https://doi.org/10.46982/gjmt.2020.106

GJMT Global Journal of Medical Therapeutics

Open Access Case Report

A Rare Case of Ductal Carcinoma in Situ in Ectopic Breast Tissue in the Vulva: A Case Report

Ashraf Farrag[1,2]*, Waleed Jafar[1], Osman Ahmed[3], Taleb Buhlaiaqh[1], Jawaher Ansari[4]

How to cite this article: Farrag A, Jafar W, Ahmed O, Buhlaiaqh T, Ansari J. A rare case of Ductal carcinoma in situ in ectopic breast tissue in the vulva: A case report. Glob J Med Therap. 2020;2(3):7-10. https://doi.org/10.46982/gjmt.2020.106

Abstract-- Ectopic breast tissue can be found along the rudimentary mammary line, which extends from the axilla to the inguinal region and disappears during the process of embryogenesis. Like normal breast tissue, this ectopic tissue is prone for malignant transformation. Most of the reported cases were invasive ductal or lobular carcinomas however, only 2 cases of ductal carcinoma in situ (DCIS) in ectopic breast tissue have been reported so far. Diagnosis and management of this rare pathological finding can be challenging. Here we report an interesting case of a 53-year lady with DCIS arising from ectopic breast tissue in the left vulva. The patient was diagnosed after surgical excision of a long standing painless left vulvar lesion. Only postoperative hormonal treatment in the form of tamoxifen was given without any evidence of disease recurrence after 3 years of follow up. We discuss the challenges faced during diagnosis and outline management options for this disease entity.

Keywords: Ectopic breast cancer, Ductal carcinoma in-situ, Vulvar Cancer

INTRODUCTION

Primary vulvar cancer is uncommon, accounting for only 2–5% of gynecologic malignancies. More than 80% of vulvar cancers are squamous cell carcinomas, with the remaining percentage comprising adenocarcinomas, basal cell carcinomas, melanomas and sarcomas [1]. Greene and colleagues first reported a case of infiltrating ductal carcinoma arising from ectopic breast tissue in the vulva [2]. Ectopic breast tissue can be found anywhere along the primitive embryonic milk lines that extends from the axilla to the inguinal region [3]. To date, there have been about 30 reported cases in English literature of primary ectopic breast cancer in the vulva. The ductal type was the most commonly reported histologic subtype (42%), followed by adenocarcinoma (35%), mucinous (10%) and lobular (7%) [4]. However, there have been only 2 reported cases of DCIS arising from ectopic breast tissue in the vulva [5, 6]. Herein we report an interesting and rare case of DCIS in ectopic breast tissue in the vulva and discuss the differential diagnosis and management challenges.

CASE PRESENTATION

A 53-year-old female presented with a two-year history of lump over the inner aspect of left labia. The lesion was reddish-brown in color, measured 2 x 2 cm and was associated with vulvar discomfort. The patient's past medical history included type 2 diabetes mellitus for which she was taking metformin regularly. She was para 7+0 and pre-menopausal. Her Eastern Cooperative Oncology Group (ECOG) performance status was 0. General examination was unremarkable with no palpable abnormal masses or lymph nodes, including both breasts and axillae. She underwent excision biopsy of the vulvar lesion. Histopathology revealed a lesion with irregular borders and irregular aggregates of epithelial cells. Cytological assessment showed the lesion to be well-differentiated, lacking nuclear pleomorphism or mitotic figures. Differential diagnosis for this lesion included microcystic adnexal carcinoma, either syringomatous carcinoma or sclerosing sweat duct carcinoma. Further assessment revealed the presence of ectopic mammary tissue in the vulva with fibrocystic changes including adenosis and cysts. Adjacent to the benign ectopic breast tissue, ducts were expanded by malignant cells with apocrine features suggestive of ductal carcinoma in situ (DCIS). There was no evidence of invasive ductal carcinoma. Immunohistochemistry (IHC) revealed diffuse positivity for cytokeratin 7 (CK7), Gross cystic disease fluid protein 15 (GCDFP-15), carcinoembryonic antigen (CEA), mammaglobin and for estrogen receptor (ER) in 10% of cells. IHC showed negative staining for S100, CK 5/6, progesterone receptor and Human epidermal growth factor receptor-2 (HER-2). The panel of myoepithelial markers (P63, smooth muscle myosin heavy chain (SMMHC), Calponin and CK14) were positive; confirming the in-situ behavior of this lesion. Margin was focally positive for DCIS but orientation of the specimen was not possible to determine the exact location (figure 1).

