## **Case Report**

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# Paget's disease of breast with an unusual presentation of involvement of overlying skin of breast: a case report

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#### ABSTRACT

Paget's disease of breast is also known as Paget's disease of the nipple & mammary Paget's disease, involving the skin of nipple & areola. It is rare type of cancer with tumors inside the same breast which may be either ductal carcinoma in-situ or invasive breast cancer. We report a case with Paget's disease of breast which is not only involving the nipple-areola complex but also involving surrounding skin of breast.

Keywords: Paget's disease, Ductal carcinoma in-situ, Invasive carcinoma, Nipple-areola complex

#### **INTRODUCTION**

Paget's disease of breast is rare type of breast cancer and most commonly identified in the setting of scaly erythematous nipple or an erythematous, eczematous rash near the nipple.<sup>1-3</sup> Nipple pruritus can also be a manifestation of Paget's disease.<sup>2</sup> In the presence of these features, Paget's disease of breast can be a diagnostic challenge as possibility of Paget's disease of breast is overlooked & diagnosis of dermatitis/eczema is made & treated with topical steroid.<sup>2,4</sup> Diagnosis hence remains elusive for long period.

Paget's disease of breast generally involves nipple and areola. This case report is unique in regard to its unusual presentation as there was involvement of almost entire breast skin along with its nipple-areola complex.

#### CASE REPORT

A 78 years old women (with no comorbidity and prior history of laparoscopic cholecystectomy for gall stones) presented with gradually progressive eczematous lesion over nipple, areola and left breast skin for last 15 years. This lesion partially responded to steroid therapy advised by local practitioner with partial resolution and flaring up of lesion. She consulted department of surgical oncology, SMS hospital, Jaipur. On examination, there were multiple eczematous, crusty lesions involving almost whole of left breast skin including nipple-areola complex (Figure 1a-b), with no palpable lump in the breast and no axillary lymphadenopathy. Based on these clinical findings, lupus vulgaris, Bowen's disease and Paget's disease of breast were taken as differential diagnosis.



Figure 1: Showing Paget's disease of left breast showing multiple eczematous, crusty lesion involving breast skin with destruction of nipple areola complex. Mammography showed no lesion within breast (Figure 2a-b). MRI breast showed only diffuse subcutaneous tissue and skin thickening without any underlying infiltration noted in left breast region with maximum thickness 6.7 mm along medial aspect (Figure 3a-b). Skin punch biopsy from left breast lesion was performed.



Figure 2: Mammography in medio-lateral and craniocaudal view showing no lesion within left breast, nipple is not visible in left breast.



#### Figure 3: Breast MRI is showing skin and subcutaneous tissue thickening of left breast with absence of nipple and no lump visible. Right breast appears normal.

Histopathological examination showed single cells and clusters of cells spread throughout the epidermis. Cells had abundant eosinophilic cytoplasm, irregular large nucleus with prominent nucleoli. Underlying dermis was infiltrated with lymphocytes and plasma cells (Figure 4a). Epidermis showed hyperkeratosis, parakeratosis and mild irregular hyperplasia. On IHC, these cells were positive for GATA-3, Her-2-neu and negative for CK-5/6, p63, S-100, HMB 45 (Figure 4b-f). These findings were consistent with the diagnosis of Paget's disease of breast. Markers ruled out the possibility of Bowen's disease and melanoma in situ.



Figure 4: H and E section showing atypical cells in the epidermis-(a). On IHC, the tumour cells were positive for Her2 neu-(d) and GATA 3-(b) and were negative for CK5/6 and P63 (inset)-(c). Cells were negative for HMB-45 (e) and S-100 (f).

In view of extensive skin involvement, the case was discussed with the patient and she was convinced to get a simple mastectomy done. Axillary sentinel lymph node biopsy was also performed. Final surgical pathological examination of mastectomy specimen was consistent with Paget's disease of breast.

