



Male breast cancer originating in an ectopic breast tissue in the umbilicus

A Case Report



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Nikolaos Kopanakis*, Olympia Tzaida**, Georgios Nikolaou*, Dimitrios Ermidis*, Vassiliki Manou*, Elias Efstathiou*, John Spiliotis*

Metaxa Cancer Hospital, Piraeus, Greece

*Department of Surgery

**Department of Pathology

Male breast cancer originating in an ectopic breast tissue in the umbilicus. A case report

INTRODUCTION: Accessory breast tissue is a rare finding in the general population with an incidence of 1-2%. Carcinomas of accessory breast tissue account for ~0.3% of breast cancers, 5% of which are arising within a supernumerary breast. They are usually diagnosed at a later stage compared with breast cancer, due to their rarity and low clinical suspicion.

CASE PRESENTATION: We present the case of a 58 years old male who was admitted to our hospital for an umbilical hernia, surgical repair. During surgery a small skin biopsy was excised and sent for pathological examination as routine procedure. The histological report revealed the presence of a poorly differentiated carcinoma. Immunochemical analysis confirmed adenocarcinoma of breast origin.

CONCLUSION: Carcinomas of accessory breast tissue are rare and therefore they are usually of advanced stage in time of diagnosis. Few cases have been reported in literature of accessory breast tissue carcinomas in men. To the best of our knowledge, this is the only case in the literature, of ectopic breast tissue cancer in the umbilicus.

KEY WORDS: Ectopic breast, Male breast cancer, Umbilicus

Introduction

Human mammary development begins with the emergence of a two- to four-cell layer ectodermal mammary streak located laterally on the embryonic trunk and extending from the axilla to the groin. Regression of

most of this streak occurs, whereas tissue in the pectoral region remains, forming the mammary ridge ¹. In about 1% - 2% of the general population, incomplete regression results in anomalous breast tissue, which may remain anywhere along the original mammary streak but most frequently in the axillary region ².

Ectopic breast tissue refers to supernumerary and aberrant breast tissue. The incidence ranges from 0.6% to 6.0% and is highest among Japanese newborns, compared with other racial/ethnic groups ³. 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 ⁴.

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Correspondence to: Nikolaos Kopanakis, Department of Surgery, Metaxa Cancer Hospital, Piraeus, Greece (e-mail: nikopanakis@gmail.com)

The second form of ectopic breast tissue, aberrant breast, consists of an isolated fragment of glandular tissue located beyond the periphery of orthotopic breasts. Usually found in the axilla but also parasternal, subclavicular, submammary, vulvar and anal cases have been reported⁶⁻⁸. Aberrant breast is characterized by an unorganized secretory system without any connection between the inside and the outside^{5, 6}.

Ectopic breast tissue may appear as anything from subcutaneous tissue similar in appearance to a small mole to that of a fully functioning breast. Both supernumerary and aberrant breast tissue may be overlooked due to their small size. Ectopic breast tissue is at risk for benign and malignant breast disease. The most frequently reported malignant disease is infiltrating ductal carcinoma (79%), followed by medullary and lobular carcinoma (9.5%)⁶.

Case presentation

In April 2015, a 58 year old Caucasian male was admitted to our clinic for an umbilical hernia mesh repair. During surgery, an excess of hernia sac with the overlying piece of skin (1,2X0,4cm) was excised and sent for pathological examination as routine procedure. Histopathology of the specimen revealed an unexpected primary breast cancer. In gross examination the skin biopsy presented a small lesion with maximum diameter of 0,5cm. Microscopically, dermis appeared infiltrated from a poorly differentiated carcinoma arranged in solid nests and cords (pic1). Epidermis was free of cancer invasion but the arrector pili muscles were infiltrated. Lymphatic tumor emboli and necrotic areas in the dermis were also described. Surgical margins were not involved.

Immunohistochemical analysis revealed that tumor cells were immunoreactive for CK7 (pic2), estrogen receptor (ER) and progesterone receptor (PR) as well as for, Mammaglobin (pic3) and GATA3(pic4). These findings were strongly suggestive of mammary origin. Mitotic index, demonstrated by MIB1, was high (70% of tumor cells). Several others specific immunomarkers, also included in the differential diagnoses, like PSA and TTF1 were negative.

Patient was offered then a second operation in order to achieve wider surgical margins. Histopathology confirmed that the supplementary excised tissues were free of cancer invasion and revealed a small aggregation of ectopic mammary gland that had remained at the periphery of the skin biopsy (pic5).

The diagnostic procedure was completed with breast ultrasound, abdominal and chest CT scan, gastroscopy and colonoscopy that were completely normal.

An appropriate adjuvant breast hormonotherapy and chemotherapy was planning. Ten months after diagnosis, our patient is free of any signs of the disease.