[1] Department of Oncology, Prince Sultan Military Medical City, Riyadh, PO. Box 7897 Riyadh 11159, Kingdom of Saudi Arabia
[2] Clinical Oncology Department, Assiut University, Egypt
[3] Department of Pathology, Prince Sultan Military Medical City, Riyadh, PO. Box 7897 Riyadh 11159, Kingdom of Saudi Arabia
[4] Department of Oncology, Tawam Hospital, Al Ain, PO. Box 15258. Al Ain, United Arab Emirates
***Corresponding Author:** Ashraf Farrag, MD, PhD.
Email address: drashraffarrag@yahoo.com
Received: 17 July 2020
Accepted: 24 August 2020
Published: 15 September 2020

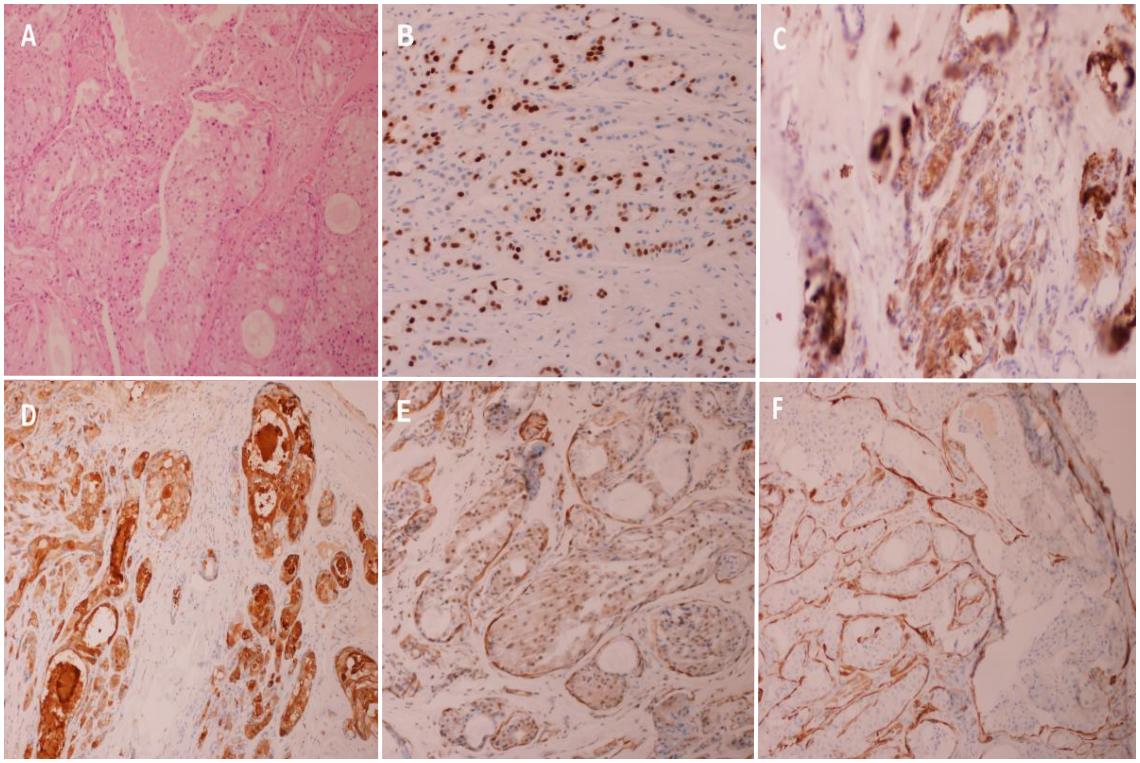

Figure 1. (A) Hematoxylin and Eosin (H&E) stained slide showing the ductal carcinoma in situ (magnification, x10). **(B)** Immunohistochemistry (IHC) staining showing positive reaction to estrogen receptor (ER), **(C)** mammaglobin, **(D)** gross cystic disease fluid protein 15 (GCDFP-15) and myoepithelial marker; **(E)** calponin and **(F)** CK14.

