

## Sentinel lymph node mapping of a breast cancer of the vulva: Case report and literature review

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### Abstract

Ectopic breast tissue is rare and typically presents as an axillary mass. Previous reports have identified ectopic breast tissue in the vulva, but malignancy is exceedingly uncommon. We present a 62 years old with

locally advanced breast carcinoma arising in the vulva demonstrates the utilization of sentinel lymph node mapping to identify metastatic lymph nodes previously unable to be identified *via* traditional surgical exploration. Our case supports the principles of adjuvant therapy for breast cancer to be applied to ectopic breast cancer arising in the vulva. A literature review highlights common key points in similar cases to guide management.

**Key words:** Vulvar cancer; Ectopic breast; Sentinel lymph node; Breast cancer; Vulvar breast cancer

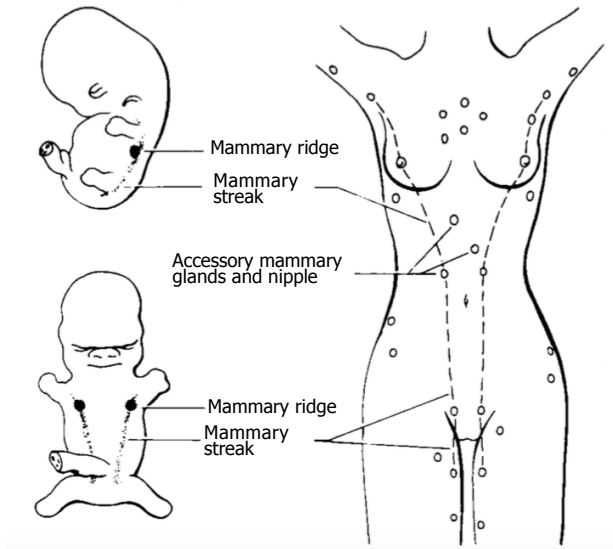
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**Core tip:** Our findings describe the presentation of ectopic breast cancer in the vulva. We demonstrate use of sentinel lymph node technology with identification of the sentinel node, only possible after the use of this technology. We conclude with a review of the literature outlining treatment of this enigmatic disease.

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### INTRODUCTION

Ectopic breast tissue has been previously reported in various locations along the primitive milk line, from the axilla to the vulva (Figure 1). Axillary ectopic breast tissue is the most frequent location and the vulva being the least common site<sup>[1]</sup>. Malignant ectopic breast tissue is rare, typically presenting as an axillary mass, with vulvar breast malignancy being exceedingly rare<sup>[1]</sup>. In 1935, Green *et al*<sup>[2]</sup> published the first case report



**Figure 1** Ectopic breast tissue has been previously reported in various locations along the primitive milk line, from the axilla to the vulva.

of adenocarcinoma arising from breast tissue in the vulva. Although 22 cases of malignant vulvar breast tissue have been reported since then, there are no clear guidelines regarding surgical or adjuvant treatment. We present a case that outlines the diagnosis and management of primary breast cancer of the vulva, highlighting diagnostic dilemmas, the utility of sentinel node mapping and reinforcing the importance of a multidisciplinary approach in the management of this rare clinical entity.

## CASE REPORT

A 62 years old Hispanic multiparous women noted a new 1.3 cm left labial mass for approximately 1 year and presented to her primary gynecologist for evaluation. She underwent a wide local excision that was noteworthy for an invasive ductal carcinoma arising in ectopic breast tissue. Final pathology was confirmed by independent review at two separate institutions. Immunohistochemical staining showed the lesion to be 95% estrogen receptor (ER) positive, 10% progesterone receptor (PR) positive, and human epidermal growth factor 2 (HER2) negative (Figure 2).

