modified mastectomy, axillary dissection	Invasive mammary carcinoma	Invasive mammary carcinoma
6	55	Excisional	Invasive mammary carcinoma	14 d	Modified mastectomy, axillary dissection	DCIS	DCIS
7	72	Excisional	Invasive mammary carcinoma	10 d	Modified mastectomy, axillary dissection	DCIS	DCIS
8	42	Excisional	DCIS	14 d	Modified mastectomy, axillary dissection	DCIS	DCIS
9	39	Excisional	DCIS, papilloma	14 d	Modified mastectomy, sentinel node biopsy	DCIS	DCIS
10	43	Excisional	DCIS	16 d	Lumpectomy axillary dissection	DCIS	DCIS
11	63	Needle	DCIS	14 d	Lumpectomy, axillary dissection	DCIS	Benign epithelium
12	42	Excisional	DCIS, micropapilloma	4 mo	Axillary dissection	Micropapilloma	Micropapilloma
13	51	Excisional	DCIS, micropapilloma	21 d	Modified mastectomy, axillary dissection	Micropapilloma	Micropapilloma
14	78	Excisional	DCIS	14 d	Modified mastectomy, sentinel node biopsy	DCIS, micropapilloma	Micropapilloma
15	56	Excisional	Invasive lobular carcinoma	15 d	Modified mastectomy, axillary dissection	Invasive lobular carcinoma	Invasive lobular carcinoma

DCIS, ductal carcinoma in situ.

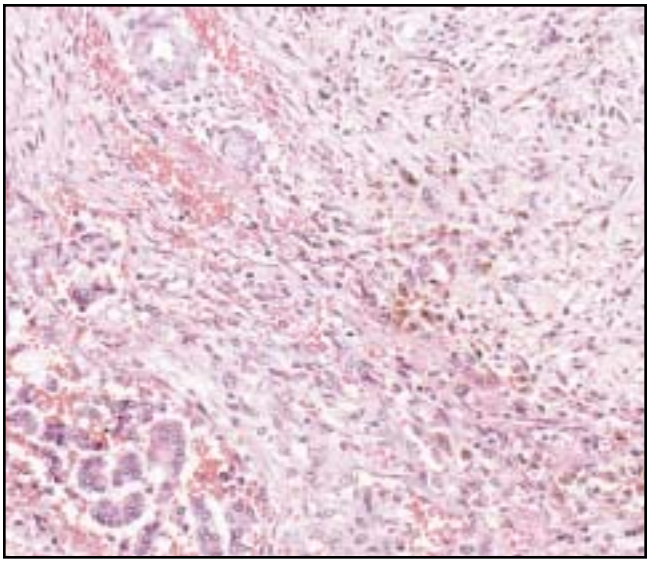

Image 1 Needle biopsy site. Well-formed granulation tissue adjacent to dislodged epithelium surrounded by an inflammatory and reparative response (H&E, ×40).

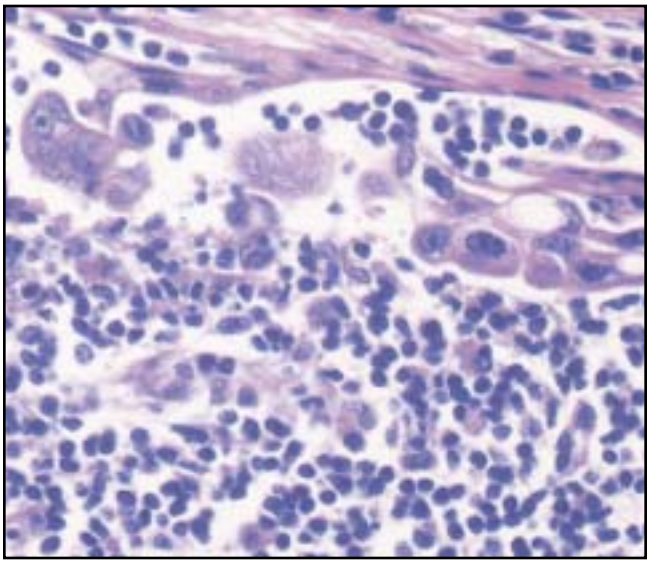

Image 2 Several small clusters of tumor cells are present in the subcapsular sinus of the draining axillary lymph node (H&E, ×200).

with follow-up of 10 years or more and found significant differences in outcome compared with patients with node-negative disease. Other authors had similar results using special techniques, such as immunohistochemistry or multiple sections, with even shorter follow-up.[11] The publication of the study by the International (Ludwig) Breast

