

Case Report

Paget's disease of the nipple

乳頭乳暈炎性癌變病

SY Cheng 鄭秀儀

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.

此病例之患者是位 45 歲女性，有八個月的左乳頭濕疹樣皮疹病史。觸診無乳房腫塊。皮膚活檢證實皮疹為乳頭乳暈炎性癌變 (Paget's disease)。病人隨後接受乳腺癌的有關檢查。乳腺軟性 X 光檢查顯示左側乳房外上部有異常微小鈣化。最後，施行左側乳房切除術，組織病理標本檢查證實病者患有乳腺管高度分化原位癌。

Keywords: Nipple, Paget's disease

關鍵詞：乳頭，乳頭乳暈炎性癌變病

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

Social Hygiene Service, Department of Health, Hong Kong

SY Cheng, FHKCP, FHKAM(Medicine)

Correspondence to: Dr. SY Cheng

Cheung Sha Wan Dermatological Clinic, 3/F, West Kowloon Health Centre, 303 Cheung Sha Wan Road, Kowloon, Hong Kong



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 micro-calcifications at the superio-lateral quadrant of the left breast. The right mammogram was normal. Biopsy of the suspicious micro-calcification 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.¹ Paget's disease of the nipple was reported as the presenting sign in 0.5% to 4.3% of all cases of breast cancers.² 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.^{3,4} However, there was exception to this rule both in men and women.⁵

Paget's disease of the nipple occurs in patients between 50 and 60 years of age.⁶ 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).⁷ 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.⁶ Up to 60% of patients have associated breast mass.^{6,8} Vesicular eruptions on the nipple may be the early feature. On the other hand, bleeding, crusting, ulceration and nipple retraction signify late manifestations.⁹

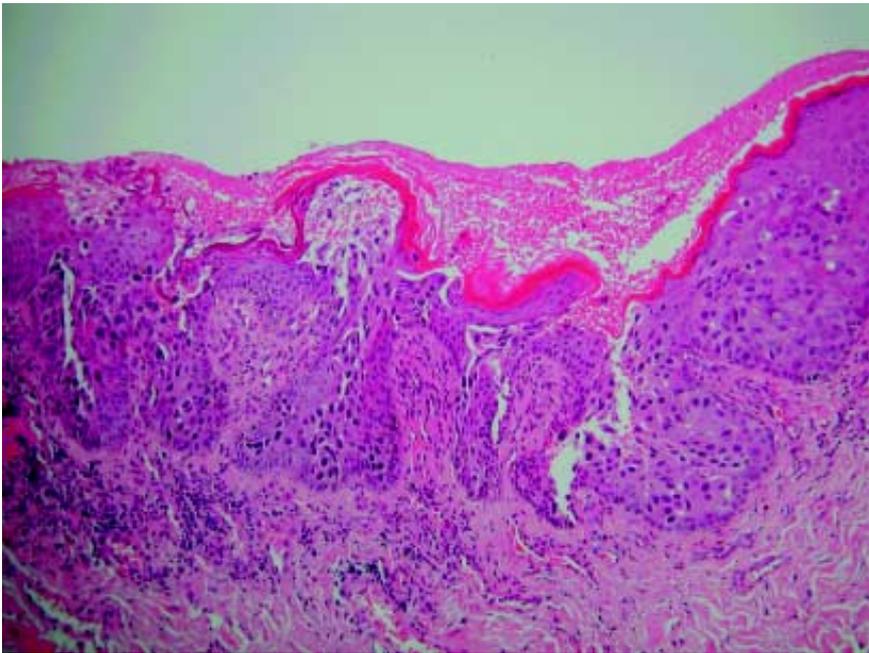


Figure 2. H&E stain, original magnification 10x10. The epidermis shows islands of Paget cells. They are large, rounded cells that are devoid of intercellular bridges and contain a large nucleus and ample pale cytoplasm. Flattened basal cells are seen lying between Paget cells and the underlying dermis. (By courtesy of KC Yau, Public Health Laboratory Centre, Department of Health)