The patient underwent a magnetic resonance imaging of the breast that was negative for a breast primary malignancy. Approximately 1 mo after initial presentation in September of 2012, the patient was referred to gynecologic oncology and underwent a partial radical vulvectomy at the prior vulvar scar site. Final pathology was negative for residual disease and the patient, given absence of metastatic disease declined adjuvant therapy. The patient initiated close surveillance and had a Fluoro-deoxyglucose (FDG) Positron emission tomography (PET) scan in January 2013 with findings of suspicious left inguinal-femoral lymphadenopathy, with standard uptake value (SUV) of 8.1.

The patient was counseled to undergo left inguinal-femoral lymphadenectomy (LND). The dissection was completed superficial to the cribiform fascia and final pathology identified 14 lymph nodes ranging from 1.2-2.5 cm that were all negative for tumor. On follow up examination in April 2013, the patient was found to have a 1-2 mm firm, non-tender nodule under her healing scar. In office biopsy confirmed recurrent invasive ductal carcinoma, with identical histology to the previous primary lesion. A repeat wide local excision was performed in June 2013. Pathology from that surgical resection was negative for tumor.

A PET-CT in August 2013 was repeated and was significant for suspicious left inguinal lymph node measuring 1.1 cm × 1.6 cm with SUV of 8.2 (Figure 3). The patient returned to the operating room with preoperative technetium 99 lymphoscintigraphy and lymphazurin blue (injected into the previous left surgical site) lymph node localization (Figure 4). An inguinal incision was created and the Geiger counter was used to identify "hot" areas. Dissection continued until area of maximum radioactivity was encountered. A hot, blue, slightly firm, 1.2 cm left sentinel was identified superficial to the cribiform fascia and excised. Intraoperative frozen section was positive for metastasis and comprehensive LND was performed. Two additional left sentinels (both hot and blue) were positive for ductal carcinoma. A right-sided sentinel node was not identified, but given contralateral positive nodes a comprehensive right LND was performed. Final pathology (Figure 2) confirmed three positive sentinels and 14 negative left and right inguinofemoral nodes.

Metastatic workup was negative and the patient underwent intensity modulated radiation therapy (4500 cGy) with 5900 cGy boosts to the left groin. Chemotherapy included weekly taxol followed by adriamycin and cyclophosphamide. Following adjuvant therapy she started maintenance therapy with an aromatase inhibitor.

She is currently without evidence of disease recurrence 13 mo after sentinel lymph node detection.

## DISCUSSION

Ectopic breast tissue is rare and accounts for 0.2%-0.6% of all breast cancers. Only 4% of these ectopic breast cancers are located in the vulva, making vulvar breast cancer exceedingly rare<sup>[3]</sup>. Ectopic breast tissue originates in the fetus at the ectodermal mammary streak extending from the axilla to the groin as demonstrated in Figure 1. Most of this structure disappears with small portions persisting in the thorax. This primordial ectoderm penetrates the underlying mesenchyme and gives rise to small solid out buddings that canalize and form the lactiferous ducts and alveoli of the mammary gland<sup>[4,5]</sup>.

There have been 22 reported cases since Greene's index case report in 1935. The majority of these patients

