Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Septic disruption of lactiferous ducts with heterogeneous carcinoma of the breast in a lactating woman

Mohammed Naim,¹ Vanesa T John,¹ Kavita Gaur,¹ Afzal Anees²

¹ Department of Pathology, JNMC AMU Aligarh, Aligarh, India

² Department of Surgery, JNMC AMU Aligarh, Aligarh, India

Correspondence to Mohammed Naim, profmnaim@gmail.com

Summary

This report documents the diagnostic histopathological features of heterogeneous breast carcinoma following sepsis and disruption of the lactiferous ducts in a lactating woman and discusses the pathogenesis. Sections from the nipple revealed disrupted collecting lactiferous ducts presenting with intraduct precarcinoma and carcinoma of the epidermoid type, and attached reparative sprouts lined by lactiferous cells. Breast lobules showed generalised benign adenotic change with various foci of carcinoma microscopically identifiable as intraduct primitive lactiferal ectodermal carcinoma, lactating carcinoma, primitive neuroendocrine carcinoma and myoepithelioid granulomatous carcinoma. The findings led to the conclusion that the lactiferous ducts are susceptible to sepsis and disruption, which may predispose a patient to breast carcinoma. The pattern of carcinoma suggested that lactiferous epithelial cells behaved colonially, with different metaplastic changes, precarcinoma and carcinoma.

BACKGROUND

Normal breast ducts contain at least three types of epithelial cells: luminal, basal/myoepithelial and stem cells,¹ ontogenically evolved from the glycogen-rich polygonal cells of primitive lactiferal ectoderm (PLE) of placode and mammary bud.² Myoepithelial cells in the ducts are spindle shaped and oriented parallel to the long axis in a continuous layer, while in acini these cells are stellate shaped and arranged in loose-basket network around the luminal cell layer.³ Stem cells are indistinct except in the terminal buds⁴ and are responsible for a high incidence of benign lobular adenotic neoplasms and breast cancers.⁵

The diagnosis of breast cancer can be complicated by tumour heterogeneity.⁶ This report documents the diagnostic histopathological features of heterogeneous breast carcinoma following septic disruption of the lactiferous ducts in a lactating woman, and discusses the pathogenesis.

CASE PRESENTATION

A 25-year-old lactating multigravida woman presented with a history of an itching papule on her right nipple during the third month of breast feeding, tender swelling of the nipple with fever, aspiration of pus under local practitioner's prescription, discharge from the aspiration site for the next 3 days, healing, feed rejection, stiffness in the affected breast and a palpable lump by the fifth month of the disease. Preoperative diagnosis by fine needle aspiration (FNA) biopsy was suggestive of malignancy. Excised breast tissue with an axillary lymph node of 1 cm size was submitted for histopathological diagnosis.

Images (figure 1) show the breast measuring 6 cm in diameter with puckering of the areola and nipple (A), the cut surface showing a whitish friable tumorous mass with irregular patches of brown discolouration (B), the section

from nipple displaying disrupted lactiferous ducts in the strata under cutaneous glands (C, D), the proximal segments of disrupted ducts transformed into epidermoid cysts (E, F, G), occasionally retaining openings on the skin surface plugged by keratin, and distally extending into a tortuous branching/terminating sprout lined by lactiferous cells (E, F), distal disrupted segment(s) presenting proximally as an extending reparative lactiferous sprout and the parent duct having intraduct epidermoid carcinoma (H, I) or epidermoid metaplasia (J) and apocrine change (K).

Sections from the tumour beyond the nipple (figure 2) displayed a widespread benign lobular adenotic neoplasm comprising of periodic acid–Schiff (PAS) stain-positive lactating acini (A) and non-secretory acini showing apocrine change with desquamation (B), foci of intraduct (C) and intraductular (D) carcinoma comprised of large polygonal PAS-positive cells morphologically similar to the PLE cells,² minute foci of apocrine change and desquamation in the intraduct carcinoma producing irregular or cribriform luminal spaces (E), argyrophillic fibrils radially arranged at the intraduct carcinoma periphery or forming patches in the central area (E, F), foci of lobular lactating carcinoma with abundant PAS-positive secretion and cuboid columnar secretory cells (G, H), foci of comedo lined by very small carcinoma cells of neurocrine appearance (I) and lobular carcinoma having PAS-negative argyrophillic cuboid columnar papillary component identified as primitive neuroendocrine carcinoma (PNEC) or (J, K), axillary lymph node with metastasis of lactating carcinoma (L).

Sections from the brown patchy areas (figure 2) showed lobular carcinoma presenting polygonal cells intermingled with myoepithelioid and tumour giant cells (M, N, O, P) qualifying the lesion as myoepithelioid granulomatous or giant cell carcinoma. A cytospin verified differentiation of

Figure 1 Images from the surface and cut surface of the breast and sections of nipple 175×125 mm (300 DPI).

Figure 2 Images from sections of the tumour beyond the nipple 175×125 mm (300 DPI).

myoepithelioid/histioid cells among the polygonal carcinoma cells (Q). The myoepithelial carcinoma component presented with productive fibrosis (R). At the lobular periphery polygonal carcinoma cells were seen transforming into exfoliating stellate myoepithelial cells with giant cell variants and fibrous cells, reducing the lobular neoplasm into islands without basement membrane amid the expanding pool of derivative myoepithelioid granulomatous carci-

noma (S, T). Collecting ducts with intraduct carcinomas identifiable in lobular areas also displayed transformation of polygonal carcinoma cells to myoepithelioid cells (U), which lacked longitudinal orientation³ and were arranged circumferential to the long axis of duct, displayed hyperchromatic fused binucleate (chromosome shaped) or stellate pleomorphic nuclei and exfoliated forming a myoepithelioid granulomatous carcinoma component (V, W), at

places presenting as sclerosing nodules around the intraduct carcinoma (X).

