

## Synchronous bilateral paget's disease of breast associated with invasive breast cancer

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### Abstract

Paget's disease is an uncommon condition which presents with eczematoid lesions involving the nipple-areolar complex in elderly women. This condition is almost always seen unilaterally. Bilateral disease is extremely rare, incidence of which is unknown with only sporadic case reports available. About ten case reports of bilateral Paget's disease are published, out of which only three had associated invasive carcinoma [1]. We present case report of synchronous bilateral Paget's disease with Ductal Carcinoma in Situ (DCIS) and invasive carcinoma of both breasts.

### Keywords

paget's disease; ductal carcinoma in situ; invasive breast cancer

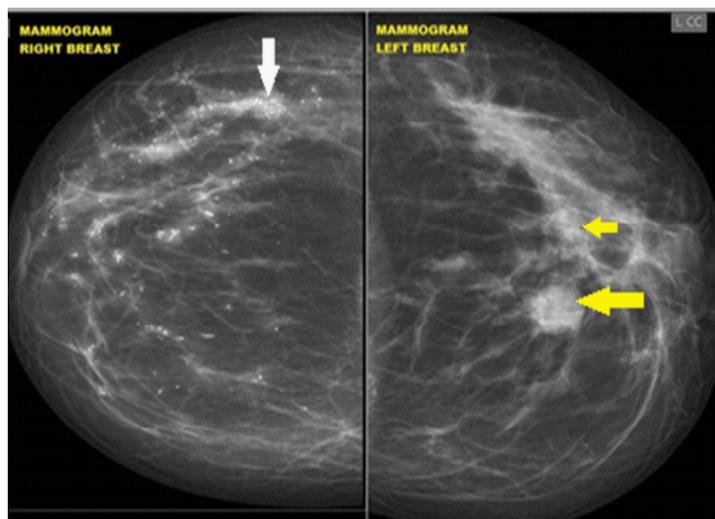
### Introduction

Paget's disease is a rare and distinct clinical entity. The skin lesions are often misdiagnosed as eczema and treated symptomatically. In about more than 90 % of the cases it is associated with invasive or in-situ carcinoma of the ipsilateral breast. Thorough clinical evaluation, imaging and full thickness biopsy is essential in all cases to rule out underlying in-situ or invasive carcinoma.

### Case Report

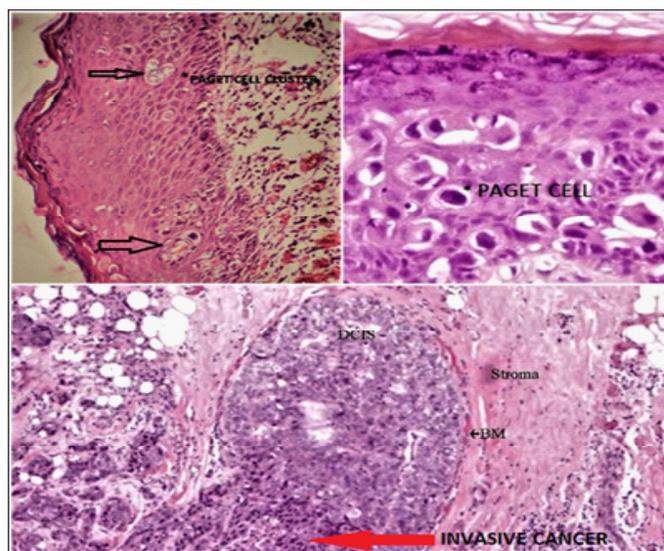
A 35-year-old pre-menopausal lady presented with skin changes of areola and nipple of both sides. There was no history of itching, bleeding from the site, breast or axillary lump. She had a full-term normal delivery six months before, and she was lactating the new born for the past six months. There was no significant past medical or surgical history. She attained menarche at 13 years and had no other significant gynecological history. There was no family history of breast or ovarian cancer. General physical examination was unremarkable. Local examination of both breasts and axilla was done. There was no palpable lump in either breast or axilla. Eczema and erosion of bilateral areola and nipple was noted. All routine investiga-

tions were normal. A clinical diagnosis of Paget's disease of both breasts was made. Mammogram showed extensive scattered microcalcifications in both breasts. An ill-defined rounded opacity with spiculations was seen in the central part of left breast (Figure 1).