#### DISCUSSION

Paget's disease of breast is rare type of cancer involving the skin of nipple and usually the areola.<sup>1,5</sup> Velpeau described the eczematous lesion of Paget's disease but it was Sir James Paget who first described the association with underlying breast cancer in 1874.67 There are two theories proposed for the origin of Paget's disease of breast; epidermotropic theory and in situ malignant transformation theory. The first theory states that the changes typical of Paget's disease arise in the ductal cells primarily and later on spread along the basement membrane through the lactiferous sinuses to the nipple. This theory is accepted by virtue of the fact that the most patients with Paget's disease have underlying breast cancer and the cells from the nipple are histologically similar to the associated invasive carcinoma. The in situ malignant transformation theory on the other hand proposes that Paget's disease primarily originates in the epidermal cells of nipple by malignant transformation of keratinocytes and is not associated with any coexisting neoplastic process in the affected breast.<sup>1,2,4</sup>

It occurs in both women and men but most cases occur in women commonly between the age group of 24 to 84 year with average age at the diagnosis being 55 year. It accounts for 1-4% of all cases of breast cancer.<sup>1,2,5</sup> The lesions are typically unilateral and most of the people with Paget's disease of breast have underlying carcinoma within the same breast which may be either ductal carcinoma in-situ or invasive cancer (may or may not be multifocal) but it may be absent in 33% of cases.<sup>3,5,8</sup>

To our knowledge, there are few case reports of Paget's disease of breast with involvement of nipple areola complex in literature, but none have reported with extensive breast skin involvement.

The symptom of Paget's disease of breast is itching, tingling or redness of nipple areola, diagnosis is often mistaken for benign skin condition such as dermatitis or eczema.<sup>2,8</sup> It may be associated with flaky, crusty or thickened skin on or around the nipple, flattened nipple. There may be bloody/yellowish nipple discharge.<sup>2</sup> The differential diagnosis includes contact dermatitis, Bowen's disease, psoriasis, basal cell carcinoma, nipple adenoma, erosive adenomatosis of nipple, and Toker cell hyperplasia.<sup>9</sup>

Diagnosis can be achieved by surface biopsy, shave biopsy, punch or wedge biopsy.<sup>2</sup> A proper full thickness tissue biopsy from the edge of lesion along-with cytological examination of exudates is helpful in ascertaining the histology as well as hormone receptors evaluation.<sup>10</sup>

Histology may reveal hyperkeratosis, parakeratosis or acanthosis of the epidermis and infiltration with classical Paget cells that are large, ovoid, have pale vacuolated cytoplasm and hyperchromatic nuclei.<sup>1,11</sup> MRI is an excellent investigation which helps in diagnosis.<sup>4,12,13</sup> It plays an important role in selecting candidates for breast conserving therapy out of those patients with mammary Paget's disease with no clinical evidence of an underlying breast carcinoma.<sup>14</sup>

Treatment options include; lumpectomy including nipple areola complex with whole breast radiation therapy or total mastectomy±sentinel node biopsy with or without breast reconstruction, central lumpectomy including nipple areola complex±sentinel lymph node biopsy without radiation therapy.<sup>2,15-17</sup> Depending upon stage and other features of underlying breast tumor (presence or absence of lymph node involvement, ER/PR receptors and HER 2neu protein over expression in tumor cells, adjuvant therapy and/or hormonal therapy may also be recommended.<sup>2,16</sup>

Unfavorable prognosis of Paget's disease depends on the presence of invasive cancer, axillary lymph node spread, histological type of breast cancer, age >60 years.<sup>18-20</sup> In Paget's disease with no underlying malignancy or lymph node spread, the 5-year survival is 92-94% and from 82% to 91% at 10 years. As per Yang et al, 5 and 10 year survival rates for the patients with negative lymph nodes and positive lymph nodes were 92.0%, 76.5% and 50%, 25.0% respectively.<sup>21</sup> Early and accurate diagnosis of the disease by means of skin biopsy enables breast conservative surgery when the lesion is confined to the epidermis of the nipple. Although the clinical behavior in men is similar to that in women, men appear to have a worse prognosis, with an estimated 5 year survival rate of 20-30%.<sup>3,22-25</sup>

#### CONCLUSION

In a patient with progressive eczematous, crusty lesion involving the skin of breast along-with nipple areola complex without any underlying breast lump, skin biopsy must be considered earlier to rule out associated malignancy and treat accordingly the malignancy or dermatological conditions.

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