OUTCOME AND FOLLOW-UP

Outcome and follow-up will be reported separately.

DISCUSSION

The lactiferous sprouts in this case were diagnostic of disruption and failed reunion of lactiferous ducts with consequent epidermoid precarcinoma and carcinoma of the disrupted duct segments. Milk stagnation under stress of lactation stimuli could be responsible for signalling the lactiferous epithelium to reacquire non-secretory or ontogenic character² and carcinogenesis. Collecting ducts in the nipple developed precarcinomas and carcinomas of the epidermoid type, while the reparative sprouts in the nipple and continuing ducts and ductules in lobules presented with lactiferous lining with adenotic change and foci of lactiferous primitive ectodermal carcinoma, primitive neuroendocrine carcinoma, myoepithelioid granulomatous carcinoma and metastasising lactating carcinoma; findings that cannot be explained by single cancer stem cell and clonal selection hypothesis.⁷ Duct segment-wise variations in metaplasia, precarcinoma and carcinoma in the form of primitive, metaplastic primitive or differentiated types, in the present case, may suggest that under an altered bioenvironment epithelial cells of various ductal and canalicular segments behaved as different symbiotic colonies, undergoing varied adaptive changes, thereby presenting as heterogeneous metaplasia, precarcinoma and carcinoma of the breast. The epidermoid response of the mature collecting duct epithelium could be due to deficient stem cells and predominant basal cell component. One experimental study has shown dissection of the mammary bud stalk followed by epidermal fate of the lactiferous epithelium.⁸ Intraduct in situ squamous cell carcinoma has also been reported in the literature in one case.⁹

Lobular adenotic neoplasm (LAN), a known precancerous state,⁵ showed foci of lobular intraduct carcinoma comprising of PAS-positive polygonal cells morphologically similar to the PLE cells of the mammary bud,² with expression of argyrophillic filaments and lumina formation by apocrine change, pathognomonic of primitive lactiferous ectodermal carcinoma (PLEC), that displayed areas of metaplastic PNEC and differentiation into lactating carcinoma (LC) and myoepithelial granulomatous carcinoma (MGC). These features differentiate PLEC and derivatives from other stem cell cancers. Myoepithelial cells with pleomorphic hyperchromatic nuclei, a disoriented loose arrangement and tumour giant cells differentiate the myoepithelial

granulomatous component of the carcinoma from other granulomatous diseases of the breast such as tuberculosis and sarcoidosis. Myoepithelial tumours¹⁰ and primitive neuroectodermal tumour (PNET)¹¹ have been reported in the breast, but heterogeneous carcinoma comprising PLEC, PNEC, LC, MGC and epidermoid carcinoma with respective variant precarcinomas and metaplasias as observed in our case have not been documented in the literature to date.

Learning points

- ▶ Lactiferous ducts are susceptible to sepsis and disruption.
- ▶ Duct disruption with improper repair may give rise to metaplasia, dysplasia and subsequent malignant events.
- ▶ The pattern of different precarcinoma and carcinoma evolving in different segments of the duct tree, as in this case, may be suggestive of colonial behaviour of lactiferous epithelial cells, so that different segments/colonies undergo different metaplastic changes, contributing to heterogeneity.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Livasy CA**, Karaca G, Nanda R, *et al*. Phenotypic evaluation of the basal-like subtype of invasive breast carcinoma. *Mod Pathol* 2006;**19**:264–71.
2. **Kellokumpu-Lehtinen P**, Johansson RM, Pelliniemi LJ. Ultrastructure of human fetal mammary gland. *Anat Rec* 1987;**218**:66–72.
3. **Adrian MC**, Inman JL, Petersen OW, *et al*. Myoepithelial cells: good fences make good neighbors. *Breast Cancer Res* 2005;**7**:190–7.
4. **Anbazhagan R**, Osin PP, Bartkova J, *et al*. The development of epithelial phenotypes in the human fetal and infant breast. *J Pathol* 1998;**184**:197–206.
5. **Celis JE**, Moreira JM, Gromova I, *et al*. Characterization of breast precancerous lesions and myoepithelial hyperplasia in sclerosing adenosis with apocrine metaplasia. *Mol Oncol* 2007;**1**:97–119.
6. **Polyak K**. Breast cancer: origins and evolution. *J Clin Invest* 2007;**117**:3155–63.
7. **Melchor L**, Benítez J. An integrative hypothesis about the origin and development of sporadic and familial breast cancer subtypes. *Carcinogenesis* 2008;**29**:1475–82.
8. **Hens JR**, Wysolmerski JJ. Key stages of mammary gland development: molecular mechanisms involved in the formation of the embryonic mammary gland. *Breast Cancer Res* 2005;**7**:220–4.
9. **Hayes MM**, Peterse JL, Yavuz E, *et al*. Squamous cell carcinoma in situ of the breast: a light microscopic and immunohistochemical study of a previously undescribed lesion. *Am J Surg Pathol* 2007;**31**:1414–9.
10. **Al-Nafussi A**. Spindle cell tumours of the breast: practical approach to diagnosis. *Histopathology* 1999;**35**:1–13.
11. **Golshan M**, Kuten A, William J, *et al*. Metaplastic carcinoma of the breast with neuroglial differentiation. *Breast* 2006;**15**:545–9.

This pdf has been created automatically from the final edited text and images.

Copyright 2010 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Mohammed N, John VT, Gaur K, Anees A. Septic disruption of lactiferous ducts with heterogeneous carcinoma of the breast in a lactating woman. *BMJ Case Reports* 2010;10.1136/bcr.02.2010.2754, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow