Pigmented Mammary Paget Disease

Dermoscopic, In Vivo Reflectance-Mode Confocal Microscopic, and Immunohistochemical Study of a Case

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Background: Pigmented mammary Paget disease represents a rare variant of mammary Paget disease that clinically and dermoscopically simulates a melanoma. We report a case of pigmented mammary Paget disease mimicking a melanoma and describe the dermoscopic, reflectance-mode confocal microscopic, histological, and immunohistochemical features.

Observations: A 70-year-old woman had a 5.5 × 4-cm pigmented plaque with a thin, scaly surface on her left breast; the plaque had slowly but progressively grown during the preceding 10 years. Dermoscopic examination showed a diffuse, light brown pigmentation with irregular black dots, small gray-blue structures, and irregular vessels. Confocal microscopic features, such as large reflecting cells with dark nuclei spreading upward in pagetoid fashion, were suggestive of melanoma. Histological evaluation integrated with immunohistochemical staining showed pigmented mammary Paget disease.

Conclusions: This case demonstrates that the diagnosis of pigmented mammary Paget disease cannot be determined by clinical examination and dermoscopy alone. Therefore, immunohistochemical staining should be performed in growing lesions with equivocal clinical and dermoscopic aspects that are characterized by abundant pagetoid infiltration in hematoxylin-eosin–stained sections to avoid overlooking pigmented mammary Paget disease.

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Pigmented Paget disease is a rare clinicopathological variant of mammary Paget disease that mimics malignant melanoma clinically, histopathologically, and dermoscopically.1-3 We report a case of pigmented mammary Paget disease that was difficult to diagnose despite the use of such advanced noninvasive diagnostic techniques as dermoscopy and in vivo reflectance-mode confocal microscopy (RCM), which have been demonstrated to improve diagnostic accuracy in dermatological oncology.4-11

REPORT OF A CASE

A 70-year-old white woman presented with a 5.5 × 4-cm itchy plaque with a thin, scaly surface on the superior quadrant of her left breast. The lesion had asymmetric, light brown pigmentation on one side and an irregularly pinkish-red coloration on the remaining area (Figure 1). The lesion had been slowly but progressively growing for 10 years. Before surgery, the lesion was examined by means of dermoscopy (FotoFinder; TechScreen Software GmbH, Bad Birnbach, Germany) and in vivo RCM (Vivascope 1000; Lucid Inc, Rochester, NY).6

On dermoscopy, the lighter portion of the lesion corresponded to a whitish-pink area with irregular linear vessels resembling an area of regression (Figure 2A), whereas the darker portion was characterized by light brown diffuse pigmentation with irregular black dots and small gray-blue structures (Figure 2B). Although the criteria were not completely specific, the dermoscopic features suggested a diagnosis of melanoma10 or lichenoid keratosis.11

According to our diagnostic protocol for dermoscopically equivocal lesions, RCM images were recorded at different levels to a maximum depth of 200 µm on the darker portion of the lesion. The superficial epidermal layers were characterized by a disarranged pattern and large, round, atypical cells with reflective cytoplasms and dark nuclei, similar to melanocytes, spreading upward in pagetoid fashion12 and intermingled with bright, reflective particles corresponding to an inflammatory infiltrate (Figure 2C). Numerous large, reflective cells with long dendritic branches within the stratum corneum were also observed (Figure 2D). At the dermoepidermal junction, small to medium-sized papillae without distinct edges were clearly observable.9 According to previously pub-
lshed data, we considered these RCM features to be suggestive of melanoma.8,9,12

Findings from histological examination with hematoxylin-eosin staining showed large atypical cells with hyperchromatic eccentric nuclei and macro nucleoli scattered throughout all levels of the epidermis. These neoplastic cells lay along and above the epidermal basal layer, sporadically arranged in small, irregular aggregates. The cells' morphologic features and their arrangement in the epidermis were similar to those seen in in situ melanomas and, to a lesser extent, in intraepithelial squamous cell carcinomas; this prompted further investigation by means of immunohistochemical staining. The malignant cells stained positively for cytokeratin MNF-116 (Figure 3C) and focally for estrogen receptor. Moreover, staining for c-erb-b2 expression was strongly positive (Figure 3B). On the other hand, results were negative for the anti–gross cystic disease fluid protein–15 monoclonal antibody, which is characteristic of apocrine differentiation. Pagetoid cells were also negative when stained for S100 protein and Melan-A, whereas dendritic cells, which were scattered throughout the superficial epidermal layers, were positive when stained for S100

Figure 1. Clinical appearance of the lesion shows an eczematous-like plaque with a thin, scaly surface and an ill-defined, irregular, light brown peripheral area. The indicated whitish-pink (arrow) and pigmented (arrowhead) areas underwent dermoscopic imaging (Figure 2A and B, respectively).

Figure 2. Dermoscopy and reflectance-mode confocal microscopy (RCM) of the lesion. A, A dermoscopic image of the whitish-pink area shows irregular linear vessels (original magnification ×20). B, A dermoscopic image of the pigmented area shows irregular black dots and small gray-blue structures (original magnification ×50). C, An RCM image shows large atypical cells (arrowheads) and bright particles within the superficial layers (original magnification ×1000). D, An RCM image shows dendritic cells (asterisk) at the stratum corneum (original magnification ×1000).
protein (Figure 3A). The main histological features together with the immunohistochemical profile of the intraepidermal neoplastic cells established a diagnosis of pigmented mammary Paget disease.

Because Paget disease can be the first sign of breast cancer, the patient underwent further clinical examination, ultrasonography, chest radiography, and mammography. No signs of intraductal or invasive breast cancer were detected. At 8 months of follow-up, the patient was still disease free.

**COMMENT**

Pigmented mammary Paget disease represents a rare variant of mammary Paget disease that is often clinically and histologically similar to melanoma.1-3 Dermoscopic results that showed a nonspecific pattern with irregularly diffuse pigmentation and regression-like structures suggested a diagnosis of melanoma have been previously reported.4 To assess a correct diagnosis for this melanocytic lesion, we used dermoscopy together with RCM, which enabled the visualization of the underlying cytological and architectural aspects at a nearly histological resolution.5-9 On RCM, the presence of large atypical cells arranged in pagetoid fashion and resembling a pagetoid melanocytosis usually seen in malignant melanocytic lesions, together with the epidermal disarrangement and papillae without distinct edges, suggested a superficial spreading melanoma.8,9,12 Hematoxylin-cosin staining alone was not sufficient to establish the correct diagnosis because the lesion was characterized by numerous pagetoid cells with unclear morphologic features. Immunohistochemical analysis provided conclusive evidence: most of the Paget cells stained positively for c-erb-b2 expression.13

Our case confirms the difficulty of making a correct presurgical diagnosis, even when using the most advanced in vivo diagnostic tools. Traditional histological analysis was also unable to define the nature of the lesion, suggesting that immunohistochemical analysis should be considered mandatory in lesions featuring a prominent pagetoid infiltration to avoid mistaking pigmented mammary Paget disease for something else and overlooking a possible unacknowledged underlying malignancy.

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