

# ACTAS Derma-Sifiliográficas

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## CASE FOR DIAGNOSIS

### Asymptomatic Pigmentation on the Breast Pigmentación Asintomática en la Mama

#### Clinical History

A 39-year-old woman with no past history of interest consulted for progressive, asymptomatic pigmentation of the right nipple that had started 1 year earlier.

#### Physical Examination

She presented an irregular, hyperpigmented macule of bluish color affecting the right nipple (Figure 2). Irregular bluish-black pigmentation with areas of erythema and whitish areas of regression were visible on dermoscopy, with peripheral grey “salt and pepper” mottling (Figure 2). There were no other breast lesions and no palpable axillary lymph nodes.

#### Histopathology

Histological study showed the presence of cells with a large amount of clear cytoplasm and large atypical nuclei with prominent nucleoli; there were isolated cells and others grouped into small nests throughout the full thickness of the epidermis. There was a moderate lymphocytic infiltrate in the superficial dermis with abundant melanophages

and dilated capillaries (Figure 3). Immunohistochemical staining was positive for human epidermal growth factor receptor-2 (HER-2 or C-erb-B2) and negative for human melanoma black-45 (HMB-45) and cytokeratin-7 (CK-7). Due to the negativity of this last analysis, testing was requested for other epithelial markers (pancytokeratin [AE1/AE3], monoclonal cytokeratin antibody [Cam] 5.2, and epithelial membrane antigen [EMA]), all of which were positive.

#### Additional Tests

Mammography and magnetic resonance imaging of both breasts showed no evidence of disease.



Figure 1



Figure 2

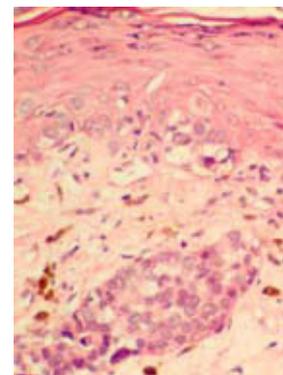


Figure 3 Hematoxylin-eosin,  $\times 100$ .

What Is Your Diagnosis?

## Diagnosis

Pigmented Paget disease of the breast.

## Clinical Course and Treatment

The nipple-areola complex was excised, revealing the presence of an infiltrating ductal carcinoma. No metastatic cells were found in the biopsy of the sentinel lymph node in the right axilla.

## Discussion

Pigmented Paget disease of the breast, first described by Pieson and Benisch in 1985,<sup>1</sup> is an uncommon clinical-pathological variant of Paget disease of the breast; just over 20 cases have been reported in the literature.<sup>1-6</sup> Pigmented Paget disease of the breast usually presents as an erythematous macule of eczematous appearance; there is a rare pigmented variant that can clinically, dermoscopically, and histologically simulate melanoma.<sup>2-6</sup> Dermoscopy reveals a nonspecific pattern with regression structures and the presence of diffuse and irregular pigmentation. This pigmentation may be secondary to a proliferation of melanocytes, to melanin phagocytosis by the pagetoid cells, or to the presence of numerous melanophages in the dermis.<sup>3</sup>

From a histological point of view it is important to establish a correct differential diagnosis with melanoma. In situ melanoma the atypical melanocytes are arranged along the dermoepidermal junction, both as nests and as individual cells and, occasionally, throughout the epidermis, whereas the cells in pigmented Paget disease of the breast are found in all the suprabasal layers of the epidermis, and the nuclei of the melanocytes show no signs of atypia or pleomorphism.<sup>3,5</sup> The definitive diagnosis of pigmented Paget disease of the breast is established by the combination of histological and immunohistochemical findings. Paget cells are positive for a number of cytokeratins (CK-7, AE1, AE3, Cam 5.2), other epithelial markers (carcinoembryonic antigen, EMA, and mucoproteins), and anti-HER-2, which is positive in 80%-90% of cases. In our patient, the lesion was clearly negative for CK-7, which has a sensitivity close to 100% in Paget disease of the breast.<sup>3,6,7</sup> In melanoma, the intraepidermal pagetoid melanocytes are characteristically positive for S-100 and HMB-45, whereas this situation is very rare in the cells of Paget disease of the breast.<sup>2-6</sup>

The differential diagnosis of pigmented Paget disease of the breast also includes pigmented carcinoma of breast, usually associated with palpable nodules or masses beneath the pigmented skin, pigmented basal

cell carcinoma, and pigmented skin metastases from carcinoma of the breast.<sup>6</sup>

We would like to highlight the importance of using histological study to establish an early diagnosis in any atypical pigmented lesion that affects the nipple-areola complex, as the clinical and dermoscopic findings do not enable us to differentiate melanoma from an epithelial tumor such as pigmented Paget disease of the breast.

## Conflicts of Interest

The authors declare no conflicts of interest.

## References

1. Peison B, Benisch B. Paget's disease of the nipple simulating malignant melanoma in a black woman. *Am J Dermatopathol.* 1985;7:165-9.
2. Requena L, Sanguenza M, Sanguenza OP, Kutzner H. Pigmented mammary Paget disease and pigmented epidermotropic metastases from breast carcinoma. *Am J Dermatopathol.* 2002;24:189-98.
3. Petersson F, Ivan D, Kazakov DV, Michal M, Prieto VG. Pigmented Paget disease. A diagnostic pitfall mimicking melanoma. *Am J Dermatopathol.* 2009;31:223-6.
4. Oiso N, Kawara S, Inui H, Kawada A. Pigmented spots as a sign of mammary Paget's disease. *Clin Exp Dermatol.* 2009;34:36-8.
5. Beltran C, Orlandini V, Stokkermans-Dubois J, Vergier B, Fauchier JM, Doutre MS, et al. Pigmented Paget's disease of the breast. *Ann Dermatol Venereol.* 2008;135:213-6.
6. Longo C, Fantini F, Cesinaro AM, Bassoli S, Seidenari S, Pellacani G. Pigmented mammary Paget disease: dermoscopic, in vivo reflectance-mode confocal microscopic, and immunohistochemical study of a case. *Arch Dermatol.* 2007;143:752-4.
7. Gutiérrez-Pascual M, Gómez-de la Fuente E, Vicente-Martín FJ, Pinedo-Moraleda F. Enfermedad de Paget extramamaria: descripción de dos casos tratados con cirugía micrográfica de Mohs. *Actas Dermosifiliogr.* 2009;100:239-40.

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