

A Case of Pigmented Mammary Paget's Disease

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Pigmented mammary Paget's disease is a uncommon clinicopathologic variant of mammary Paget's disease, and this mimics malignant melanoma both clinically and histopathologically. Herein, we report on a rare case of pigmented mammary Paget's disease. An 81-year-old woman presented with 2.5×1 cm sized, red and brown, eczematous plaque on her right areola, and she'd had this lesion for 3 years. Histopathology showed large, atypical cells with large nuclei and abundant pale cytoplasm throughout the epidermis. Dispersed melanocytes were noted in the epidermis and some of the Paget's cells contained melanin within their cytoplasm. Immunohistochemical studies demonstrated that the intraepidermal pagetoid cells were positive for cytokeratin 7; in contrast, they were negative for S-100, Periodic-acid Schiff (PAS), Alcian blue at PH 2.5, HMB-45 and carcinoembryonic antigen (CEA). We recommend that pigmented mammary Paget's disease should be included in the differential diagnosis of pigmented lesions on the nipple.

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Key Words: Pigmented mammary Paget's disease

INTRODUCTION

Mammary Paget's disease is the result of intra-ductal mammary carcinoma that extends to the epidermis of the nipple and areola through a lactiferous duct. Pigmented mammary Paget's disease is a uncommon clinicopathologic variant of mammary Paget's disease, and this mimics malignant melanoma both clinically and histopathologically¹. The characteristic pigmentation is mostly due to the presence of dispersed melanocytes within the tumor and melanophages in the stroma². Only a few such cases have been described after the first reported case of pigmented mammary Paget's disease in 1990¹⁻¹¹. Herein, we report on a rare case of pigmented mammary Paget's disease.

CASE REPORT

An 81-year-old woman presented with an eczematous plaque on her right areola, and she had this lesion for 3 years. Physical examination revealed a 2.5×1 cm, sited red and brown, eczematous plaque on the right areola. Her right nipple was distorted and the borders of the areola were darkly pigmented (Fig. 1). A palpable breast mass was noted beneath



Fig. 1. Clinical appearance at admission.

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the plaque, but there was no axillary lymphadenopathy. The remaining physical examination was normal. Routine laboratory examinations, including the complete blood count, blood chemistry analysis and urinalysis, were within the normal limits.

We performed an incisional biopsy that included the pigmented area. Histopathology showed large, atypical cells with large nuclei and abundant pale cytoplasm throughout the epidermis. The atypical cells presented as solitary units and small aggregations in the epidermis. There was a diffuse inflammatory infiltrate that was mainly composed of

lymphocytes that filled the papillary dermis and obscured the dermoepidermal junction. The pattern of spread of the intraductal carcinoma was shown in the lactiferous ducts. The number of melanocytes in the basal layer was increased, and some of the Paget's cells contained melanin within their cytoplasm.

The immunohistochemical studies demonstrated that the intraepidermal pagetoid cells were negative for S-100, periodic-acid Schiff (PAS), Alcian blue at PH 2.5, HMB-45 and carcinoembryonic antigen (CEA). In contrast, they were positive for cyto-