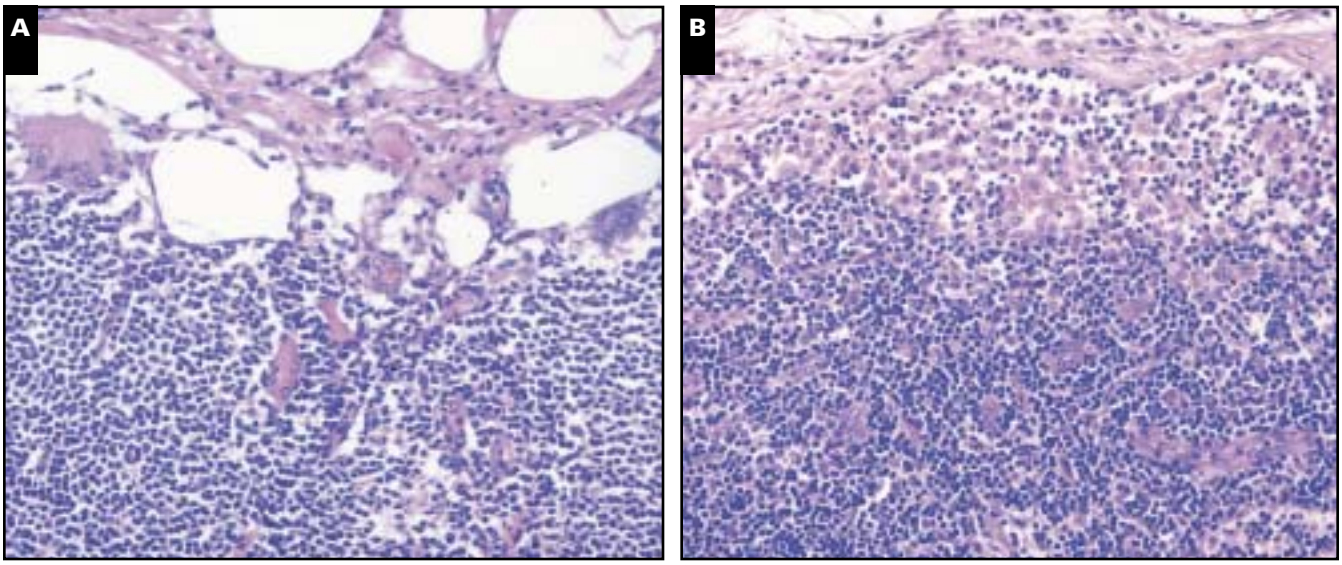

Image 3 A, Foreign body–type multinucleated giant cell and foamy macrophages in the subcapsular sinus of the axillary lymph node (H&E, ×100). B, Hemosiderin-laden macrophages, lymphocytes, and debris in the subcapsular sinus (H&E, ×100).

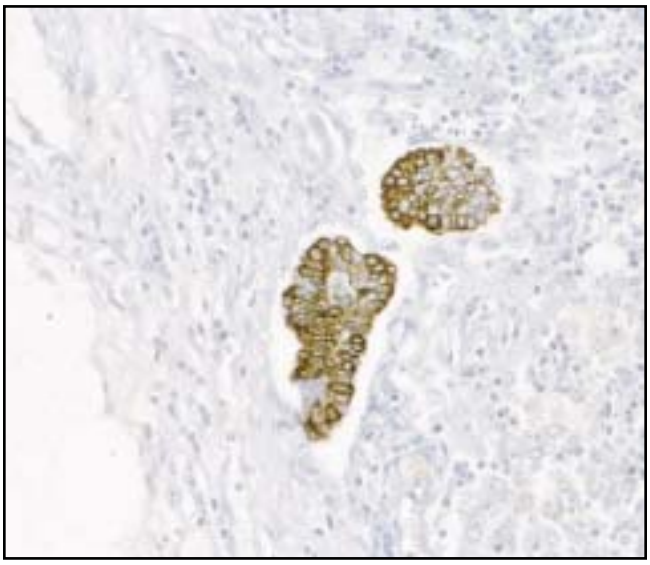

Image 4 Papillary fragment in the lymph node of a patient with micropapillomas and ductal carcinoma in situ (cytokeratin, ×200).

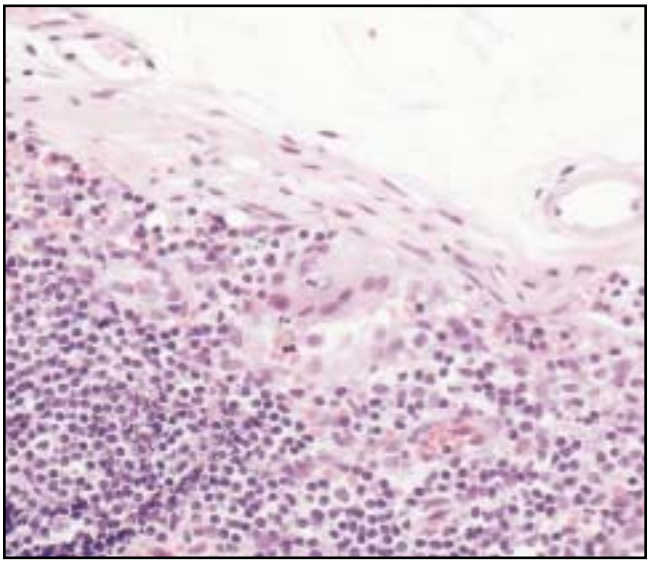

Image 5 Distorted benign gland in the subcapsular sinus with associated inflammatory response (H&E, ×200).

