Case Report

Paget's disease of the nipple
乳頭乳暈炎性癌變病

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This is a report of a 45-year-old Chinese woman who presented with an eight-month history of unilateral eczematous like rash on her left nipple-areola area. No breast mass was palpable. The skin biopsy confirmed the lesion to be Paget’s disease of the nipple. Mammogram showed abnormal microcalcifications at the superio-lateral quadrant of the left breast. A left mastectomy was done and the histopathology of the mastectomy specimen confirmed an underlying high grade ductal carcinoma in-situ.

Keywords: Nipple, Paget's disease

Introduction

Paget's disease of the nipple is a manifestation of underlying breast cancer which may mimic ordinary nipple eczema. Hence, it is important to make the diagnosis early so that appropriate investigation and treatment be given. The following is a case report of a 45-year-old lady with the disease.

Case report

The patient is a 45-year-old housewife. She complained of an eight-month duration of persistent itchy rash, blood stained discharge and erosion of her left nipple. Her past health was good. There was no family history of breast cancer. On physical examination, there was erythematous exudation of the left nipple-areola complex (Figure 1). No vesicle, nipple retraction
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Figure 1. Erythematous exudative plaque of the left nipple-areola area.

or breast mass was detected. No lymphadenopathy was palpable. The major clinical differential diagnoses were Paget’s disease of the nipple and eczema.

Incisional skin biopsy of the left areola showed abundant Paget cells in the epidermis (Figure 2). There was no invasion of the Paget cells into the dermis, which consisted of a marked chronic inflammatory infiltrate. The low molecular weight keratin stain (Cam 5.2) was positive (Figure 3). The diagnosis was Paget’s disease of the nipple.

A mammogram examination was performed for the patient which showed abnormal segmentally distributed linear and branching microcalcifications at the superio-lateral quadrant of the left breast. The right mammogram was normal. Biopsy of the suspicious microcalcification area confirmed it to be ductal carcinoma in-situ. Left modified radical mastectomy was done. The surgical specimen showed high-grade ductal carcinoma in-situ, with focal areas suggestive of early stromal invasion. The surgical margins and the axillary lymph nodes were not involved.

Discussion

Paget’s disease of the nipple is a superficial manifestation of an underlying infiltrating or non-infiltrating breast carcinoma. The disease was named after Sir James Paget. In 1874, he described that 15 female patients had chronic eczematous eruption of the nipple and areola and subsequently these patients developed an infiltrating carcinoma of the mammary gland. Paget’s disease of the nipple was reported as the presenting sign in 0.5% to 4.3% of all cases of breast cancers. On the other hand, almost all patients with Paget’s disease of the nipple were associated with an underlying breast carcinoma of ductal origin, either in situ or invasive. Studies found that 92-97% of patients with Paget’s disease had associated underlying breast carcinoma. However, there was exception to this rule both in men and women.

Paget’s disease of the nipple occurs in patients between 50 and 60 years of age. It occurs rarely in men, where it carries a worse prognosis than in women. The disease may be diagnosed late, with a mean duration of symptoms prior to presentation as 6.5 months (range 1 to 54). The disease presents classically as an unilateral, well-demarcated, slightly infiltrated, erythematous, exudative or scaly plaque involving the nipple-areola complex. The lesion frequently appears on the nipple, then spreads to the areola but seldom extends to the surrounding skin. The patient often complains of nipple discharge, pain or itch. However, 10% of patients are asymptomatic. Up to 60% of patients have associated breast mass. Vesicular eruptions on the nipple may be the early feature. On the other hand, bleeding, crusting, ulceration and nipple retraction signify late manifestations.
Figure 2. H&E stain, original magnification 10x10. The epidermis shows islands of Paget cells. They are large, rounded cells that are devoid of intercellular bridges and contain a large nucleus and ample pale cytoplasm. Flattened basal cells are seen lying between Paget cells and the underlying dermis. (By courtesy of KC Yau, Public Health Laboratory Centre, Department of Health)

Figure 3. Cytokeratin (Cam5.2) stain, original magnification 10x10. The cytoplasm of the Paget cells is highlighted by the low molecular weight cytokeratin (Cam5.2) immunohistochemical stain. (By courtesy of KC Yau, Public Health Laboratory Centre, Department of Health)
Eczema is the major differential diagnosis. Other differential diagnoses include contact dermatitis, frictional hyperkeratosis, psoriasis, bacterial, viral or fungal infection. Malignant diseases such as Bowen's disease, superficial basal cell carcinoma, melanoma or skin metastasis should be excluded. The accurate diagnosis relies on high index of suspicion. Any eczema or even only vesicular eruption on the nipple without other clinical sign should be regarded as Paget's disease of the nipple until proven otherwise. Unilateral distribution, persistent soreness or itching of the papillary area should strongly lead to suspicion. However, skin biopsy is essential to establish the diagnosis.

The histologic hallmark is the finding of abundant Paget cells in the epidermis. Paget cells are round and much larger than their neighbouring keratinocytes. They contain pale vacuolated cytoplasm, enlarged polymorphic and hyperchromatic nuclei and prominent nucleoli. Mitoses are often present. The cytoplasm of the Paget cells is highlighted by the use of the low molecular weight cytokeratin (Cam 5.2) immunohistochemical stain.

Two theories explained the pathogenesis. The epidermotropic theory postulates that Paget cells are actually ductal carcinoma cells that have migrated along the basement membranes of underlying ducts to the epidermis of the nipple. On the other hand, in-situ transformation theory regards Paget cells as transformed malignant keratinocytes, which appear in situ. Most immunohistochemical studies have tended to favour the epidermotropic theory while the in-situ theory is supported by ultrastructural studies.

In the absence of a palpable breast mass, mammography is used to detect and locate subclinical underlying tumours, clusters of suspicious microcalcifications, or both. The sensitivity of the mammography varies from 24% to 97%, being higher in patients with palpable mass. Paget's disease of the nipple, even without an underlying palpable or radiologically visible breast mass, should be considered diagnostic of underlying breast carcinoma. The disease can be treated with surgery, radiotherapy and/or chemotherapy as in other breast carcinomas. Recently, breast-conserving surgeries have been done in selected patients. During follow up, one should also look for any skin changes, which could be a manifestation of local recurrence. Patients with post-radiotherapy skin changes should be warranted to have early skin biopsy in order to rule out local recurrence.

There was a clear difference in the prognosis of patients presenting with both nipple changes and breast mass, as opposed to those with nipple changes only. Palpable breast mass is associated with higher incidence of multifocal disease and positive lymph node involvement. The five year survival rates for patients with Paget's disease of the nipple were 43% for those with breast mass and 92% for those without breast mass.

References