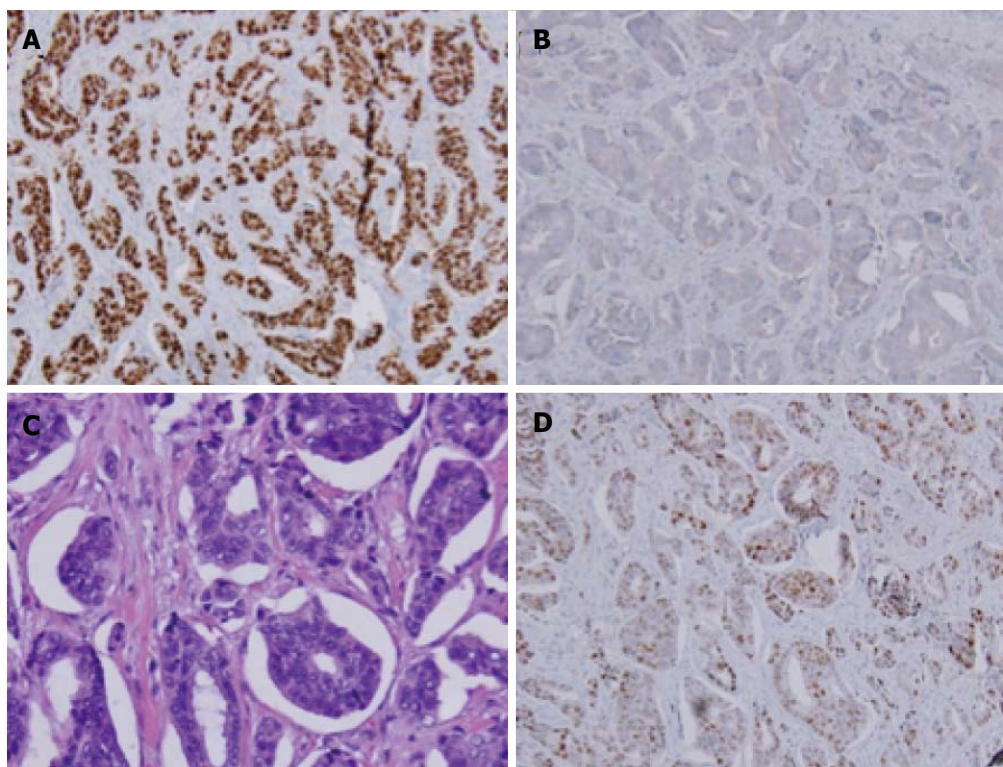


Figure 2 Estrogen receptor staining of primary tumor (A), Her2neu staining of primary tumor (B), metastasis to the lymph node (C), progesterone receptor staining of primary tumor (D).

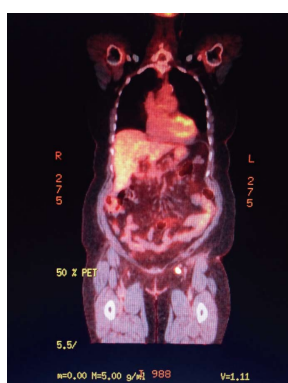


Figure 3 Patient returned to the operating room with preoperative technetium 99 lymphoscintigraphy and lymphazurin blue (injected into the previous left surgical site) lymph node localization.

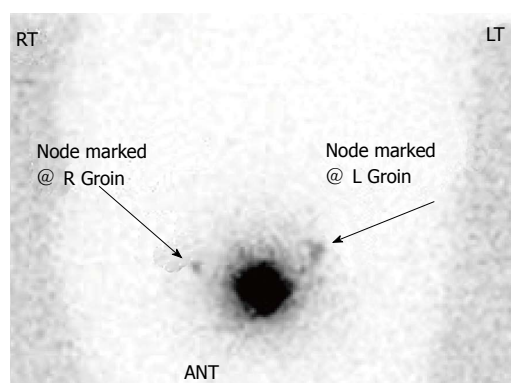


Figure 4 Ectopic breast tissue originates in the fetus at the ectodermal mammary streak extending from the axilla to the groin. RT: Radiation therapy.

presented with an innocuous solitary lesion of the vulva (Table 1); upon surgical excision, adenocarcinoma or ductal carcinoma arising in normal appearing breast tissue was identified. Extensive preoperative imaging is traditionally used to exclude metastasis of a primary breast malignancy. Two of these reported cases were indeed metastatic from a primary breast lesion<sup>[6,7]</sup>. Adjuvant chemotherapy and radiation treatment protocols are heterogeneous (Table 2) given the rare frequency of these lesions, and absence of standardized treatment paradigms. Anti-hormonal therapy has been used in 14 (13 Tamoxifen and 1 Aromatase) patients with ER/PR positive specimens with various outcomes. The use of trastuzumab in

HER2 positive cases has not been previously reported.