Discussion

The mammary gland develops from the ectodermal layer during embryogenesis. On the sixth week of gestation appears the milk line that extends from the axilla to the groin area⁷. This line normally disappears, except in the thoracic region, where the normal breasts will develop. However, breast tissues will develop in the ectopic area if the milk line remnants fail to regress during embryogenesis.

The incidence range of ectopic breast is 0.6% to 6.0% and is more common in the Far East⁸. It can be seen in both sexes. The most common location of ectopic breast is the axilla. Other less common locations are the face, thighs, perineum, groin, vulva, and shoulders^{7,9-11}. Ectopic breast tissue comes in two forms: supernumerary and aberrant. A supernumerary breast consists of a ductal system communicating with the overlying skin meanwhile aberrant breast is characterized by an unorganized secretory system without any connection between the inside and the outside^{5,6}. Ectopic mammary tissue, whether supernumerary or aberrant, may present characteristics analogous to orthotopic tissue in terms of function and, more importantly, pathologic degeneration. In a 1994 review of 82 cases of ectopic breast cancer, Marshall et al found an increased incidence of cancer in aberrant breast tissue but no increased incidence in cancer within supernumerary breasts⁶. Other studies have shown no such increased risk¹.

Carcinomas of accessory mammary tissue account for ~0.3% of all breast cancers, 5% of which are within a supernumerary breast⁶. 95% of ectopic breast cancers occur in aberrant breast tissue compared with just 5% in a supernumerary breast¹³. They present most commonly in the axilla and the most common histological type is infiltrating ductal carcinoma, 50–79%, with 9.5% medullary and lobular carcinomas⁶.

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.

Aberrant breast tissue is generally undetectable in the absence of pathologic signs, such as manual detection of a nodule. Early diagnosis of carcinoma in ectopic breast tissue requires early pathological diagnosis since the clinical diagnosis is unreliable¹². When a nipple-areolar complex is not present the mass may be misdiagnosed as a lipoma, lymph node, sebaceous cyst, or hidradenitis suppurativa¹⁴.

Male breast cancer is extremely rare compared with female breast cancer. Thus, the occurrence of male accessory breast cancer is extremely uncommon and to the best of our knowledge, no case of male umbilical accessory breast cancer has been reported.

Generally, accessory breast cancer must be pathologically demonstrated to be located adjacent to normal breast ducts or lobules that are not connected with the prop-

er mammary gland, and it is also necessary to exclude the possibility of a metastatic lesion from another primary cancer¹⁵. Metastatic carcinoma from the breast or other origins must be considered, as well as the diagnosis of a primary origin.

In our case, as the adenocarcinoma was poorly-differentiated, the morphological distinction was extremely difficult. We had firstly to determine whether the mass was a primary malignant neoplasm from the accessory dermal units that were, however, morphologically normal or a metastatic carcinoma from distant organs like the gastrointestinal tract, the lung or the prostate. These possible metastatic origins were all excluded by the use of appropriate immunohistochemical markers. The study was secondarily completed by extensive imaging. Positive reaction for mammaglobin, GATA3, ER and PR was strongly suggestive for a mammary origin.

Roorda et al¹⁶ reported that for the diagnosis of accessory breast carcinoma physical examination and pathological examination after needle aspiration and biopsy excision are useful tools in the same manner as normal breast carcinoma. Immunohistochemical analysis plays a very important role, completing the pathological examination.

Immunohistochemical markers, including the estrogen and progesterone receptors and CK7, are useful in the pathological diagnosis of mammary carcinoma.

Mammaglobin represent another significant immunomarker of breast cancer¹⁷. Lewis et al¹⁸ reported that mammaglobin is a more sensitive, but less specific, marker of breast cancer compared with GCDPF-15, as mammaglobin is not only expressed in breast carcinoma tissue but also in benign breast epithelium, while normal breast tissue does not express GCDPF-15^{17,18}. In our case the expression of GCDPF-15 was negative. GATA3 is a novel immunomarker for breast and urothelial cancer. It is a nuclear transcription factor that shows superior sensitivity to GCDPF-15 and mammaglobin with a strong association with ER α useful also as a predictor of response to hormonal therapy of breast cancer patients^{19,20}. This marker has also been demonstrated positive in our case. In addition the presence of ectopic mammary gland tissue in the specimen of the re-excision supported the suggestive diagnosis of breast carcinoma.

Interestingly, after establishing the diagnosis of umbilical accessory breast cancer in our patient, we were informed that a sister of him had also an aberrant breast gland, a finding not remarkable since that time, suggesting a familial predisposition for ectopic breast tissue of the presented case.

Conclusion

To the best of our knowledge this is the first case of accessory breast carcinoma located in the umbilicus.

Immunohistochemistry was necessary in order to complete the diagnosis. Treatment was surgical excision in the same manner as common breast cancer followed by adjuvant hormone therapy plus chemotherapy. Misdiagnosis or late diagnosis of that cases is often due to the unusual presentation. Awareness of the possibility for development of breast carcinoma in this rare ectopic site is crucial for the patient management and disease outcome.

