

# Diagnosis and Treatment of Cancer Arising in Ectopic Breast Tissue

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**abstract** Ectopic breast tissue is a frequently seen anomaly, and this tissue is subject to all of the disease processes of the normal breast, including cancer. Although cancer in ectopic breast tissue is extremely rare, the diagnosis should be kept in mind when evaluating new masses. This report reviews the subject of ectopic breast tissue and describes the uses of sentinel lymph node biopsy for a cancer arising in an ectopic breast. □

## CASE REPORT

A 64-year-old gravida 3, para 3, postmenopausal female with a supernumerary breast in the left upper abdominal position was evaluated for a palpable mass within the third breast, just inferior to the small but well-formed nipple-areolar complex.

The patient initially became aware of the accessory breast tissue during puberty, at age 11, when she noted discomfort associated with menses. During her first full-term pregnancy, at age 24, she reported substantial engorgement of the accessory breast, but no lactation. She had been compliant with a routine screening program of her right and left breasts, including yearly mammography, physician examination, and monthly self-breast examination, all of which had been normal. She had no significant medical problems, no previous history of cancer, and took no medications. Her family history included a sister diagnosed with breast cancer at age 52.

Physical examination revealed two well-formed symmetric, pendulous breasts without nipple changes or palpable abnormalities. Recent bilateral mammogram was negative. There was no axillary, cervical,

supraclavicular, or inguinal adenopathy. Beginning inferior to the inframammary fold was a non-ptotic breast mound 10 cm x 8 cm x 4 cm in height from the abdominal wall with a small but well-formed areola and nipple. A firm, 2-cm, non-tender, mobile mass was noted centrally and inferiorly within the accessory breast mound

with no associated skin changes or discharge from the supernumerary nipple.

Further evaluation of this mass included ultrasound, which demonstrated a hypoechoic mass with posterior acoustic shadowing, and mammography in a special medial-lateral view, which demonstrated a 2-cm spiculated lesion suspicious for malignancy (*Figure 1*). Fine-needle aspiration (FNA) of the mass revealed



FIGURE 1. Medial lateral mammographic view showing left breast and ectopic breast with skin marker (X) over the palpable tumor.

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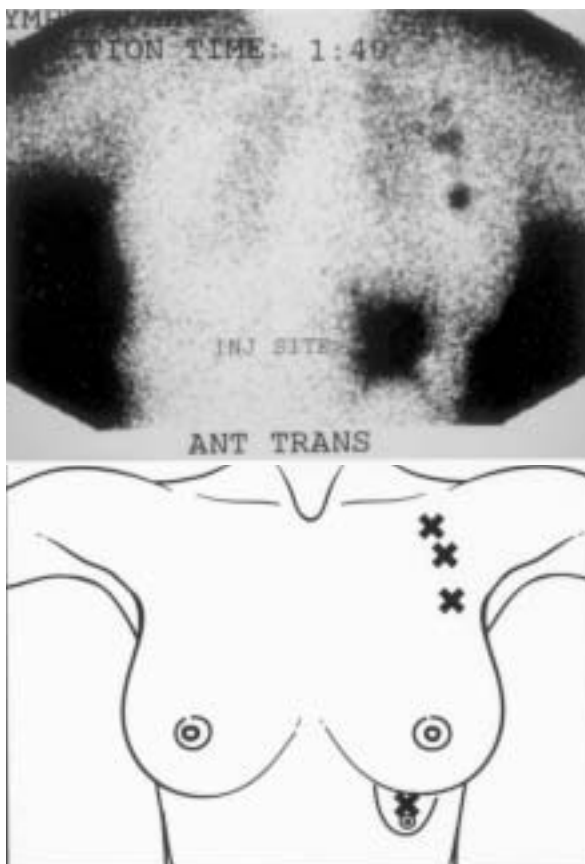


FIGURE 2. Lymphoscintigram showing injection site (X) in ectopic breast and uptake in axilla (XXX).

malignant cells consistent with adenocarcinoma. Subsequent extent-of-disease evaluation by bone scan and computerized tomography (CT) scans of the chest, abdomen, and pelvis revealed no evidence of distant metastatic disease.

We scheduled the patient for accessory-breast mastectomy, intraoperative sentinel lymph node (SLN) mapping with node biopsy, and possible axillary dissection for a clinical T2 N0 M0 breast cancer.