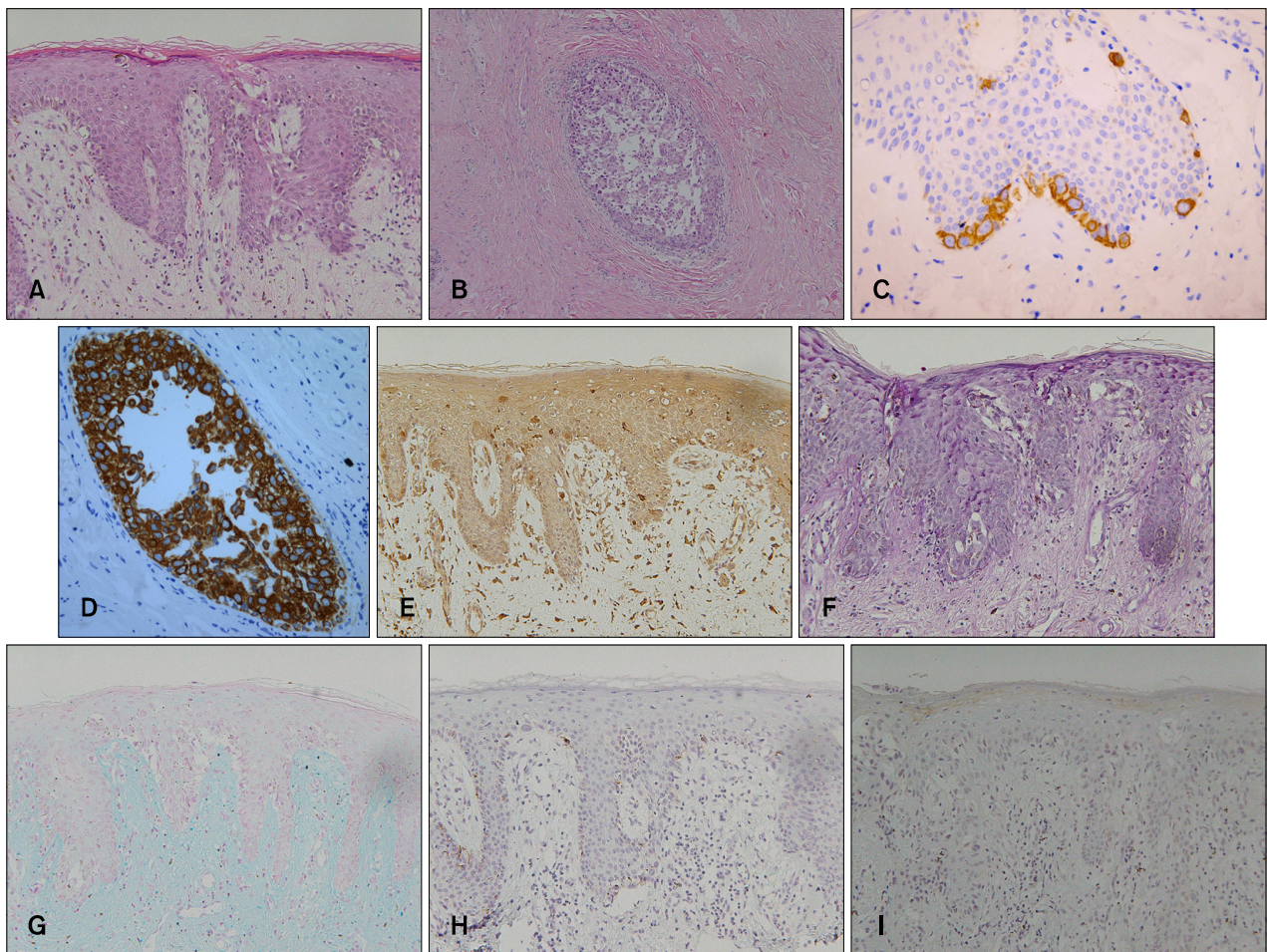


Fig. 2. The Paget's cells with large hyperchromatic nuclei and abundant pale cytoplasm were present throughout the epidermis. Dispersed melanocytes were noted in the epidermis and some of the Paget's cells contained melanin within their cytoplasm (A) (H&E, $\times 200$). The tumor cells were also found in the lactiferous ducts, where they formed clusters (B) (H&E, $\times 200$). The intraepidermal pagetoid cells and intraductal pagetoid cell were positive for cytokeratin 7 (C, D) (cytokeratin 7, $\times 400$). In contrast, they were negative for S-100 (E) (S-100, $\times 200$), Periodic-acid Schiff (F) (PAS, $\times 200$), Alcian blue at PH 2.5 (G) (Alcian blue at PH 2.5, $\times 200$), HMB-45 (H) (HMB45, $\times 200$) and carcinoembryonic antigen (I) (CEA, $\times 200$).

keratin 7 (Fig. 2).

Mammography revealed a shadow within the right breast, but no evidence of metastases was found. Simple mastectomy was recommended, but the patient failed to appear for follow-up.

DISCUSSION

Pigmented mammary Paget's disease is a rare clinicopathologic variant of mammary Paget's disease¹. It was first reported in 1990 by Ho et al³, and only a few such cases have been described afterwards¹⁻¹¹. It has been described as hyperpigmented patches or plaques involving the areola and nipple, which may simulate melanoma both clinically and histopathologically. For patients with breast carcinoma, 4.4% of the cases show epidermotropism². In rare instances, malignant melanoma may affect the mammary areola¹², and a collision of primary malignant melanoma and ductal carcinoma of the breast¹³ has also been described. The histopathologic differential diagnosis of pigmented mammary Paget's disease should include melanoma in situ. In melanoma in situ, nests of neoplastic melanocytes and single melanocytes are presented along the dermoepidermal junction and they are scattered throughout all levels of the epidermis, but they are almost always in direct contact with the papillary dermis, whereas the neoplastic cells of mammary Paget's disease are scattered through the suprabasal layers of the epidermis¹. Moreover, the intrapidermal pagetoid melanocytes in melanoma, (primary and epidermotropic metastatic melanoma) usually strongly express S-100 protein and HMB-45, whereas they do not express cytokeratin 7^{1,14}. Cytokeratin 7 is the immunohistochemical stain of choice for making the diagnosis of Paget's disease¹⁵. The high sensitivity of cytokeratin 7 makes it useful to diagnose a case of pigmented mammary Paget's disease that resembles malignant melanoma¹¹.

In this present case, single cells or nests of Paget's cells were scattered through the suprabasal layers of the epidermis and increased number of melanocytes were observed in the epidermis. Immunohistochemically, special staining for PAS was negative. In contrast with extramammary Paget's disease, the Paget's cells in Paget's disease of the breast stain with PAS in only some of the cases. The lesion may clinically mimic malignant melanoma. However, the

intraepidermal pagetoid cells in this case were negative for S-100 and HMB-45, but they were positive for cytokeratin 7. Thus, a diagnosis of pigmented Paget's disease was established, and the possibility of melanoma in situ was excluded.

Hyperpigmentation of the lesion was the most striking clinical feature in this case. Many of the Paget's cells contained abundant granular or dusty melanin within their cytoplasm. The exact mechanism for the melanocytic proliferation and melanin content within the cytoplasm of Paget's cells is unknown. Several histogenetic theories have been proposed. The local production of melanocytic chemotactic factor by breast cancer cells and pigment blockade of the melanocytes have been postulated as the cause for the clinical pigmentation in some cases of mammary Paget's disease¹⁶. Dusty melanin has also been described within the cytoplasm of the neoplastic cells of mammary Paget's disease, without an increased number of melanocytes^{3,4}. Another possibility would be phagocytosis of the melanin pigment from the melanocytes by the epithelial cells of the carcinoma¹⁷. Therefore, the clinical hyperpigmentation of some cases of mammary Paget's disease may be a result of either proliferation of dendritic melanocytes that contain abundant melanin or the phagocytosis or transfer of melanin from melanocytes to the cytoplasm of the cancer cells.

In this report, we have presented a rare case of pigmented mammary Paget's disease, and this may mimic malignant melanoma both clinically and histopathologically. Therefore, a detailed pathologic evaluation, including immunohistochemical staining, is essential for making the correct diagnosis. Pigmented mammary Paget's disease should be included in the differential diagnosis of pigmented lesions on the nipple.

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