Magnetic resonance imaging (MRI) scan of the pelvis did not reveal any residual abnormality in the vulva. Fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) showed no detectable metabolically active lesion to suggest either residual or metastatic disease. Bilateral breast mammography and ultrasound showed no evidence of microcalcifications, suspicious lesions or any architectural distortion.

The case was discussed in our gynecology multidisciplinary meeting and it was decided to arrange for further re-excision as the initial surgical procedure was excision biopsy and there was suspicion of a focal positive margin. However, on clinical review it was felt that in the absence of clinically visible residual lesion in the vulva, re-excision is unlikely to add any additional benefit.

She was offered adjuvant radiotherapy to the vulva to minimize risk of disease recurrence similar to DCIS of breast cancer. However, after a discussion of the benefits and risks of pelvic radiotherapy the patient declined this. Extrapolating from the breast DCIS studies she was commenced on tamoxifen 20 mg once daily after discussing the potential side effects.

After 3 years of diagnosis, she remains on adjuvant tamoxifen with no clinical or radiological evidence of disease recurrence either in the vulva or breast. She remains on regular follow-up with the gynecologists for clinical assessments along with annual mammographic evaluation.

DISCUSSION

Traditionally, vulvar adenocarcinoma of mammary-like glands was considered to originate from the remnant of the embryonic milk line which extends from the axilla to the inguinal region. This remnant tissue can be prone to all physiological and pathological changes of normal breast tissue including malignant transformation. However, another theory suggested that the origin of this mammary-like tissue came from distinctive variant of anogenital skin glands which have eccrine and apocrine features makes them the most likely source of a series of lesions occurring in the anogenital region including invasive vulvar adenocarcinoma [7]. Currently, neither of these theories is universally accepted and the histogenesis of these tumors remains controversial [8].

Histological diagnosis of primary breast carcinoma of the vulva usually based on a combination of morphological and IHC criteria. A morphology consistent with breast carcinoma and the presence of non-neoplastic breast tissue or carcinoma in situ component are characteristic findings. IHC criteria comprise positive estrogen and/or progesterone receptor expression in addition to common breast cancer–associated markers including CEA, CK7, and mammaglobin [9]. Moreover, it is necessary to exclude metastases from primary breast carcinoma or adenocarcinoma arising from other organs [10].

The above criteria were applied to our case as histopathological assessment showed morphological features of DCIS of the breast and normal breast-like tissue was detected around the DCIS elements. The tumor tissue was

positive for ER, CK7, CEA and Mammaglobin by IHC. Radiological evaluation including bilateral mammography and PET/CT were negative for another primary breast cancer or any systemic disease dissemination.

The above findings collectively confirmed the diagnosis of DCIS in ectopic breast tissue in vulva in our case. The site of the lesion in our case was at the left vulva just lateral to the clitoris in keeping with the normal position of the milk line and consistent with the site of most cases of adenocarcinoma arising in ectopic mammary tissue.

Due to its rarity, DCIS or invasive carcinoma in the ectopic breast tissue of the vulva have no specific treatment guidelines. Most of the reported cases were treated according the guidelines for primary breast cancer based on the tumor stage and biological subtype.

In the previously reported two cases of ectopic mammary DCIS in the vulva [5, 6], the authors reported free surgical margins. In the case reported by Castro et al [5], the patient had a surgical re-excision to obtain free margins. No postoperative treatment was offered in both cases. In our case we had a slightly different approach where our patient had a focally positive margin and didn't go for surgery again. Also, we preferred to keep her on postoperative hormonal treatment based on positive hormonal receptors status.