Cancer Study Group[11] brought a flurry of letters questioning the methods, conclusions, and recommendations.[12,13]

More recently, no significant difference in survival was found when patients with micrometastatic deposits were compared with patients with node-negative breast cancer.[14] In a study of invasive lobular carcinoma, Trojani et al[15] showed that micrometastases detected by immunohistochemical studies had no prognostic significance. It therefore is imperative that the presence of breast epithelium of any size in axillary lymph nodes be described and diagnosed with care.

Altered RBCs and hemosiderin-laden macrophages are essential for the diagnosis of benign transport of breast epithelium, and the diagnosis should be made with caution without their presence. We regard the proximity of these cells to the debris of the recent biopsy event as a guarantee that they occurred together in time and space. This microscopic finding is the usual, expected, reparative response to hemorrhage and trauma in the regional draining lymph nodes.

As noted in our results, this phenomenon is not restricted to breast cancer epithelium. Four of our cases revealed benign epithelium in the subcapsular sinus of the draining lymph node, and in all cases, this epithelium was

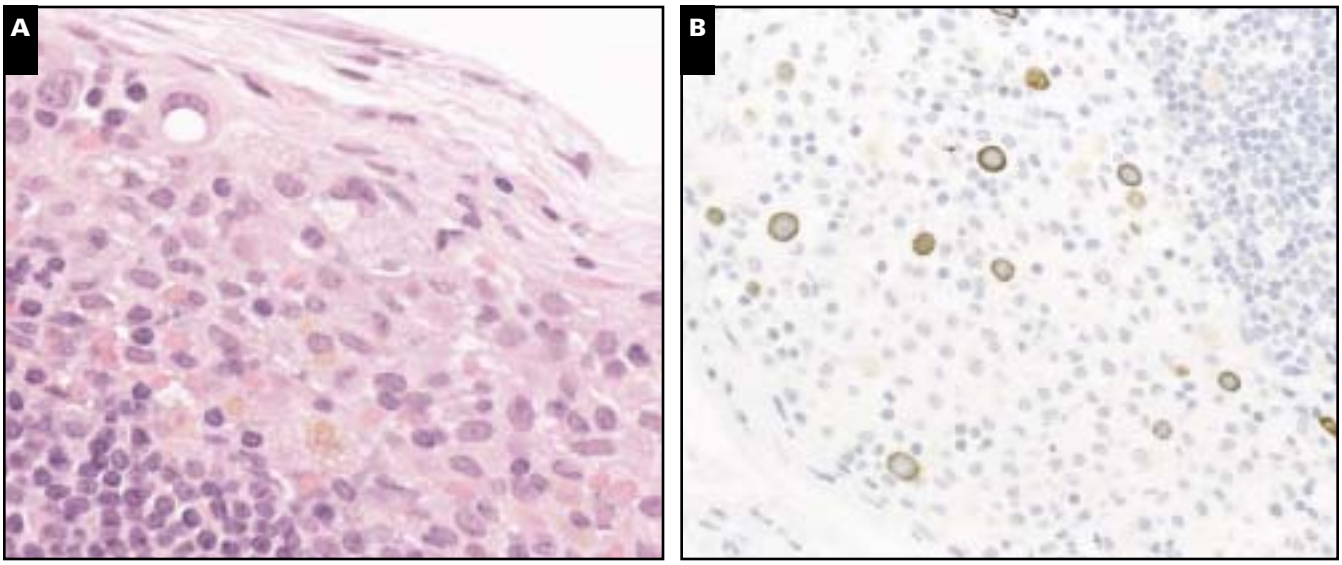

Image 6 Single cells scattered in the subcapsular sinus of the axillary lymph node (A, H&E, ×40; B, cytokeratin, ×40).

found with postbiopsy cellular debris. In these cases, we think that adjacent papillomas or normal breast tissue was displaced surgically when the initial lesion was manipulated. Identical nodal findings after surgical manipulation of benign and malignant breast lesions support our benign transport hypothesis.