The presence of metastatic tumor in regional lymph nodes remains the most significant prognostic factor for several malignancies, including breast cancer. Sixteen patients underwent inguinal LND with all 16 patients having lymph node involvement. Survival and adjuvant therapy data are outlined in Table 2. Sentinel lymph node mapping is a technique that minimizes morbidity while maintaining diagnostic accuracy by isolating the first or "sentinel" node to drain the affected area burdened with tumor. This is traditionally performed with injection of the tumor with isosulfan blue and a radiolabeled colloid, most often technetium 99. This technique was pioneered by Morton in the treatment



Table 1 Clinical presentations of vulvar-breast cancer

Ref.	Year	Age (yr)	Location	Size (cm)	Symptoms and duration	Duration (mo)
Greene <sup>[2]</sup>	1935	59	Right labia majora	20 × 15	Mass	12
Hendrix <i>et al</i> <sup>[14]</sup>	1956	58	Right Labia minora	3	Ulcerated mass	84
Guerry <i>et al</i> <sup>[16]</sup>	1976	62	Right labia minora	1.5	Mass	4
Guercio <i>et al</i> <sup>[15]</sup>	1984	49	Left labia majora	2	Mass	Unk
Cho <i>et al</i> <sup>[16]</sup>	1985	70	Right labia majora	3 × 4	Mass	30
Simon <i>et al</i> <sup>[17]</sup>	1988	60	Right labia majora	2 × 2	Ulcerated mass	36
Rose <i>et al</i> <sup>[18]</sup>	1990	68	Right labia majora	3.5 × 3.5	Mass	36
Di Bonito <i>et al</i> <sup>[19]</sup>	1992	46	Right labia majora	1.5	Ulcerated mass	24
Bailey <i>et al</i> <sup>[20]</sup>	1993	65	Right labia majora	3 × 2	Ulcerated mass	36
Levin <i>et al</i> <sup>[21]</sup>	1994	62	Left clitoris	2.5	Mass	Unk
Kennedy <i>et al</i> <sup>[7]</sup>	1997	71	Left labia majora	5	Ulceration and dysuria	1
Irvin <i>et al</i> <sup>[4]</sup>	1998	64	Left lateral mons	3	Indurated mass	48
Gorisek <i>et al</i> <sup>[22]</sup>	2000	81	Left labia majora	2 × 3	Ulcerated mass	Unk
Piura <i>et al</i> <sup>[23]</sup>	2002	69	Left labia majora	3	Ulcerated mas	Unk
Chung-Park <i>et al</i> <sup>[24]</sup>	2002	47	Right labia minora	2	Ulcerated mass	12
Yin <i>et al</i> <sup>[25]</sup>	2003	84	Mons	5	Swelling	24
Lopes <i>et al</i> <sup>[26]</sup>	2006	44	Left vulva	2	Mass	48
Fracchioli <i>et al</i> <sup>[27]</sup>	2006	57	Left vulva	1	Mass	Unk
North <i>et al</i> <sup>[28]</sup>	2006	49	Right labia minora and clitoris	1.5	Pain and pressure	Unk
			Left groin	2		
Naseer <i>et al</i> <sup>[29]</sup>	2011	57	Right labia majora	1.5	Non painful lesion	Unk
McMaster <sup>[30]</sup>	2013	60	Left labia majora	3	Pedunculated ulcerated mass	6
Bogani <i>et al</i> <sup>[13]</sup>	2013	71	Left labia Majora	4	Painful ulcerated mass	Unk
			Left groin	3		

Unk: Unknown.

of melanoma in the early 1990's<sup>[8]</sup>. The assessment of regional lymph nodes in breast cancer paralleled the work in melanoma, in an effort to limit the morbidity of axillary lymph node dissection<sup>[9]</sup>. Numerous clinical trials have detailed the effectiveness and reduced morbidity associated with sentinel lymph node dissection in breast cancer patients in both the primary surgical setting and following neoadjuvant therapy. Current American Society of Clinical Oncology (ASCO) guidelines recommends sentinel lymph node mapping as standard of care in breast cancer<sup>[10]</sup>.

