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REVIEW BREAST

Ectopic Breast Cancer: Case Report and Review of the Literature

Elisa Francone · Marco J. Nathan · Federica Murelli · Maria Santina Bruno · Enrico Traverso · Daniele Friedman

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Abstract Ectopic breast tissue comes in two forms: supernumerary and aberrant. Despite morphologic differences, ectopic breast tissue presents characteristics analogous to orthotopic breast tissue in terms of function and, most importantly, pathologic degeneration. Data in the literature concerning its precise incidence, the probability of malignant degeneration, and its standardized management are scarce and controversial. This study selected more than 100 years of literature, and this report discusses a case of ectopic breast cancer treatment, suggesting novel therapeutic advice that could bring considerable clinical advantages, improve cosmetic results, and reduce the psychological impact on patients.

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Keywords Breast cancer · Ectopic breast · Extra nipple · Supernumerary breast

Introduction

Ectopic breast tissue comes in two forms: supernumerary and aberrant [1]. A supernumerary breast consists of a ductal system communicating with the overlying skin, usually located along the "milk line", which extends from the axilla to the groin. It frequently responds to hormonal stimulation and undergoes physiologic changes as a complete functioning breast [2]. This form of ectopic tissue is subject to the same diseases and alterations, whether benign or malignant, that affect orthotopic breasts [3, 4].

Two varieties of supernumerary breast should be distinguished: polymastia and polythelia. Polymastia is an accessory gland that occurs as a consequence of the mammary ridge failing to regress during embryonic development. The gland may be found in association with an areola–nipple complex (classes 1–4) [5]. Polythelia presents itself in the form of an areola and/or a nipple lacking glandular tissue (classes 5–7) [5].

The second form of ectopic breast tissue, aberrant breast, consists of an isolated fragment of glandular tissue located beyond the periphery of orthotopic breasts. It is most commonly found in the axilla. However, parasternal, subclavicular, submammary, vulvar and anal cases also have been reported [6–8]. Aberrant breast is characterized by an unorganized secretory system without any connection between the inside and the outside.

Case Report

In March 2004, a 43-year-old Caucasian woman with a nonsignificant medical history approached our Department with a painless fixed solid nodular mass under a known supernumerary nipple located below the orthotopic right mammary gland in the midclavicular line (Fig. 1). Mammography and ultrasonography identified a suspicious mass lesion, and fine-needle aspiration cytology confirmed the diagnosis of malignancy. The results of clinical and

E. Francone (✉) · F. Murelli · M. S. Bruno · E. Traverso · D. Friedman
Department of Surgery, Breast Unit, IRCCS AOU San Martino-IST, Largo Rosanna Benzi 8, 16132 Genoa, Italy
e-mail: elisafrancone@gmail.com

M. J. Nathan
Department of Philosophy, Columbia University, 1150 Amsterdam Avenue, New York, NY 10027, USA

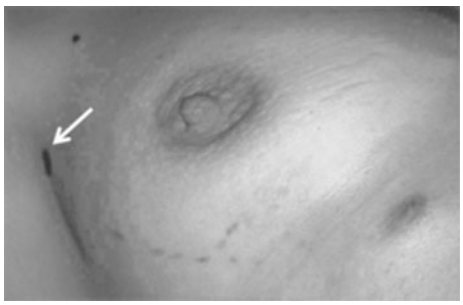

Fig. 1 Supernumerary nipple located below the right breast. The *arrow* indicates the sentinel lymph node projection

instrumental examination of the bilateral breasts and axillas were negative.

The patient underwent a wide local excision of the supernumerary breast tissue. The sentinel lymph node procedure was applied and, as expected [8, 9], the lymphatic drainage of the specific cancer site was flowing toward the omolateral axilla. Because histopathologic intraoperative examination showed evidence of metastatic disease, axillary lymph node dissection (levels 1 and 2) was performed. Histopathologic examination of the specimen led to the diagnosis of infiltrating ductal breast cancer. Only the sentinel lymph node (pT1c/G2/N1a) was involved. Immunohistochemical evaluation results were positive for estrogen receptor (65 %) and progesterone receptor (50 %). In 35 % of the neoplastic cells, the MIB-1 proliferation marker was positive.

