Case Report

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Paget's disease of the male breast

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ABSTRACT

Paget's disease of the breast is a rare type of breast cancer presenting as an eczematous eruption over of nipple and/or areola. It accounts for 0.8% of all breast cancers. Of all malignant breast cancer, 1% occurs in male patients. The incidence of Paget's disease in male breast is extremely rare. Most of the cases have an underlying breast cancer. It has a different tumor biology that dictates a favorable clinical behavior and outcome. This unique entity therefore merits reporting.

Keywords: Paget's disease, Male breast, Mammary Paget's disease, Breast cancer

INTRODUCTION

Paget's disease (PD) is a rare type of breast cancer. It presents as an eczematous eruption over the nipple/areola or both and it is usually associated with underlying breast cancer. The presentation may varies from eczema, scaling, ulceration, bleeding or a painful nipple. The incidence of male breast cancer is less than 1% of all breast cancers and PD in male is extremely rare. PD may be associated with an underlying in situ or invasive cancer. As it resemblance to chronic eczema both, misdiagnosis and under-diagnosis are common. The average delay in treatment of the disease is about 6-8 months from the onset of symptoms. He Biopsy should be considered as early as possible to prevent undue delay in the management. Further, PD in males should be treated aggressively for better results.

CASE REPORT

A 60 year old man presented with 4 month history of itching and eczematous scaling of left nipple areolar complex. His problem had not resolved with use of a

topical ointment. On examination, there was retraction of nipple with distortion of nipple-areolar complex on the left side (Figure 1). There was 2 x 1.5 cm hard lump underneath the left nipple-areolar complex. Central group of left axillary nodes (3 in number) were palpable, hard and mobile. There was no history of breast or related cancer in his family.



Figure 1: Showing eczematoid lesion with destruction of left nipple areola complex.

Fine Needle Aspiration Cytology (FNAC) from the lump was suggestive of ductal carcinoma and FNAC from lymph node was positive for malignancy. Work up for systemic metastasis was negative. Modified radical mastectomy was done. Histopathology revealed Paget's disease of the left nipple with evidence of underlying invasive ductal carcinoma and eight positive lymph nodes with extracapsular extension. Resected specimen margin was free of tumor. Patient was given adjuvant radiotherapy followed by chemotherapy. There was no recurrence of tumor during the 4 years follow up.

DISCUSSION

PD of the breast was first described in 1874 by Sir James.¹ The incidence of breast cancer in male is infrequent, accounting for nearly 0.8% of all breast cancers.⁵ The mean age of PD in male is 60 years, but ranges from 43 to 81 years.

Pathogenesis

Two main hypotheses have tried to explain its nature and origin:⁶ The more accepted theory is the epidermotropic (ductal) theory which postulates that the Paget's cells are ductal in origin. The normal tight junctions between keratinocytes are disrupted due to tumor cells. Which allows seepage of intercellular fluid to the skin surface. The basement membrane of the ducts and lobules is in continuity with the basement membrane of the skin thus permitting the duct cancer cells to migrate along the basal membrane of underlying ducts to the epidermis of the nipple. Therefore, ductal carcinoma in situ (DCIS) can be present in both the epidermis and the breast ductal system in the absence of stromal invasion. About 50% cases of PD are due to ductal carcinoma in situ (DCIS) alone and the remainder to DCIS associated with an invasive carcinoma.7

The heregulin-alpha, a motility factor released by keratinocytes of the nipple, plays a key role in the pathogenesis of PD by attracting breast cancer cells to spread throughout the epidermis. Heregulin-alpha and SK-BR-3 cells rapidly induces spreading, the formation of pseudopodia, and chemotaxis, leading to rapid translocation and dispersal of cells. Pseudopodia are necessary in spreading, attachment and locomotion of cells. HER2/neu is preferentially located on pseudopodia and microvilli. The motility factor acts on its receptors HER3 or HER4 or both, as well as on their co-receptor HER2/neu, which are expressed by Paget cells, to induce chemotaxis and subsequent spread of Paget cells throughout the nipple epidermis.

