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.

Arch Dermatol. 2007;143:752-754
lished data, we considered these RCM features to be sug-
gestive of melanoma.8,9,12

Findings from histological examination with hema-
toxin-eosin staining showed large atypical cells with
hyperchromatic eccentric nuclei and macronucleoli scat-
tered throughout all levels of the epidermis. These neo-
plastic 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 melano-
mas and, to a lesser extent, in intraepithelial squamous
cell carcinomas; this prompted further investigation by
means of immunohistochemical staining. The malig-
nant cells stained positively for cytokeratin MNF-116
(Figure 3C) and focally for estrogen receptor. More-
over, staining for c-erb-b2 expression was strongly posi-
tive (Figure 3B). On the other hand, results were nega-
tive for the anti–gross cystic disease fluid protein–15
monoclonal antibody, which is characteristic of apo-
crine differentiation. Pagetoid cells were also negative
when stained for S100 protein and Melan-A, whereas den-
dritic cells, which were scattered throughout the super-
ficial epidermal layers, were positive when stained for S100

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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.\(^1,2\) Dermoscopic results that showed a nonspecific pattern with irregularly diffused pigmentation and regression-like structures suggesting a diagnosis of melanoma have been previously reported.\(^2\) 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.\(^7-9\) 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-eosin 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 pre-surgical 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.

Accepted for Publication: September 25, 2006.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Longo and Pellacani. Acquisition of data: Longo, Fantini, and Bassoli. Analysis and interpretation of data: Longo, Fantini, Cesinaro, Seidenari, and Pellacani. Drafting of the manuscript: Longo, Cesinaro, and Pellacani. Critical revision of the manuscript for important intellectual content: Longo, Fantini, Bassoli, Cesinaro, Seidenari, and Pellacani. Obtained funding: Seidenari. Study supervision: Pellacani.

Financial Disclosure: None reported.

Funding/Support: This study was partially supported by a grant from the Fondazione Cassa di Risparmio di Modena.

REFERENCES