Sentinel node mapping in vulvar cancer is a more contemporary topic with evolving literature, and has paralleled some advances in penile carcinoma lymphatic mapping. GROINS-V, an observational study, followed 403 patients with primary vulvar tumors less than 4 cm treated with sentinel node mapping. Eight patients had groin recurrence with a false negative rate of 5.9% and a false negative predictive value of 2.9%<sup>[11]</sup>. Similar results were replicated in GOG protocol 173<sup>[12]</sup>, a phase 3 multi-institutional study of intraoperative lymphatic mapping in patients with invasive squamous cell carcinoma of the vulva. Inclusion criteria included depth of invasion > 1 mm and primary tumor size 2-6 cm. Four hundred and fifty-two patients underwent sentinel node mapping with 418 patients having a sentinel node identified. Eleven (8.3%) patients with negative sentinel lymph nodes had groin recurrence. The false negative rate in primary lesions < 4 cm was 2%, but with lesions > 4 cm the false negative rate was 4%<sup>[11]</sup>. It is important to note that all patients in GOG protocol 173 underwent comprehensive LND after sentinel LND

regardless of its status. GROINS-V also identified a statistically significant decrease in wound breakdown, cellulitis, and lymphedema in patients undergoing sentinel lymph node mapping. Both studies provide evidence to support the incorporation of sentinel LND in the management of vulvar malignancies.

Our case utilized sentinel lymph node mapping at time of recurrence and precisely aided in the identification of the metastatic lymph nodes. This technology was not utilized in the primary surgical management due to uncertainties on how it would perform when the primary lesion was comprised of ectopic breast tissue. However, after failing to identify the PET positive nodes with standard LND, SLD was employed to identify and excise the lymph nodes.

Primary breast cancer originating in the vulva is rare and management strategies stem from individual case reports or case series. Current literature supports the use of sentinel lymph node mapping in vulvar cancer and we anticipate that future cases will utilize this practice. Bogani *et al*<sup>[13]</sup> as well as our case have been the only published literature to utilize sentinel lymph node mapping after a previous LND. Both cases identified positive sentinel lymph nodes that were previously unable to have been resected. These findings may support the up-front use of sentinel lymph node localization.

From our review of the literature there are several key concepts in managing this rare malignancy. First, exclusion of a primary breast malignancy needs to be confirmed by pretreatment imaging and physical examination. Next, occurrence of positive nodes is

