

## Invasive ductal carcinoma arising in ectopic breast tissue of the axilla. Case report and review of the literature

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**SUMMARY:** Invasive ductal carcinoma arising in ectopic breast tissue of the axilla. Case report and review of the literature.

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*Mammary carcinoma arising in ectopic breast tissue is an uncommon occurrence. Most reported cases have involved ductal carcinoma, but other types, such as medullary, papillary, and lobular carcinomas, have been described. For pathologists, the diagnosis of mammary carcinoma arising in ectopic breast tissue can be difficult, especially in the axilla, where carcinoma of adnexal origin must be excluded.*

*We describe a 51-year-old woman who developed invasive secretory ductal carcinoma in ectopic left axillary breast tissue and micrometastatic carcinoma in an ipsilateral axillary lymph node. The carcinoma arose in a left axillary mass that had been present for several years, from which she had secreted fluid during prior menstrual periods.*

**RIASSUNTO:** Carcinoma duttale infiltrante in tessuto mammario ectopico dell'ascella. Descrizione di un caso clinico e revisione della letteratura.

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*Il carcinoma della mammella che insorge da tessuto mammario ectopico è evenienza alquanto rara. Nella maggioranza dei casi si tratta del duttale infiltrante anche se vengono riportati casi di midollare e papillare. La sua diagnosi differenziale, quando insorge in sede ascellare, è estremamente difficoltosa inducendo spesso a diagnosi per patologia degli annessi cutanei.*

*Descriviamo il caso di un carcinoma duttale secretante situato nell'ascella sinistra e con micro metastasi ai linfonodi omolaterali. Il carcinoma prese origine da una tumefazione, di dimensioni limitate, comparsa anni prima nell'ascella sinistra; tale lesione aveva sempre secreto in occasione dei periodi mestruali.*

**KEY WORDS:** Ectopic breast tissue - Invasive ductal carcinoma - Treatment.  
Tessuto mammario ectopico - Carcinoma duttale infiltrante - Trattamento.

### Introduction

Accessory breast tissue is a relatively common occurrence that has a high incidence of being misdiagnosed. Various diagnoses of such structures include lipoma, lymphatic malformation, lymphadenitis and sebaceous cysts. Clinically, cases of accessory breast tissue may be asymptomatic or patients may report discomfort during menstruation, pain, discharge, and restriction of arm movement. Many patients may wish to have ectopic tissue excised for cosmetic reasons or to relieve anxiety over

the possibility of malignancy. Potential accessory breast tissue in a patient merits further investigation by the clinician, as this tissue has the ability to undergo all the pathological changes of the normal breast and the presence of ectopic breast tissue may indicate underlying congenital anomalies.

In ancient times, multiple breasts were associated with fertility. The goddess Artemis is one of the most well known of the female deities endowed with multiple breasts. During the centuries of witch-hunts, supernumerary breasts and nipples were deemed Devil's marks. Men and women found with this accessory breast tissue were often tortured and killed. One of the most referred to cases of accessory breast tissue is from 1827 and involves Therese Ventre of Marseilles, France. Ventre had an accessory breast on the lateral aspect of her left thigh that enlarged during puberty and produced milk when she became pregnant. The famous woodcut showing Ventre's children nursing from both of her normally posi-

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tioned right breast and left thigh breast is frequently depicted.

The prevalence of accessory breast tissue has been shown to be dependent on few factors, including gender, ethnicity, geographical area, and inheritance.

Overall, the occurrence averages between 0.22 per cent and 6 per cent of the general population. Women report a higher rate of polymastia and polythelia than do men. Instances of ectopic breast tissue are higher in black Americans, white Americans, Native Americans, Japanese, Israeli Jews, and Arabs. Studies on white European children show a very low frequency of 0.22 per cent. Most instances of accessory breast tissue is sporadic, however, familial cases have been described in up to 10 per cent of the affected population. Family pedigrees have mapped the two most common methods of inheritance to be autosomal dominant with incomplete penetrance and X-linked dominance. Each of these modes of inheritance shows variability in their phenotypic expression among generations.

Any combination of accessory breast tissue, including nipples, areola, and glandular breast tissue, can be found in addition to the two normally developed breasts on the chest. Most commonly, this tissue develops along the embryonic mammary ridge that extends from the axilla to the groin. Incomplete regression of this ridge during embryologic formation gives rise to ectopic breast tissue. Aberrant breast tissue has been reported to arise from extra sites, including the face, posterior neck, chest, buttock, vulva, hip, shoulder, posterior and/or lateral thigh, perineum, as well as the mid-back. Several theories have been developed to account for breast tissue found outside the embryonic milk line. One theory suggests that the milk ridges become displaced, whereas another posits that accessory breast tissue may occur anywhere apocrine sweat glands are found.

In 1915 Kajava classified the expression of accessory breast tissue into eight categories still in use today: complete supernumerary nipple (SN) with nipple, areola and glandular breast tissue, which is known as polymastia; SN with nipple and glandular tissue without areola; SN with areola and glandular tissue without nipple; aberrant glandular tissue only; SN with nipple, areola and pseudomamma, which is fat tissue that replaces the glandular tissue; SN with nipple only, which is known as *polythelia*; SN with areola only, which is known as *polythelia areolaris*; and a patch of hair only, which is known as *polythelia pilosa*. The most common type of accessory breast tissue is polythelia. Axillary accessory breast tissue is found in 60 per cent to 70 per cent of all affected patients. This tissue is separate from the direct extension of the axillary tail of Spence. Accessory breast tissue is not usually identified at young age. The tissue frequently becomes symptomatic during menarche, pregnancy, or lactation as it responds to normal fluctuating levels

of hormones. Ectopic breast tissue has been known to change size cyclically with menstruation, to increase in size during pregnancy, and to lactate while nursing.

Patients with accessory breast tissue may also be more prone to other congenital anomalies. Although there is some dispute over the findings, research indicates a correlation between ectopic breast tissue and urogenital abnormalities. Urogenital anomalies occur in 1 per cent to 2 per cent of the general population, whereas an estimated 14.5 per cent of patients with accessory breast tissue have been diagnosed by ultrasound with kidney and/or urinary tract abnormalities. This high association has led some researchers to suggest that there may be a common supernumerary breast tissue/renal field defect.

Accessory breast tissue has also been associated with underlying cardiovascular disorders, although the relation between the two has yet to be definitively established. Congenital heart anomalies with pulmonary hypertension, cardiomyopathy arising from myocardial infarction, and systemic hypertension are notably related to polythelia. Ectopic breast tissue in patients is an important cutaneous indicator of conduction system abnormalities, such as bundle branch block or third degree heart block.

Polythelia is a well-established clinical finding in Simpson-Golabi-Behmel Syndrome. Simpson-Golabi-Behmel Syndrome is an X-linked recessive disorder characterized by pre- or postnatal overgrowth, facial dysmorphic features, polythelia, heart malformations, cleft palate, and postaxial polydactyly.

Accessory breast tissue has not been conclusively linked to renal or cardiovascular disorders, however many clinicians choose to follow up affected patients with renal ultrasound and a full cardiovascular workup or screening of any congenital or acquired disorders.

## Case report

A 51-year-old, gravida 1, para 1 woman presented with a firm mobile mass in the left axilla that had been present for several years. The patient reported that the mass was recently "changing and becoming erythematous". She described the secretion of liquid material from this area. A well-formed nipple or areolar structure was not identified. Her past medical history was significant only for long-standing hypertension and occasional urinary tract infections. She had not prior breast complaints or breast surgeries. Mammograms and breast MRI were normal. The contralateral axillary tissue was unremarkable on physical examination. Her maternal aunt and paternal first cousin had prior breast cancer.

The patient underwent an incisional biopsy of the lesion. The specimen consisted of an unoriented, elliptical, pale, tan to dark gray, focally roughened, nodular skin lesion measuring 1.6 x 0.7 x 0.6 cm, which was entirely submitted for histologic evaluation. The lesion, located in the deep dermal-subcutaneous region, was a lobulated circumscribed tumor mass composed microscopically of a monomorphic population of ductal cells with cribriform and microcystic architecture. Many microlumens contained pale pink to amphiphilic secretion.

The carcinoma cells had vacuolated, eosinophilic to amphophilic cytoplasm and low to intermediate nuclear grade. The borders of the lesion involved the inked surgical margin. The carcinoma displayed no nuclear reactivity for estrogen or progesterone receptors and was also HER-2/neu-negative. One glandular structure reminiscent of a mammary lobule was identified in the deep dermis adjacent to the tumor. The overlying epidermis was histologically unremarkable.

The patient subsequently underwent a re-excision of the left axillary biopsy site, which revealed residual carcinoma adjacent to the incisional biopsy. Inked surgical margins were negative. This specimen also included ectopic breast tissue consisting of lobules as well as skin adnexal glands. Although the distinction of ectopic breast tissue from adjacent skin adnexal glands can be difficult, glands from the former can be found organized in discernible lobules, whereas the latter generally do not have this configuration. The mammary glandular tissue was intermixed with adnexal glands, a superficial distribution indicative of ectopic tissue rather than an axillary extension of the mammary tail of Spence. A limited left lymphadenectomy revealed micrometastatic carcinoma histologically similar to the axillary tumor in 1 of 2 level III lymph nodes. At the time of the left axillary re-excision, a left breast biopsy was performed for a mass remote from the axilla. Histologically, the breast biopsy showed ductal hyperplasia in a radial sclerosing pattern.