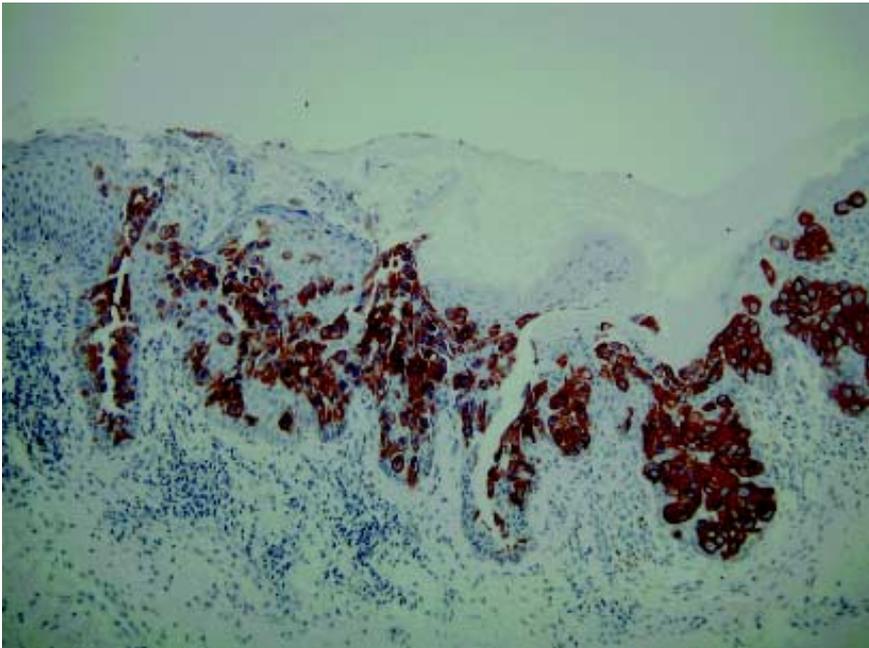


Figure 3. Cytokeratin (Cam5.2) stain, original magnification 10x10. The cytoplasm of the Paget cells is highlighted by the low molecular weight cytokeratin (Cam5.2) immunohistochemical stain. (By courtesy of KC Yau, Public Health Laboratory Centre, Department of Health)

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.⁹ 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.⁹ On the other hand, in-situ transformation theory regards Paget cells as transformed malignant keratinocytes, which appear in situ.⁹ 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.⁹ 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.⁴

References

1. Connolly SM. Mammary and extramammary Paget's disease. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI. *Dermatology in General Medicine*. 5th edition, New York: McGraw Hill, 1999. p. 919-24.
2. Othter PJ, Balslev E, Blichert-Toft M. Paget's disease of the nipple. A continuing enigma. *Acta Chir Scand* 1990; 156:343-52.
3. Yim JH, Wick MR, Philpott GW, Norton JA, Doherty GM. Underlying pathology in mammary Paget's Disease. *Ann Surg Oncol* 1997;4:287-92.
4. Ashikari R, Park K, Huvos AG, Urban JA. Paget's disease of the breast. *Cancer* 1970;26:680-5.
5. Jones RE Jr. Mammary Paget's disease without underlying carcinoma. *Am J Dermatopathol* 1985;7: 361-5.
6. Inwang ER, Fentiman IS. Paget's disease of the nipple. *Br J Hosp Med* 1990;44:392-5.
7. Chaudary MA, Millis RR, Lane EB, Miller NA. Paget's disease of the nipple: a ten year review including clinical, pathological, and immunohistochemical findings. *Breast Cancer Res Treat* 1986;8:139-46.
8. Whitaker-Worth DL, Carlone V, Susser WS, Phelan N, Grant-Kels JM. Dermatologic diseases of the breast and nipple. *J Am Acad Dermatol* 2000;43(5 Pt 1): 733-51.
9. Jamali FR, Ricci A Jr, Deckers PJ. Paget's disease of the nipple-areola complex. *Surg Clin North Am* 1996;76: 365-81.