Cases identified by our group as benign transport differ from those seen in nodal heterotopic epithelial inclusions. These benign epithelial lesions may present any of the patterns found elsewhere in the breast.[16] In these cases, often seen in women with a diagnosis of tubular carcinoma,[17] glandular structures are banal and are without the attendant signs of previous tissue disruption. Interestingly, Fisher et al considered a history of previous biopsy as significant when determining causation.[17]

We analogize these findings to those of McDivitt et al[18] of embolic involvement of an axillary node by benign breast lesions, and we suggest that the mechanism of embolism is mechanical force into lymphatic channels. In our consultation service, transport of benign elements into peritumoral lymphovascular spaces, similar to the findings of Youngson et al,[6,7] after breast biopsy has been observed not infrequently. The recent work by Diaz et al[19] confirmed the relatively high rate of tumor displacement after large-gauge needle core biopsy. Other authors have suggested that mechanical force may disrupt and embolize susceptible tissues. Partial detachment of the placenta during continued contraction is readily accepted as the mechanical force behind trophoblastic and/or amniotic fluid emboli in the systemic vasculature and lung.[20] Perrone[21] believed the colonic glands she noted in lymph nodes obtained at colon resection 2 weeks after a colonoscopic biopsy of an adenocarcinoma were a result of mechanical trauma. Weeks et al[22] described benign nodal inclusions in pediatric patients with renal neoplasms, apparently as a result of rupture of obstructed renal tubules and clearance by local lymphatics. Clement et al[23] in 1996 described 2 cases of hyperplastic mesothelial cells in abdominal lymph nodes and agreed that these probably were present owing to the disruptive effect of ascites on hyperplastic mesothelium as proposed by Brooks et al[24] in their study of mediastinal lymph nodes in patients with pleural effusions. In both studies, the displaced mesothelium was located in the subcapsular sinus.[23,24] Vilela et al[25] described embolization of mesothelial cells in lymphatic spaces secondary to a pressure gradient in a patient with severe ascites. This forced transport of cells also elicited an inflammatory response, and it is this finding that differentiates this particular case from benign nodal mesothelial inclusions.[25]

The clinical implications of benign transport of tumor elements to axillary nodes in patients with a diagnosis of breast cancer are unclear. We believe that these findings most likely are of no clinical significance and a microscopic reflection of what must be a frequent event at the time of mechanical manipulation. The transport of benign glands to the sinus as seen in one of our cases lends much credence to that claim. Whether the tumoral enforced inhabitants of the lymph node have any true metastatic capability is unknown. Injected, highly selected, single tumor cells derived from cell lines with demonstrated metastatic capacity can have widespread metastatic capability experimentally, albeit to restricted organ systems.[26] Equally as important, in experimental work, it has been shown that the transient presence of single tumor cells in the peripheral blood is without untoward effect.

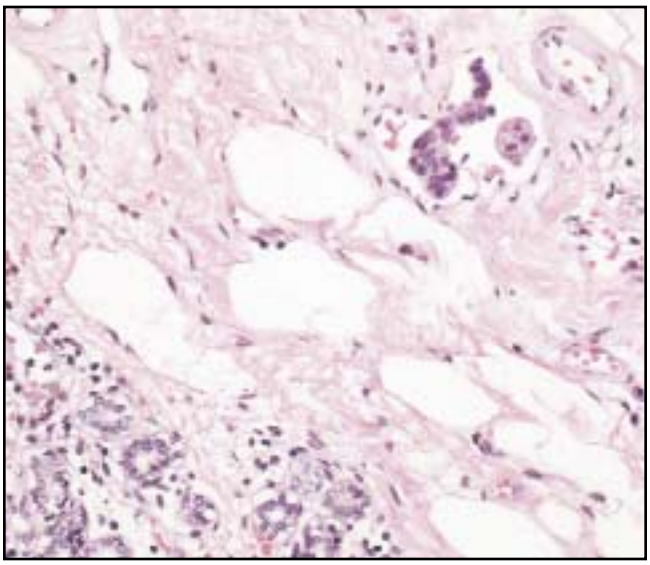

Image 7 Excision specimen with disrupted tumor fragments in lymphatic spaces near the biopsy site (H&E, ×100).

Verification of the clinical import of this novel finding can be solved only with long-term studies with observation and follow-up. At present, we suggest that widespread metastases are not a risk but still recommend careful follow-up of patients for whom this diagnosis is made.

Conclusions

Benign transport of breast epithelium into axillary lymph nodes after needle or surgical manipulation is a diagnosis that should be made with care. Cell clusters identical to the main breast lesion, altered RBCs, and an inflammatory response usually consisting of hemosiderin-laden macrophages are necessary for the diagnosis. Although not yet proven to be a benign event, prior information on equal survival for patients with incised and excised tumors strongly supports the likelihood that these findings will have no untoward prognostic implications. We believe that this phenomenon, in itself, does not carry risk of future metastatic behavior and look forward to larger and more extensive studies in this area.

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