Riassunto

La sede ectopica di tessuto ghiandolare mammario è un'eventualità rara, con un'incidenza del 1-2% nella popolazione generale. I carcinomi insorti in questi tessuti mammari accessori rappresentano circa il 0,3% di tutti i cancri della mammella, 5% dei quali insorti su mammelle soprannumerarie. La loro diagnosi avviene in fase più avanzata che nel caso dei correnti cancri della mammella in relazione alla loro rarità ed al basso livello di sospetto clinico.

Qui è presentato il caso di un uomo di 58 anni ricoverato nel nostro ospedale per la riparazione chirurgica di un'ernia ombelicale. Durante l'intervento venne eseguita una piccola biopsia cutanea per esame istologico quale procedura usuale. Il referto istologico ha rivelato la presenza di un carcinoma scarsamente differenziato, che all'analisi immunoistochimica si è dimostrato essere un adenocarcinoma di origine mammaria.

Si conferma la rarità dei carcinomi insorti su tessuto ghiandolare mammario accessorio, che sono per lo più in fase avanzata al momento della diagnosi. Pochi di questi casi sono riportati in letteratura in relazione a tessuto mammario accessorio nel sesso maschile, ed a nostra conoscenza questo è l'unico in letteratura di tessuto mammario carcinomatoso a sede ectopica nell'ombelico.

References

1. Lesavoy M, Gomez-Garcia A, Nejdil R, Yosipuri G, Syiau T-J, Chang P: *Axillary breast tissue: Clinical presentation and surgical breast treatment*. Ann Plast Surg, 1995; 35:356-60.
2. Marshall M, Moynihan J, Frost A, Evans R: *Ectopic breast cancer. Case report and literature review*. Surg Oncol, 1994; 3:295-304.
3. Bakker JR, Sataloff DM, Haupt HM: *Breast cancer presenting in aberrant axillary breast tissue*. Commun Oncol, 2005; 2:117-22.
4. Nakao A, Saito S: *Ectopic breast cancer: a case report and review of the Japanese literature*. Anticancer Res, 1998; 18:3737-740.
5. Chan N, Penswick J: *Ectopic breast tissue presenting as an anal polyp*. Can J Surg, 2007; 50:E23-E24.
6. Marshall M, Moynihan J: *Ectopic breast cancer: A case report and literature review*. Surg Oncol, 1994; 3:295-304.
7. Pathak S, Preston J: *A rare case of multiple accessory breast tissue in the axillae, lower abdomen and vulval areas*. J Obstet Gynaecol, 2007; 27: 531-33.

8. Schmidt H: *Supernumerary nipples: Prevalence, size, sex and side predilection. A prospective clinical study.* Eur J Pediatr, 1998; 157: 821-23.
9. Koltuksuz U, Aydin E: *Supernumerary breast tissue: A case of pseudomamma on the face.* J Pediatr Surg, 1997; 32: 1377-378.
10. Camisa C: *Accessory breast on the posterior thigh of a man.* J Am Acad Dermatol, 1980; 3: 467-69.
11. Basu S, Bag T, Saha KS, et al.: *Accessory breast in the perineum.* Trop Doct, 2003; 33: 245.
12. Evans D, Guyton D: *Carcinoma of the axillary breast.* J Surg Oncol, 1995; 59:190-95.
13. Madej B, Winkler I, Burdan F: *Cancer of the accessory breast-A case report.* Adv Med Sci, 2009; 54:308-10.
14. Giron G, Friedamn I, Feldman S: *Lobular carcinoma in ectopic axillary breast tissue.* Am Surgeon, 2004; 70:312-15.
15. Yerra L, Karnad AB, Votaw ML: *Primary breast cancer in aberrant breast tissue in the axilla.* Southern Medical Journal, 1997; 90, 6:661-62.
16. Roorda AK, Hansen JP, Rider JA, et al.: *Ectopic breast cancer: special treatment considerations in the postmenopausal patient.* Breast J, 2002; 8: 286-89.
17. Xie Y1, Huang J, Xiao D, Zhong M: *Male breast cancer arising in ectopic axillary breast tissue: A diagnostic dilemma.* Oncol Lett, 2013; 5(6):1931-934. Epub 2013 Apr 11.
18. Lewis GH, Subhawong AP, Nassar H, et al.: *Relationship between molecular subtype of invasive breast carcinoma and expression of gross cystic disease fluid protein 15 and mammaglobin.* Am J Clin Pathol, 2011; 135: 587-91.
19. Asch-Kendrick R, Cimino-Mathews A: *The role of GATA3 in breast carcinomas: A review.* Hum Pathol, 2016; 48:37-47.
20. Gown AM, Fulton RS, Kandalaft PL: *Markers of metastatic carcinoma of breast origin.* Histopathology, 2016; 68(1):86-95.

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