A Case of Pigmented Mammary Paget's Disease

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Pigmented mammary Paget's disease is an 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 a 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.

(Ann Dermatol (Seoul) 20(4) 240∼243, 2008)

Key Words: Pigmented mammary Paget's disease

INTRODUCTION

Mammary Paget's disease is the result of intraductal mammary carcinoma that extends to the epidermis of the nipple and areola through a lactiferous duct. Pigmented mammary Paget's disease is an uncommon clinicopathologic variant of mammary Paget's disease, and this mimics malignant melanoma both clinically and histopathologically. The characteristic pigmentation is mostly due to the presence of dispersed melanocytes within the tumor and melanophages in the stroma. Only a few such cases have been described after the first reported case of pigmented mammary Paget's disease in 1990. 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...
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-

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**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, ×200). The tumor cells were also found in the lactiferous ducts, where they formed clusters (B) (H&E, ×200). The intraepidermal pagetoid cells and intraductal pagetoid cell were positive for cytokeratin 7 (C, D) (cytokeratin 7, ×400). In contrast, they were negative for S-100 (E) (S-100, ×200), Periodic-acid Schiff (F) (PAS, ×200), Alcian blue at PH 2.5 (G) (Alcian blue at PH 2.5, ×200), HMB-45 (H) (HMB45, ×200) and carcinoembryonic antigen (I) (CEA, ×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 disease. It was first reported in 1990 by Ho et al., and only a few such cases have been described afterwards. 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 epidermotropism.

In rare instances, malignant melanoma may affect the mammary areola, and a collision of primary disease that resembles malignant melanoma 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 epidermis. 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 and cytoplasm of the cancer cells.

The high sensitivity of cytokeratin 7 makes it useful in some cases of mammary Paget's disease. This disease should be included in the differential diagnosis of pigmented lesions on the nipple.

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 blockage of the melanocytes have been postulated as the cause for the clinical pigmentation in some cases of mammary Paget's disease. Dusty melanin has also been described within the cytoplasm of the neoplastic cells of mammary Paget's disease, without an increased number of melanocytes. Another possibility would be phagocytosis of the melanin pigment from the melanocytes by the epithelial cells of the carcinoma. 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.

**REFERENCES**

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