

QUIZ SECTION

A Hyperpigmented Plaque on the Right Nipple: A Quiz

Ying-Chi Chen¹, Chii-shuenn Yang², Yi-Ju Chen^{1*} and Jui-Lung Shen¹

Departments of ¹Dermatology and ²Pathology, Taichung Veterans General Hospital, 405 Taichung, Taiwan. *E-mail: yjchenmd@vghtc.gov.tw

A 47-year-old woman presented with a single itchy, hyperpigmented plaque over her right nipple, which had been present for 2 weeks (Fig. 1A). The lesion was approximately 3.2 × 2.5 cm in size. Nipple retraction and ulceration were absent. Physical examination revealed no palpable mass within the breasts or regional lymphadenopathy. She reported no prior systemic disease, had no family history of breast cancer, and denied taking any drugs, including contraceptives. An incisional biopsy of the plaque revealed epidermal pagetoid spreading of tumour cells, which had hyperchromatism, nuclear pleomorphism and atypical mitosis, in addition to upper dermal lymphocytic inflammation. The presence of melanin pigmentation around the tumour cells within the epidermis and marked occurrence of melanophages in the upper dermis were noted (Fig. 1B). Immunohistochemical staining results showed that the tumour cells were positive for cytokeratin 7 (CK7) but negative for S-100 and MiTF.

What is your diagnosis? See next page for answer.

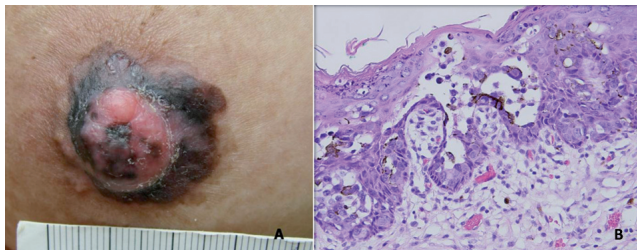


Fig. 1. (A) An itchy, brownish-to mottled-black hyperpigmented plaque with an irregular margin and some scales over the right nipple and areola. (B) Aggregation of large atypical cells in the epidermis appearing as artificial clefts associated with the presence of dense perivascular lymphocytic inflammation and prominent melanophages in the upper dermis. (Haematoxylin-eosin: ×400).

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ANSWERS TO QUIZ

A Hyperpigmented Plaque on the Right Nipple: Comment

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Diagnosis: Pigmented mammary Paget's disease

Pigmented mammary Paget's disease (PMPD) is a rare condition which is clinically, dermoscopically, and even histologically, similar to malignant melanoma (1–4). Histological examination reveal large Paget's cells with abundant pale cytoplasm and hyperchromatic nuclei, presenting as solitary units or small nests within the epidermis. Large amounts of dusty melanin pigment are observed within the cytoplasm of the tumour cells. The presence of numerous melanophages and lymphocytic inflammation over the papillary dermis is also characteristic. Immunohistochemical studies must be conducted in order to obtain an accurate diagnosis. The tumour cells of PMPD are positive for anti-keratin antibodies and other epithelial markers, such as CK7, CAM 5.2, CEA, and epithelial membrane antigen (EMA). Paget's cells also test positive for Alcian blue, diastase-periodic acid-Schiff (PAS), and gross cystic disease fluid protein-15 (GCDFP-15). Among these markers, CK7 is reported to be the most accurate diagnostic antigen because it helps to distinguish the tumour cells from the surrounding epidermal keratinocytes, and specimens from almost all of the PMPD patients test positive for this marker (4). However, the atypical tumour cells in PMPD patients are negative for the S-100 protein and melanocytic markers (Mart-1, Melan-A, HMB-45, or Fontana-Masson stains), which help differentiate PMPD from melanoma. In some circumstances, even normal epidermal dendritic melanocytes test positive for the S-100 protein. However, the dendritic melanocytes have more regular and smaller nuclei than the Paget's cells.

Other clinicopathological differential diagnoses include pigmented Bowen's disease and pigmented cutaneous metastasis from an underlying breast cancer. The tumour cells in Bowen's disease, unlike those in PMPD, are usually negative for CAM 5.2, CEA, EMA, PAS and GCDFP-15.

However, immunohistochemical examination does not help to differentiate PMPD and pigmented epidermotropic breast carcinoma. Certain characteristic histological features may help differentiate these two entities. The Paget's cells in PMPD scatter through the suprabasal layers without a junctional component. In contrast, pigmented epidermotropic breast carcinoma is characterized by tumoural aggregations in the underlying dermis and by the distribution of the neoplastic epithelial cells at the dermoepidermal junction and at all the epidermal layers (2).

Previous studies have shown that mammary Paget's disease is always associated with an underlying carcinoma of the breast, and this is also true in cases of PMPD (1–4). In the present case, mammography, breast sonography, and tests using normal serum tumour markers (CEA and CA-153) revealed no clinical evidence of underlying breast cancers. The patient underwent simple mastectomy after a skin biopsy. Pathological evaluation of surgical specimens revealed ductal carcinoma *in situ* with a small focus of microinvasive carcinoma located in the dermis of the nipple with the lesion. No tumour recurrence was observed during the subsequent follow-up period of 8 months.

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