It is recommended for patients with pure DCIS in breast to obtain a free resection margin of at least 2 mm, which was found to be associated with a reduced risk of ipsilateral breast tumor recurrence [11, 12]. However, some studies suggested that re-excision can be omitted in patients with focally positive resection margins [13]. The National Comprehensive Cancer Network (NCCN) guidelines recommend that in cases of minimal or focal DCIS involvement near the margin, clinical judgment is suggested to determine if re-excision might be avoided in individual cases [11]. In our case the margin was found to be focally positive but in the absence of clinically or radiologically visible lesion it was felt that re-excision could lead to considerable morbidity with disfigurement and sexual dysfunction and therefore avoided.

In our case, surgery was followed by tamoxifen according to the guidelines for treatment of primary DCIS of the breast. Both the NCCN and European Society of Medical Oncology (ESMO) guidelines recommend adjuvant hormonal treatment for ER positive DCIS of the breast [11, 14]. The use of Tamoxifen decreased the risk of invasive and non-invasive recurrences and reduces the incidence of contralateral breast cancer without a positive impact on survival [15]. In patients who didn't receive post-operative radiotherapy, Tamoxifen was found to be more effective in reduction of both ipsilateral and contralateral breast events [16].

The benefit of adjuvant radiotherapy for breast DCIS was shown in a 2009 meta-analysis in which radiotherapy resulted in a reduction in the risk of all ipsilateral breast events (pooled Hazard Ratio [HR] 0.49, 95% CI 0.41-0.58) [17]. The National Surgical Breast and Bowel Project (NSABP) B-17 trial compared with breast DCIS excision alone or with radiotherapy and demonstrated a lower rate of ipsilateral invasive breast cancer recurrence (8.9 versus 19.4 %), but similar overall survival (83 versus 84%) and cumulative all-cause mortality rate through 15 years (HR for death 1.08, 95% CI 0.79-1.48, 17.1 versus 15.8%) [18]. Sometimes, omitting post-operative radiotherapy (PORT) in low risk groups is a reasonable choice to avoid overtreatment and its toxicity. Sagara et al, in their retrospective study found that the survival benefit of PORT was observed only in patients with higher nuclear grade, younger age, and larger tumor size. It was suggesting that decisions for RT could be tailored on the basis of patient factors, tumor biology, and the prognostic score [19]. In contrast to breast radiotherapy, radiation to the vulva has significant early and late side effects which can considerably affect quality of life with sexual dysfunction.

Due to the possible side effects of radiotherapy and given the low likelihood of disease recurrence, the patient opted for adjuvant hormonal treatment only after surgery.

Conclusion

Although DCIS/invasive cancer of ectopic breast tissue in the vulva is a very rare clinical entity, it should be considered one of the differential diagnosis of abnormal vulvar swellings due to its specific management approach. The diagnosis is usually challenging and a high index of suspicion is required to demonstrate the combination of histological appearances and IHC findings required for the demonstration of the ectopic breast tissue together with the presence of DCIS/invasive cancer. Exclusion of synchronous primary breast cancer or other malignancies is essential to rule out metastatic disease in the vulva. Clinical trials to determine optimum treatment are not possible owing to the rarity of this condition. We recommend that treatment of similar conditions should be extrapolated from the breast DCIS/invasive cancer guidelines, in addition to the shared experience from small case series and case reports, which emphasize the importance of reporting of such cases.

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions: AF and JA contributed to the conception and design. OA prepared and commented on the pathological slides. AF, JA, TB, WJ and OA wrote and reviewed the manuscript. AF and JA supervised the case report. All authors read and approved the final manuscript.

Funding: No funding was obtained for the preparation or publication of this article.