**Figure 1:** Mammogram showing extensive scattered microcalcifications in both breasts. White arrow shows microcalcifications in right breast. An ill-defined rounded opacity with spiculations is seen in the central left breast (marked with yellow arrows).

Ultrasound of both breasts was done, which showed hypo echoic lesions in both breasts. In the right breast there was a lesion in the retro-areolar region which measured 1.1 x 0.6 cms. The left breast showed a similar lesion which measured 2.5 x 1.7 cms. Ultrasound guided fine needle aspiration was performed from the above-mentioned lesions of both breasts. Cytology from the breast lump revealed invasive ductal carcinoma of both breasts. After confirming the presence of invasive cancer by frozen section examination of the specimen, patient underwent simultaneous bilateral modified radical mastectomy and immediate breast reconstruction of both breasts with prostheses. The histopathological examination showed classical Paget's cells with extensive comedo type ductal carcinoma in situ with foci of invasive ductal carcinoma in both the breasts (Figure 2).



**Figure 2:** Histopathology slide showing classical Paget's cells (marked with black arrows and asterisk) with extensive comedo type ductal carcinoma in situ with foci of invasive ductal carcinoma (marked with red arrow); Hematoxylin and Eosin stain, 10x magnification.

Receptor assay was triple negative for oestrogen, progesterone and HER-2 –neu receptors. The patient received adjuvant chemotherapy and radiation and is on routine follow-up and has been disease free for the past four years.

## Discussion

Sir James Paget noted an association between skin lesions on the nipple and breast cancer, he described this condition for the first time in 1874 [2]. In his paper, Paget described 15 women between 40 and 60 years old, who first presented with the skin changes involving nipple-areolar complex, and subsequently progressed to development of breast cancer. He noted that all fifteen patients initially presented with an itching eczema-like rash and discharge from the nipple, which were refractory to common remedies, and within the following year progressed to cancer [2].

The vast majority of patients diagnosed with Paget's disease have an associated underlying neoplasm in the breast. In the series by Yim et al., the percentage of patients diagnosed with Paget's disease of the nipple found to have invasive or non-invasive carcinoma was upwards of 90% [3]. Full thickness biopsy of skin lesion is essential to make the diagnosis. On histopathology, there is classical finding of nests and groups of malignant Paget's cells which are glandular epithelial cells containing mucin. They have enlarged pleomorphic nuclei with clear cytoplasm and predominantly involve the lower layers of the epidermis [4]. Similar findings were noted in our patient. On immunohistochemical examination Paget's cells show over-expression with cytokeratin 7 (CK7) and also express other glandular antigens such as epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), gross cystic disease fluid protein 15 (GCDFP-15) and several mucins, but do not express either high molecular weight CKs or melanocytic antigens [4]. Imaging in the form of Mammogram and Ultrasound may have limitations in detecting underlying Ductal Carcinoma in Situ (DCIS) and an additional evaluation with Magnetic Resonance Imaging (MRI) can help detect underlying invasive cancer and DCIS [5]. In our patient, mammogram revealed extensive microcalcifications, suggestive of ductal carcinoma. Historically, patients with diagnosis of Paget's disease have been treated with mastectomy, because of a high likelihood of association with multicentric and/or multifocal breast cancer [6]. The patients with negative MRI but with Paget's in the nipple should undergo excision of the nipple-areolar complex followed by adjuvant radiation [6]. Those with underlying malignancy should undergo therapy based on the type and clinical staging of the associated malignancy. Breast conserving therapy is a feasible alternative for patients with disease limited to the central segment of the breast [7]. Prognosis depends on the stage of underlying malignancy.

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