The patient underwent a total-body computed tomography (CT) scan and bone scintigraphy, and the results were negative. Postoperative adjuvant chemotherapy (5-fluorouracil, epirubicin, and cyclophosphamide) and hormonal therapy (aromatase inhibitors), according to the standard protocol [10, 11], were performed. At this writing, 8 years later, the patient is well and disease free.

Discussion

This case study presents an opportunity to discuss the treatment of ectopic breast tissue, which is seldom mentioned in the surgical literature, and suggests some novel therapeutic considerations. Some researchers consider malignant degeneration of ectopic breast tissue to be highly probable. In particular, aberrant breast tissue is reportedly more prone to malignant transformation than orthotopic or ectopic breast tissue [2, 12] because, as suggested [13], stagnation arising in the ductal lumens is a promoting factor for the development of malignancy.

Others report that cancer in ectopic breasts tends to arise earlier than in developmentally normal breasts [8]. Still others claim that development of a benign mass or malignant degeneration, although possible, is rather unusual [3, 14, 15]. Despite morphologic differences, ectopic mammary tissue, whether supernumerary or aberrant, may present characteristics analogous to orthotopic tissue in terms of function and, more importantly, pathologic degeneration.

Histologic evidence shows that invasive ductal carcinoma is the most common malignant histotype in both orthotopic and ectopic breast tissue [4, 16, 17], as in the reported case. Furthermore, other forms of mammarian cancer frequently affecting orthotopic breasts, such as ductal carcinoma in situ (DCIS) or lobular carcinoma, reportedly occur in ectopic tissue as well [4, 15, 18].

The precise incidence of ectopic breast tissue also is uncertain. According to some authors, it occurs quite commonly and with a high incidence of misdiagnoses [19]. Others consider it a rare condition [3].

The occurrence of ectopic breast tissue ranges from 0.6 to 6 %[1] [20]. In particular, the incidence of supernumerary breast is relatively well known. It is easily detectable, and its clinical conditions have been studied for a long time [5] Polymastia occurs in less than 1 % of the population.[2] Polythelia presents an incidence calculated at about 1.0 to 1.4 %[3] and is associated with other congenital anomalies.[4]

Comprehensive data concerning the global incidence of aberrant breast tissue are harder to obtain because aberrant breast tissue is neither visible nor palpable in normal conditions. In fact, it becomes clinically diagnosable only when detectable signs are produced.

The management of ectopic mammarian tissue raises a number of controversial issues due to the rarity and complexity of the phenomenon, which is expressed in several forms and in various anatomic locations [25]. For this reason, diagnostic, therapeutic, and psychological considerations should be discussed separately.

The fact that ectopic breast tissue is not always easily detectable in the absence of pathologic symptoms renders the detection of solutions to problems concerning the timing of the diagnosis particularly challenging. Supernumerary and aberrant variants must be discussed separately. Whereas polymastia may not become evident until the influence of sex hormones during puberty, polythelia is both congenital and generally identifiable at childhood,

[1] Ectopic breast tissue affects 2 to 6 % of females, with the highest incidence among Japanese and the lowest incidence among Caucasians [8], and 1 to 3 % of males [21].

[2] Polymastia may be unilateral (more frequently on the left side) or bilateral, located along the milk line above or below orthotopic breasts [22].

[3] Polythelia generally presents itself as a unilateral lesion, most frequently located above the normal nipple (87 %) as opposed to below it (13 %) [22].

[4] Reported congenital anomalies include nervous, cardiovascular, gastroenteric, skeletal, and, particularly, renal abnormalities [2, 22–24].

particularly when the nipple is chromatically discernible. In contrast, aberrant breast tissue is generally undetectable in the absence of pathologic signs, such as manual detection of a nodule. The differential diagnosis must include other subcutaneous masses such as fibroadenoma, lipoma, hidradenitis, or follicular cyst, and also lymphadenopathy associated with benign or malignant disease, given that aberrant breast tissue is most commonly found in the axilla [12, 16].