Lymphoscintigraphy was performed using intradermal injection of 0.5 mCi of Technetium-99m-labeled unfiltered sulfur colloid injected at the supernumerary nipple. Images of the thorax, abdomen, and pelvis demonstrated uptake in three foci in the left axillary region (Figures 2, 3).

At operation, 5 cc of isosulfan blue dye was injected as close as possible to the mass within the parenchyma of the accessory breast mound. Injection was followed by lymphatic massage. Inspection with a hand-held gamma probe revealed radioactivity

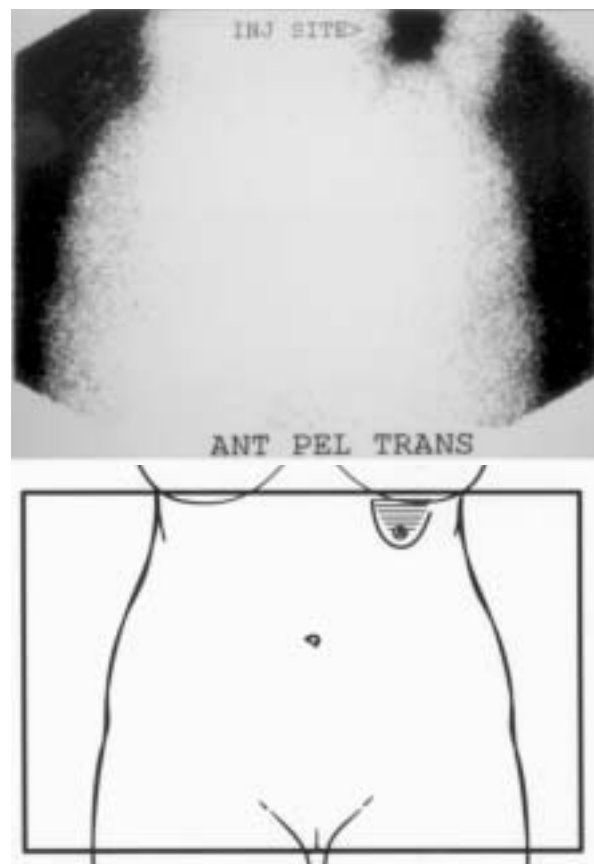


FIGURE 3. Lymphoscintigram of abdomen and pelvis showing injection site at ectopic breast but no uptake in inguinal area.

exclusively in the area of the left axilla with no appreciable counts over the supraclavicular, cervical, right axillary, internal mammary, pelvic, or inguinal regions. A single blue and hot lymph node was found and excised. Two additional hot SLNs with no apparent blue-dye staining were also excised, as well as two non-SLNs contiguous with them. Subsequent low background-radioactivity levels were achieved in the axillary bed. Intraoperative frozen sections of SLN specimens were negative for metastatic disease.

A total mastectomy of the accessory breast was performed (Figure 4). Wide excision of overlying skin of the breast mound and excision of the underlying fascia had grossly negative margins. The extent of the surgical field of the accessory-breast mastectomy was marked by Weck clips on the rectus muscle and the serratus to direct postoperative radiation, if required. Primary closure without the creation of skin flaps was possible because of the patient's lax redundant subcutaneous abdominal tissue and skin.

Upon pathologic review, a 2.4-cm invasive, high-grade mammary carcinoma with ductal and pleomorphic lobular features was identified along with ductal carcinoma in situ (DCIS). All surgical margins were negative for disease; however, the posterior margin was close. The tumor was HER-2/*neu* negative, and expressed both estrogen and progesterone receptors. All lymph nodes were negative for metastatic disease on routine pathology and additional immunohistochemical staining.

The patient subsequently underwent four cycles

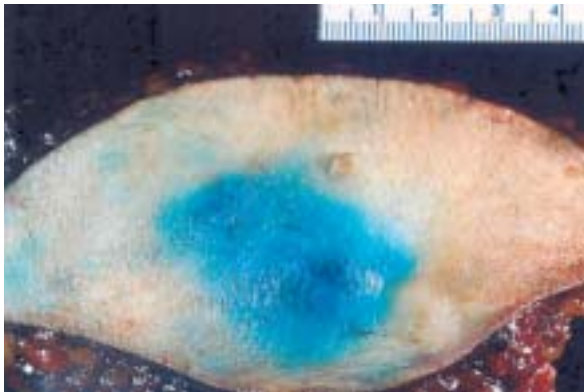


FIGURE 4. Mastectomy specimen with isosulfan blue dye staining skin over tumor just below nipple-areolar complex.

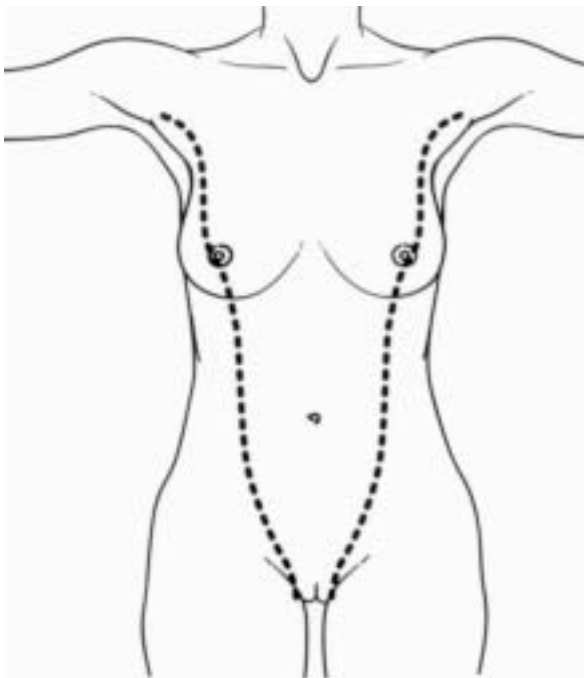


FIGURE 5. Line drawing showing "milk ridge," the site of ectopic breast mounds if normal embryonic regression fails.

of adjuvant doxorubicin (*Adriamycin*, Pharmacia Inc, Kalamazoo, Mi) and cyclophosphamide (*Cytoxan*, Bristol-Myers Squibb Oncology, Princeton, NJ) chemotherapy followed by a course of external-beam radiation therapy to the accessory-breast surgical field (5,000 cGy) with a boost (1,000 cGy) to the posterior, closest margin marked by clips. Normal breast tissue was shielded. The patient was placed on tamoxifen.

The patient remains free of disease at last follow-up, 19 months from her initial diagnosis and surgical management.

## DISCUSSION

### Embryology

The mammary ridge is a bandlike thickening of epidermis that runs from the axilla to the groin in two symmetrical ectodermal thickenings during the fifth week of embryonic development. Most of the mammary ridge disappears, but the region in the thorax persists and invaginates into the underlying mesenchyme. At 16 weeks' gestation, epithelial buds develop and then branch to form strips. The buds canalize to become the lactiferous ducts, and the strips develop into secretory alveoli. The lactiferous ducts open into a small epithelial pit, which, after birth, develops into the nipple. If the mammary ridge does not atrophy normally, ectopic breast tissue mounds and/or nipples are formed anywhere along the milk ridge (*Figure 5*), although the axilla is the most common area.<sup>1,2</sup>

Ectopic breast tissue has been found in multiple locations along the milk line from the axilla to the vulva. Ectopic breasts that arise along the milk line traditionally have been referred to as accessory or supernumerary breasts. Formation of a nipple without obvious underlying breast tissue is also common. When mammary tissue is found in the superior trunk, in the same area of the breast, but outside its periphery, it is traditionally referred to as aberrant breast tissue.<sup>3</sup> It is thought that these areas of tissue are diverticula of the ipsilateral breast that develop during the fetal period and, later in development, lose all connection to the normally placed breast.<sup>4</sup> The duct system in aberrant breast tissue is not as well organized as that of normal breasts or even accessory breasts, and the duct system does not lead to a nipple or other central focus.<sup>3</sup>

### Incidence

Ectopic breast tissue and/or nipples are a frequently seen congenital anomaly. The incidence is about 1%

in the general population, but is thought to be higher in women of Japanese descent. Iwai et al<sup>5</sup> reported the incidence of accessory breast tissue in a Japanese population to be 3.7%. The most common observed location of an ectopic nipple is just below the normally located left nipple.<sup>6</sup> Polythelia (extra nipples) has been associated with urinary anomalies, such as supernumerary kidneys, failure of renal formation, double-collecting systems, ureteropelvic-junction stenosis, multicystic kidneys, and renal carcinomas.<sup>7,8</sup>

Previous studies have indicated that ectopic breasts and accessory breasts may have a genetic basis because they have been found in more than one generation of certain families.<sup>9</sup> Extra breasts have also been found in parent-child pairs.<sup>10</sup> Males have almost the same percentage of extra nipples as do females.<sup>11</sup>

### Physiology

Ectopic breast tissue is usually overlooked until dramatic hormonal increases occur. They are often first noticed during puberty or pregnancy. At these times, response to hormonal surges can cause enlargement, tenderness, and lactation even as it does in breast tissue in the normal location. Fine-needle aspiration and cytology can be useful in differentiating ectopic breast tissue from other subcutaneous masses, such as lipomas.<sup>12</sup> Follow-up of accessory breasts should be similar to that of normally located breasts and include special instruction in self-examination and regular clinical evaluation. Routine mammographic views would usually not include accessory breast tissue.

Excision of ectopic breast tissue is indicated for cosmetic reasons. This is common in adolescents who find a third breast at puberty and feel it is "freakish."

### Diseases

Ectopic breast tissue is subject to all of the disease processes of the normal breast. Fibroadenomas, fibrocystic disease,<sup>13</sup> phyllodes tumors,<sup>14</sup> Paget's disease,<sup>15</sup> mastitis,<sup>16</sup> abscesses, as well as all varieties of breast cancer<sup>17-20</sup> have been found in ectopic breasts. Carcinoma in ectopic breast tissue is extremely rare. Chiari<sup>17</sup> found that this situation accounted for a 0.3% incidence of all breast cancers. However, it is thought that cancer is slightly more common in aberrant breast tissue than in accessory breast tissue.<sup>21,22</sup>

Although many of the earlier reports suggested a worse prognosis for patients with ectopic breast can-

cer, this is now not thought to be true. Stage for stage, this cancer is thought to have the same prognosis as cancer in the normally located breast.<sup>17</sup> The problem lies in detection. Because cancer in ectopic breast tissue is so rare, clinical suspicion is generally low.

One report describes a patient with cancer independently arising in a supernumerary breast years after a primary breast cancer in one of the normal breasts.<sup>23</sup> Since the risk of a contralateral breast cancer is higher after breast cancer, ectopic breast tissue would also have a higher risk, and postoperative exams should include ectopic breast tissue.

### Diagnosis

In general, work-up is identical to that of any breast mass. Standard mammograms do not usually show ectopic breast tissue, because of its location. With special positioning of the patient, however, ectopic breasts are sometimes imaged. In this case study, mammography of the accessory breast demonstrated the cancer; however, this breast had not been imaged on any former study. Ultrasonography may be helpful. Fine-needle aspiration can be a very valuable tool in evaluating these masses; indeed, as mentioned earlier, FNA can prove that breast tissue exists, and may be able to distinguish it from other types of masses (eg, lipomas).

Any change or mass in accessory breast tissue should be expeditiously evaluated. Excision is warranted for any suspicious nodules. At one time, preventive mastectomy of the accessory breast was advocated, because of a question of higher risk of breast cancer in ectopic sites. Since it now appears that ectopic breast tissue has no higher risk of carcinogenesis, preventive mastectomy is not required.

If cancer is diagnosed, a total mastectomy is standard. There are no reports of attempted breast conservation of accessory breasts. For treatment, a thorough mastectomy with the removal of a large amount of overlying skin is recommended. This is necessary because the skin is usually very close to the cancer in the small ectopic breast. If the skin closure of the mastectomy is tight, it is possible to dissect under the abdominal fat even to the umbilicus, and to pull up the skin to make a better closure. With cancer of the third breast, it is not necessary to consider excision of the ipsilateral normal breast, as the duct system of each breast is separate, precluding extension of the intraductal carcinoma into another breast.

**CONCLUSION**

Traditionally, lymph node staging for the ectopic breast was done by complete lymph node dissection of the closest nodal basin. The basin to be dissected was determined by Sappey's line, which runs circumferentially from the anterior inferior costal margin around to the posterior aspect of the twelfth rib. Lesions above the line are thought to drain to the ipsilateral axilla, and lesions below the line are thought to drain to the inguinal nodes. Lesions in the midline could drain to both nodal basins.<sup>4</sup>

Sentinel lymph node biopsy has been shown to be accurate in multiple large breast cancer trials. In the era of SLN biopsy, the lymph node basin draining the accessory breast tissue can be more accurately determined. We know that in cases of truncal melanoma, the tumor can drain to multiple sites including, but not limited to, the axilla and groin areas. The same may be true of breast cancer in an ectopic location. In the present case, a preoperative lymphoscintigram of the inframammary breast showed uptake only in the ipsilateral axilla, directing our efforts there. Using SLN biopsy in these situations will allow surgeons to stage ectopic breast cancers appropriately and accurately while avoiding unnecessary dissection of other nodal basins.

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