The patient received adjuvant chemotherapy consisting of adriamycin and cyclophosphamide. Taking into consideration the characteristics of the tumor and its high-grade features, it was recommended to proceed with adjuvant radioterapy. The patient completed five weeks of external beam radioterapy. Two years after surgery, she showed no signs suggestive of recurrence. Mammography continued to show no signs of malignancy.

## Discussion and conclusions

During the early weeks of embryonic development, the mammary milk lines, which represent two ectodermal thickenings along the sides of the embryo, extend from the axillary region to the groin. In normal development most of the embryologic mammary ridges resolve, except for two segments in the pectoral region, which later become breasts. Failure of any portion of the mammary ridge to involute can lead to ectopic breast tissue with (polythelia) or without (polymastia) a nipple/areolar complex. Polythelia, in particular, has been associated with urinary anomalies, such as supernumerary kidneys, failure of renal formation, and renal carcinomas, which can be explained in part by the parallel embryologic development of mammary structures and the genitourinary system.

Most instances of ectopic breast tissue occur along the milk line in the axilla and vulva. Ectopic breast tissue is subject to the same hormonal influences and risk of disease as pectoral breast tissue. During menses or pregnancy, hormonal stimulation can cause engorgement and discomfort (2). Ectopic breast tissue can undergo lactational change during pregnancy, and in the presence of a nipple-areolar complex it can give rise to lactational secretion.

A range of proliferative conditions occurring in ectopic breast tissue has been described, including cysts,

papillomas, and fibroepithelial lesions (3). Carcinomas arising in ectopic breast tissue have been well-documented. The majority have been located in axillary (2, 5) and vulvar breast tissue (6, 7). Histologically, most adenocarcinomas arising in supernumerary breast tissue have been of the ductal type (8). Other subtypes have been described, including medullary, papillary, and lobular carcinoma. Ectopic breast tissue, especially when found in the axilla, is located in the subcutaneous tissue and deep dermis of the skin, where it often mingles with normal skin appendage glands (3). For the pathologist, the morphologic distinction between carcinoma of mammary and skin appendage gland origin can be difficult in this instance. The presence of in situ carcinoma or immunoreactivity for estrogen and progesterone receptors has been used in the past to make the distinction between mammary and nonmammary carcinomas. Diagnostic uncertainty is complicated further by the existence of cutaneous mammary-like sweat glands, also known as mixed sweat glands (9). Carcinoma of mammary and adnexal origin can be morphologically indistinguishable, and immunostains, such as estrogen and progesterone receptors and BRST-2, have been found to be positive in both entities (10). At the present time, no single immunohistochemical marker can distinguish mammary carcinoma from skin appendage-derived carcinoma, and a panel of markers is likely to be more useful. Wick and coworkers (11) reported that gross cystic disease fluid protein 15 (BRST-2) was statistically significant in its lack of staining in eccrine sweat gland carcinomas as compared to ductal carcinomas of the breast. Other investigators have reported the utility of epidermal growth factor receptor; immunoreactivity for epidermal growth factor receptor was found to be strongly associated with primary sweat gland carcinomas when compared to metastatic breast carcinoma in the skin (12). Various other immunohistochemical stains, such as carcinoembryonic antigen, S100, and c-erbB-2 oncoprotein, have been found to be less useful (11, 12).

We believe that a careful search for adjacent benign breast tissue in the excised specimen is critical, and this process may involve submitting the entire specimen for histologic evaluation, as well as obtaining deeper levels on paraffin blocks. Also, all available clinicopathologic information should be considered when arriving at a histologic diagnosis. The question arises as to why this is an example of ectopic breast tissue rather than an extension of breast parenchyma into the axilla. This issue can be best explained by the observation that in our case the mammary glandular tissue was interspersed among adnexal glands. This intermingling of glands connotes an anatomically superficial location, which is not characteristic of an axillary extension of the mammary tail of Spence.

Treatment of ectopic invasive mammary carcinoma is usually accomplished by wide local excision and regional lymph node staging if there are no concomitant tumors in the breast.

This may require lymphadenectomy if sentinel lymph node mapping is not technically feasible. Mastectomy is not necessary if ectopic axillary breast tissue can be verified and no suspicious lesions are evident clinically or mammographically in the breast (3). No survival advantage was seen with mastectomy when com-

pared to local excision combined with axillary dissection or radiation (13). It has been suggested that the prognosis of patients with carcinoma arising in ectopic breast tissue may be worse than that of pectoral breast carcinoma due to earlier lymph node involvement and difficulty in achieving en bloc resection of the tumor in some primary sites (13). Other investigators, however, have reported instances of axillary breast carcinoma with negative lymph nodes treated by excision and lymphadenectomy with long-term survival (13).

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