References

1. Rogers LJ, Cuello MA. Cancer of the vulva. Int J Gynaecol Obstet. 2018; 43:4-13. https://doi.org/10.1002/ijgo.12609
2. Greene HJ. Adenocarcinoma of supernumerary breast of the labia majora in a case of epidermoid carcinoma of the vulva. Am J Obstet Gynecol 1936; 31: 660-663.
3. Prendergast PM. Anatomy of the Breast. In: Shiffman M and Di Giuseppe A, ed. Cosmetic Surgery. Berlin, Heidelberg: Springer; 2013: 47-55.
4. Matak L, Dukić B, Tupek T, Lisica-Šikić N, Mikuš M. Primary ectopic lobular breast cancer of the vulva: case report and

review of literature. J Obstet Gynaecol. 2020;40(5):727-730. doi:10.1080/01443615.2019.1623182
5. Castro CY, Deavers M. Ductal carcinoma in-situ arising in mammary-like glands of the vulva. Int J Gynecol Pathol. 2001;20(3):277-283. doi:10.1097/00004347-200107000-00012
6. Pelosi G, Martignoni G, Bonetti F. Intraductal carcinoma of mammary-type apocrine epithelium arising within a papillary hydradenoma of the vulva. Report of a case and review of the literature. Arch Pathol Lab Med. 1991;115(12):1249-1254.
7. van der Putte SC. Mammary-like glands of the vulva and their disorders. Int J Gynecol Pathol. 1994;13(2):150-160. doi:10.1097/00004347-199404000-00009
8. Benito V, Arribas S, Martínez D, Medina N, Lubrano A, Arencibia O. Metastatic adenocarcinoma of mammary-like glands of the vulva successfully treated with surgery and hormonal therapy. J Obstet Gynaecol Res. 2013;39(1):450-454. doi:10.1111/j.1447-0756.2012.01937.x
9. Lamb A, Darus CJ, Skripenova S, Weisberg T, Miesfeldt S. Association of primary breast cancer of the vulva with hereditary breast and ovarian cancer. J Clin Oncol. 2013;31(13):e231-e232. doi:10.1200/JCO.2012.45.5972
10. Ishigaki T, Toriumi Y, Nosaka R, et al. Primary ectopic breast cancer of the vulva, treated with local excision of the vulva and sentinel lymph node biopsy: a case report. Surg Case Rep. 2017;3(1):69. doi:10.1186/s40792-017-0343-x
11. National Comprehensive Cancer Network. Breast Cancer (Version 3.2020). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Accessed March 24, 2020.
12. Kuerer HM, Smith BD, Chavez-MacGregor M, et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. J Cancer. 2017;8(14):2653-2662. Published 2017 Aug 22. doi:10.7150/jca.20871
13. Olson TP, Harter J, Muñoz A, Mahvi DM, Breslin T. Frozen section analysis for intraoperative margin assessment during breast-conserving surgery results in low rates of re-excision and local recurrence. Ann Surg Oncol. 2007;14(10):2953-2960. doi:10.1245/s10434-007-9437-1
14. Cardoso F, Kyriakides S, Ohno S, et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30(8):1194-1220. doi:10.1093/annonc/mdz173
15. Staley H, McCallum I, Bruce J. Postoperative Tamoxifen for ductal carcinoma in situ: Cochrane systematic review and meta-analysis. Breast. 2014;23(5):546-551. doi:10.1016/j.breast.2014.06.015
16. Cuzick J, Sestak I, Pinder SE, et al. Effect of tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK/ANZ DCIS trial. Lancet Oncol. 2011;12(1):21-29. doi:10.1016/S1470-2045(10)70266-7
17. Goodwin A, Parker S, Ghersi D, Wilcken N. Post-operative radiotherapy for ductal carcinoma in situ of the breast--a systematic review of the randomised trials. Breast. 2009;18(3):143-149. doi:10.1016/j.breast.2009.04.003
18. Wapnir IL, Dignam JJ, Fisher B, et al. Long-term outcomes of invasive ipsilateral breast tumor recurrences after lumpectomy in NSABP B-17 and B-24 randomized clinical trials for DCIS. J Natl Cancer Inst. 2011;103(6):478-488. doi:10.1093/jnci/djr027
19. Sagara Y, Freedman RA, Vaz-Luis I, et al. Patient Prognostic Score and Associations With Survival Improvement Offered by Radiotherapy After Breast-Conserving Surgery for Ductal Carcinoma In Situ: A Population-Based Longitudinal Cohort Study. J Clin Oncol. 2016;34(11):1190-1196. doi:10.1200/JCO.2015.65.1869.