As shown by therapeutic considerations, once the diagnostic procedures are completed, ectopic breast tissue, supernumerary or aberrant, should be treated in the same way as typical breast diseases depending on the type of neoplasia and its natural development. General clinical guidelines are not standardized. Some researchers recommend the inclusion of ectopic breast tissue in screening [26] so that differential treatment can be prescribed, depending on whether the lesion is benign or malignant. In cases of benign neoplasm, lumpectomy is recommended.

In contrast, if the neoplasm is malignant, the therapy must be based on regular standard procedures for breast cancer treatment (surgery, chemotherapy, radiation therapy, and ormonotherapy) assisted by an appropriate follow-up program [3, 26]. Nodal groups selected for exploration should correspond to the specific lymphatic drainage site of the malignant tumor.[5] Ipsilateral prophylactic mastectomy has no role in the management of ectopic breast cancer tissue [13, 26].

Psychological considerations are also relevant to the treatment of congenital breast malformations. Ectopic breast tissue can be psychologically debilitating to individuals. Accurate diagnosis, counseling, and appropriate treatment for both men and for women are thus necessary in alleviating the sense of deformity and unattractiveness that often presents itself under these circumstances [20].

Conclusions

Ectopic breast tissue is seldom mentioned in the literature, and both its benign and malignant alterations are significantly underreported [26]. The problem stems in part from a general lack of awareness that these nodules have potentially dangerous implications, often underestimated by patients and physicians.

From a psychological point of view, embarrassment caused by ectopic/accessory breast tissue could be compared with gynecomastia, a possible cause in itself of significant emotional distress and social impediments [29, 30]. The feeling of self-consciousness associated with overlying accessory areolas and nipples inhibits patients, preventing them from seeking appropriate medical consultation. For these reasons, a clinical diagnosis is frequently delayed [31], rendering successful treatment more challenging.

Some researchers consider the risk of malignant degeneration negligible. Others recommend that ectopic mammarian tissue must be included in screening procedures and preemptively excised. In the case of a supernumerary breast, it is possible to intervene on healthy tissue to prevent the possible emergence of any sign, symptom, or malignant degeneration. Performing the excision usually is preventive.

In contrast, the form of excision generally performed on aberrant breast tissue is curative because, as mentioned, it is hard to diagnose before pathologic effects are manifested. It should also be considered that although these effects actually would be manifesting, a patient may not detect a palpable mass and consequently apply to a physician [32].

Preventive excision carries major benefits and is thus highly recommendable. It reduces the overall glandular volume and the permanence of in situ ectopic breast tissue potentially susceptible to malignant degeneration, thus decreasing the effects of a potential mammarian carcinoma on both the duration and the quality of patients' lives.

In addition, timely treatment allows less invasive surgical intervention. When the disease is diagnosed in time, a simple, elliptical excision, including skin, can be performed under conditions of local anesthesia, reducing both the morbidity and the duration of the postoperation hospitalization, decreasing the psychological impact on the patient, and minimizing the economic impact.

Finally, from an aesthetic point of view, by selective removal of unpleasant tissue, preventive excision allows a more localized operation than a more invasive delayed intervention. In addition, excision of ectopic tissue generally is less disfiguring than a mutilating operation on an orthotopic breast and thus is less psychologically invasive.

Practitioners who routinely perform breast exams should include the research of ectopic breast tissue in both the anamnesis and the clinical exam, making their patients aware of potential risks associated with malignant degeneration of that type of entity and informing them over therapeutic management. Practicing wide excision of ectopic breast tissue, once discovered, will potentially reduce cosmetic and psychological concerns, serving moreover as a new weapon in the battle for breast cancer prevention.

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[5] Because of complexities specific to lymphatic drainage, clinical treatment of patients with tumors such as breast cancers involves lymphatic mapping with either vital dyes and direct vision at surgery or radiopharmaceuticals for scintigraphic mapping with a gamma camera and intraoperative identification of sentinel lymph nodes using a specially built probe [27, 28].

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