The second theory is that the Paget's cell is an epidermoid cell transformed in situ without a direct connection with the underlying carcinoma of the breast. It is supported by histological studies in cases without an underlying carcinoma of the breast. PD of the breast presents as nipple erythema and mild eczematous scaling

and flaking, progressing to nipple crusting, skin erosions and ulceration. Skin erythema and an exudate resembling chronic eczema is due to the presence of intercellular fluid in the skin surface due to the disruption of normal tight junctions between keratinocytes. The tumor cells can spread into the areola and surrounding skin of the breast. The incidence of axillary lymph node involvement is 50-65% in patients with a palpable mass and 0-15% in patients without a palpable mass.

The differential diagnosis includes malignant melanoma and Bowen's disease (intraepithelial squamous cell carcinoma). These can be differentiated by morphological characteristics of the cells and IHC. ¹¹

Diagnosis

A sample can be obtained by nipple scrape or full thickness biopsy. The presence of Paget's cells and a lactiferous duct secures the diagnosis. Most of the patients with PD have an underlying breast carcinoma. It may present with (54%) or without (46%) a mass. ¹⁰ If there is a palpable mass, trucut biopsy or fine needle aspiration cytology has to be done.

The risk factors for male breast cancer are testicular abnormalities, infertility, obesity, cirrhosis or Klinefelter's syndrome. These were not seen in our patient.

The mammographic evaluation is performed in all cases with clinical findings of PD. It helps to detect the underlying carcinoma, to exclude multifocal disease. It also acts as a tool for follow-up of the patients, who undergoes Breast Conservative Surgery (BCS). The findings include skin thickening, nipple retraction, microcalcifications, or a mass at the level of the nippleareolar complex. In the breast parenchyma there may be a discrete mass or masses, asymmetry, architectural calcifications. distortion, or malignant mammographic findings may be negative in up to 50% of cases. In such cases ultrasonography (US) should be considered as a part of initial evaluation. Magnetic Resonance Imaging (MRI) can have a role when the results of mammography or US are negative. MRI allows detection of otherwise occult disease. It also accurately demonstrates the extent of disease, multicentric cancer. and permits underlying cancer to be ruled out. It is helpful when considering BCS.¹²

Immunohistochemistry (IHC)

PD of the nipple is characterized by overexpression of human epidermal growth factor receptor-2 (HER-2)/neu. The oestrogen and progesterone receptors will be expressed in 10% of cases. Proliferative activity of cancer cells, Ki-67 antigen expression in PD cancer cell may be a potential prognostic factor. ¹³ Paget's cells are positive for CK7 in nearly all cases and may also express Epithelial Membrane Antigen (EMA), carcinoembryonic

antigen (CEA), Gross Cystic Disease Fluid Protein 15 (GCDFP-15). The antigen NY-BR-1 is a useful diagnostic marker. Our case was positive for HER-2/neu and negative for oestrogen and progesterone receptors.

Treatment

Treatment includes mastectomy plus axillary node sampling or clearance, BCS with radiotherapy, nipple sparing mastectomy, cryosurgery, photodynamic therapy (PDT). Adjuvant treatment may be considered depending on nodal and receptor status.³ PD local recurrence can be found in a significant proportion after nipple-sparing mastectomy.¹⁶ Though minimally invasive strategies like PDT, cryosurgery in selected cases have been tried;^{17,18} modified radical mastectomy with axillary clearance is the conventional treatment of choice. However, studies have shown breast conserving surgery with radiotherapy to be a feasible and safe option in properly selected patients.¹⁹

The presence of underlying breast mass, positive axillary node and overexpression of HER-2/neu receptor have been shown to have poor survival.²⁰

Patients with direct dermal invasion from PD had a favorable outcome during the available follow-up period. This type of dermal involvement must be distinguished from locally advanced invasive carcinomas with skin invasion classified as T4b in the American Joint Cancer Commission staging system, as cancers with other types of skin invasion are associated with a poor prognosis.²¹

Although there seems to be no significant difference in the tumor histology in male and female, the former appears to have a poor prognosis. The five-year survival rate in males is 20 to 30% and in females 30 to 50 %.

CONCLUSION

We report a classic case of PD of the male breast with underlying infiltrating ductal carcinoma. Dermatitis like lesions and nipple erosions in male and female patients should arouse suspicion of PD. Biopsy should be promptly considered as early as possible to prevent undue delay in diagnosis. Further, PD in males should be treated aggressively for better outcomes.

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