CASE REPORT

Invasive papillary breast cancer with Paget's disease: first reported association and literature review

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Accepted 20 December 2017

SUMMARY

Invasive papillary carcinoma of the breast and Paget's disease are both rare entities. We report the first known case of invasive papillary carcinoma associated with Paget's disease in a woman who presented clinically with a nipple mass. While invasive papillary carcinoma has been reported to have an indolent course without need for overtreatment, our patient had unusual unfavourable histological features. Literature review of this rare subtype was performed.

BACKGROUND

Invasive papillary cancer and Paget's disease are both rare entities, accounting for less than 1% and 0.5%–5% of all newly diagnosed breast cancers, respectively.^{1,2} Paget's disease had been reported to be associated with an underlying cancer in >90% of cases.² However, it had not been reported in association with invasive papillary carcinoma. Invasive papillary carcinoma tends to be slow-growing and has favourable histological features.³ We report the first known association of invasive papillary carcinoma with Paget's disease, presenting with unusual aggressive features.

CASE PRESENTATION

A 52-year-old woman presented with a right nipple lump of 3 months' duration. On examination her right nipple was ulcerated with a retroareolar mass (figure 1).

INVESTIGATIONS

Mammogram (figure 2) revealed an enlarged right nipple with a retroareolar mass. Ultrasound showed

Figure 2 Right craniocaudal and mediolateral oblique mammograms demonstrating retroareolar mass with an enlarged nipple (arrow).

this suspicious mass to be 2.5 cm, infiltrating and replacing the nipple (figure 3) with two right axillary indeterminate lymph nodes. An MRI found an additional indeterminate lesion in the ipsilateral upper inner quadrant (UIQ) of the breast.

The patient underwent a right nipple punch biopsy, which revealed papillary carcinoma with Paget's disease. Right axillary node biopsy showed isolated tumour cells.

Her staging scans revealed no distant metastasis.

TREATMENT

The patient underwent a right mastectomy and axillary clearance. Final histopathology revealed a 25 mm grade III invasive papillary carcinoma (figure 4) associated with 20 mm of high-grade ductal carcinoma in situ (DCIS) and Paget's disease. The tumour was oestrogen receptor (ER)-negative and progesterone receptor (PR)-negative. Human epidermal growth factor receptor 2 (HER2) was positive. P63 was negative. Lymphovascular invasion (LVI) was present. One of 10 lymph nodes showed micrometastasis.

OUTCOME AND FOLLOW-UP

Postoperatively, the patient was discharged after an overnight hospital stay. She recovered well and underwent chemotherapy (doxorubicin, cyclophosphamide and docetaxel) with immunotherapy (trastuzumab) and radiotherapy. She is currently 6 months post operation.

DISCUSSION

Invasive papillary carcinoma is an extremely rare subtype. It typically presents with bloody nipple discharge, breast lump or radiographic abnormalities.⁴ Presenting with an ulcerated nipple mass,

Figure 1 Ulcerated right nipple with retroareolar mass.

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To cite: Lim GH, Chinthala JP, Gudi MA. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222817

Figure 3 Right ultrasound showing a suspicious retroareolar mass infiltrating and replacing the nipple. Region of interest; ROI

as in our patient, was unknown of in patients with invasive papillary cancer. This unusual presentation could, however, be secondary to associated Paget's disease. While it is not apparent if the Paget's disease in our case was related to the DCIS or invasive papillary cancer, Paget's disease with DCIS or most reported sparse cases of invasive papillary cancer would not have such aggressive features, as demonstrated in our patient.

Mammogram and ultrasound were the most commonly reported imaging modalities used for invasive papillary carcinoma⁵ and Paget's disease, with the latter demonstrating nipple areolar complex abnormalities, similar to our patient. There were limited reports on the use of MRI in invasive papillary carcinoma, although MRI had been documented to be useful in patients with Paget's disease as it was able to detect occult disease, accurately showing the extent of disease.^{6,7} MRI, in our case, revealed an indeterminate mass in the UIQ, which subsequently did not have any pathological correlate. This could be due to the sensitivity nature of MRI^{6,8}; hence, its role in imaging these rare subtypes needs to be further defined.

Histologically, invasive papillary carcinoma has been characterised by smaller size, lower grade, positivity of ER/PR, HER2 negativity and no nodal involvement.^{9,10} In the absence of DCIS, a metastasis needs to be excluded. In our case, there was an extensive background of DCIS, consistent with breast origin. Our patient, however, had a high-grade tumour, ER/PR negativity, HER2 positivity, nodal metastasis and LVI. We postulate that this atypical aggressive nature may be related partly to the presence of Paget's

Figure 4 (A) H&E 200× showing an invasive tumour with a papillary architecture. (B) 100× staining for cytokeratin 7 (CK7) highlighting the foci of Paget's disease in the overlying skin.

Learning points

- ▶ Invasive papillary carcinoma of the breast and Paget's disease are both rare entities.
- ▶ This is the first known association of invasive papillary carcinoma with Paget's disease.
- ▶ While invasive papillary carcinoma tends to have an indolent course without need for overtreatment, our patient had unusual unfavourable histological features.

disease, which may be a poor prognostic factor when associated with invasive papillary carcinoma, since Paget's disease could potentially result in ulceration of the nipple areola complex, as shown in our patient, and result in a higher stage disease. In fact, Paget's disease has been associated with a poorer prognosis in invasive cancers compared with invasive cancers alone.²

As invasive papillary carcinoma is often associated with a lower recurrence rate and longer disease-free interval,¹¹ studies have advocated not to overtreat this indolent subtype.¹² Surgical options included wide local excision, with or without adjuvant radiotherapy, or mastectomy, although the latter was reported to be less frequently performed.^{3,12} In our case, in view of the central location of the cancer and the large mass to breast size ratio, a mastectomy with axillary clearance was performed. The patient then underwent chemotherapy, immunotherapy and radiotherapy as per multidisciplinary tumour board's recommendation. This case highlighted that the treatment for patients with invasive papillary carcinoma associated with Paget's disease should be individualised and may need to be more aggressive than that for invasive papillary carcinoma alone.

In conclusion, we report the first known association of invasive papillary carcinoma with Paget's disease with an unusual presentation of aggressive features.

Contributors Conception of study: MAG. Data collection: GHL and JPC. Data analysis: all authors. Manuscript writing: all authors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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