**Table 2** Previously published reports

Ref.	Treatment	Histology	ER	PR	Her2-neu	LN	Status	Follow up (mo)
Greene <sup>[2]</sup>	None	AC + S	NA	NA	NA	NA	DOD	1
Hendrix <i>et al</i> <sup>[14]</sup>	Surgery	AC	NA	NA	NA	NA	DOD	4
Guerry <i>et al</i> <sup>[6]</sup>	Surgery	DC	NA	NA	NA	NA	DOD	24
Guercio <i>et al</i> <sup>[15]</sup>	Surgery + RT	LO	NA	NA	NA	11/24	NED	36
Cho <i>et al</i> <sup>[16]</sup>	Surgery + tamoxifen	AC	+	+	NA	2/9	NED	24
Simon <i>et al</i> <sup>[17]</sup>	Surgery + tamoxifen + cyclophosphamide, adriamycin, 5FU Recurrence cisplatin/etoposide then carboplatin/etoposide	AC	+	+	NA	3/11	DOD	27
Rose <i>et al</i> <sup>[18]</sup>	Surgery + RT + tamoxifen	DC	+	-	NA	1/15	Unk	Unk
Di Bonito <i>et al</i> <sup>[19]</sup>	Surgery	Unk			NA	11/13	NED	4
Bailey <i>et al</i> <sup>[20]</sup>	Surgery + tamoxifen	DC	+	+	NA	2/20	NED	12
Levin <i>et al</i> <sup>[21]</sup>	Surgery + tamoxifen Recurrence restarted tamoxifen/RT	AC	+	-	+	4/11	NED	24
Kennedy <i>et al</i> <sup>[7]</sup>	Surgery + adriamycin/cyclophosphamide	Unk	-	-	NA	9/9	NED	15
Irvin <i>et al</i> <sup>[4]</sup>	Surgery + cytoxan/Mtx/5FU + RT + tamoxifen	AC	+	+	NA	1/14	NED	4
Gorisek <i>et al</i> <sup>[22]</sup>	Surgery + tamoxifen	AC	+	+	NA	NA	NED	19
Piura <i>et al</i> <sup>[23]</sup>	Surgery + adriamycin/cyclophosphamide/paclitaxel + RT + tamoxifen	AC	+	+	NA	7/15	NED	14
Chung-Park <i>et al</i> <sup>[24]</sup>	Surgery	MU	+	+	-	NA	NED	36
Yin <i>et al</i> <sup>[25]</sup>	Surgery	MU	+	+	-	1/11	NED	9
Lopes <i>et al</i> <sup>[26]</sup>	Surgery + docetaxel/doxorubicin/cyclophosphamide + tamoxifen	MU	+	NA	-	2/13	Unk	Unk
Fracchioli <i>et al</i> <sup>[27]</sup>	Surgery + 5FU/adriamycin/cyclophosphamide + tamoxifen Recurrence-paclitaxel	AC	-	NA	NA	7/7	Rec Unk	36 Unk
North <i>et al</i> <sup>[28]</sup>	Surgery + cyclophosphamide/epirubicin/5FU + weekly docetaxel + tamoxifen	DC	+	+	-	5/7	Unk	Unk
Naseer <i>et al</i> <sup>[29]</sup>	Surgery + 5FU/epirubicin/cyclophosphamide + weekly docetaxel + RT + aromatase	DC	+	+	-	3/13	Unk	Unk
McMaster <i>et al</i> <sup>[30]</sup>	Surgery + RT	DC	+	NA	NA	NA	Unk	Unk
Bogani <i>et al</i> <sup>[13]</sup>	Surgery + epirubicin/cyclophosphamide + tamoxifen	DC	+	+	NA	1/8	NED	24

AC: Adenocarcinoma; DC: Ductal carcinoma; DOD: Dead of disease; LO: Lobular; MU: Mucinous; Mtx: Methotrexate; NA: Not applicable; NED: No evidence of disease; Rec: Recurrence; RT: Radiation therapy; S: Squamous; Unk: Unknown; 5FU: 5-fluorouracil.

high and can be difficult to locate; primary surgical excision (radical vulvectomy) with sentinel lymph node dissection to help identify the sentinel lymph node should be considered.

Systemic chemotherapy based on adjuvant therapy platforms for breast cancer with docetaxel or paclitaxel, plus doxorubicin, and cyclophosphamide should be considered. Given the biologic parallels between primary breast and vulvar breast cancer, treatment paradigms mimicking primary breast cancer are a rational approach and are advisable. This is supported by the median survival of patients treated with adjuvant therapy for breast cancer had a mean survival of 30 mo in comparison to 12 mo for those receiving a vulvar treatment (surgery followed by radiation). Finally, patients with estrogen and progesterone receptor positive specimens may be maintained on tamoxifen or aromatase inhibitors.

## COMMENTS

### Case characteristics

A 62 years old Hispanic women presented with a 1.3 cm left labial mass.

### Clinical diagnosis

Suspected neoplasm originating from the left labia.

### Differential diagnosis

Gartners duct cyst, labial myoma, vulvar squamous cell carcinoma, and vulvar

melanoma.

### Pathological diagnosis

Histologic examination identified the ectopic breast tissue and carcinoma present in excised specimen.

### Treatment

Excisional procedure.

### Related reports

Previous reports of vulvar breast cancer present similarly with an isolated labial mass, treated with surgical excision, however many do not receive chemotherapy that parallels breast cancer treatments.

### Experiences and lessons

When vulvar breast cancer is encountered, the physician should exclude a primary breast malignancy, perform an excision procedure, and utilize sentinel lymph node mapping as recommended in breast cancer.

### Peer-review

Well written case report.

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