

UC Davis

Dermatology Online Journal

Title

Pigmented lesion of the nipple - a clinicopathological challenge

Permalink

<https://escholarship.org/uc/item/1qv340vp>

Journal

Dermatology Online Journal, 22(10)

Authors

Vide, Júlia
César, Artur
Rodrigues Pereira, Pedro
et al.

Publication Date

2016

DOI

10.5070/D32210032907

Copyright Information

Copyright 2016 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

Photo vignette

Pigmented lesion of the nipple - a clinicopathological challenge

Júlia Vide¹, Artur César¹, Pedro Rodrigues Pereira², Filomena Azevedo¹

Dermatology Online Journal 22 (10): 14

¹ Serviço de Dermatologia e Venereologia, Centro Hospitalar de São João EPE, Porto, Portugal

² Serviço de Anatomia Patológica, Centro Hospitalar de São João EPE, Porto, Portugal

Correspondence:

Júlia Vide
juliavide@gmail.com

Abstract

Differential diagnoses of pigmented lesions of the nipple include melanocytic nevus, melanosis of the nipple, seborrheic keratosis, pigmented basal cell carcinoma, melanoma and Paget disease. The histologic exam with appropriate immunohistochemistry is a fundamental tool to achieve a correct diagnosis. We present a patient with a pigmented lesion of her right nipple revealing mammary Paget disease and elucidate diagnostic obstacles and prognostic importance of early breast cancer detection.

Key-words: Mammary Paget's disease; melanoma; tumor biomarkers; immunohistochemistry

Case synopsis

A 42-year-old woman was referred to our department regarding a nonpruritic pigmented lesion on the right nipple. That lesion had been slowly growing for 2 years. There was no excoriation of the nipple, no retraction, no palpable masses, and no lymphadenopathy.

Physical examination revealed an irregular hyperpigmented macule, 10x8 mm, involving the lateral quadrants of the right nipple (Figure 1).



Figure 1. Dark brown pigmented asymmetric macule in the right nipple.

On dermoscopy, a non-specific brown reticular pigmentation was observed (Figure 2).

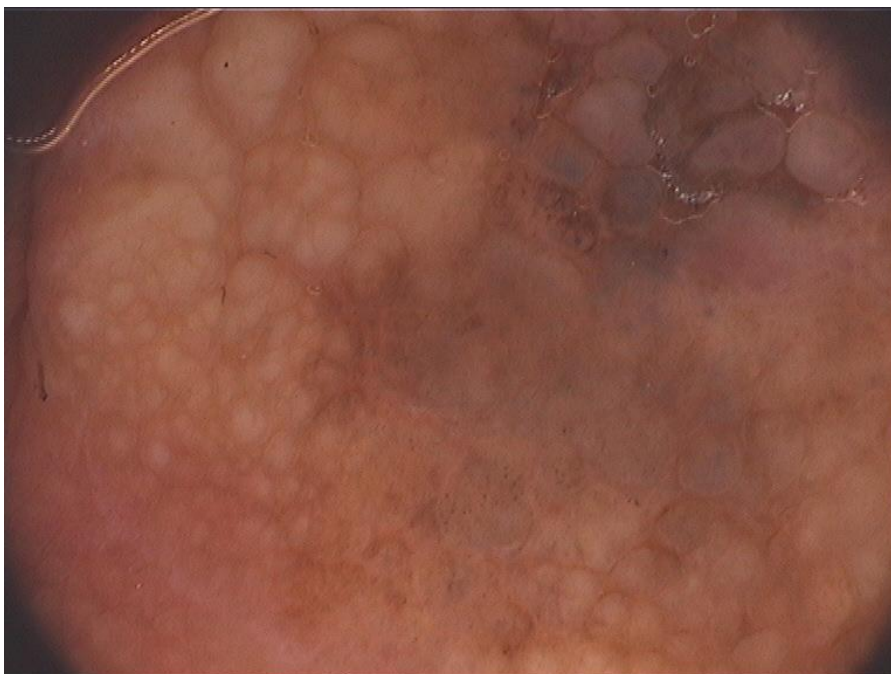


Figure 2. Unspecified brown reticular pigmentation on dermoscopy.

The skin biopsy disclosed a junctional proliferation characterized by atypical cells with enlarged nuclei and pale cytoplasm, some of which contained brown melanin granular pigment, with intraepithelial dissemination and no invasion. Also, rare mitosis (1/mm²), a discrete lympho-plasmocytic infiltrate, and melanophages were observed (Figure 3).

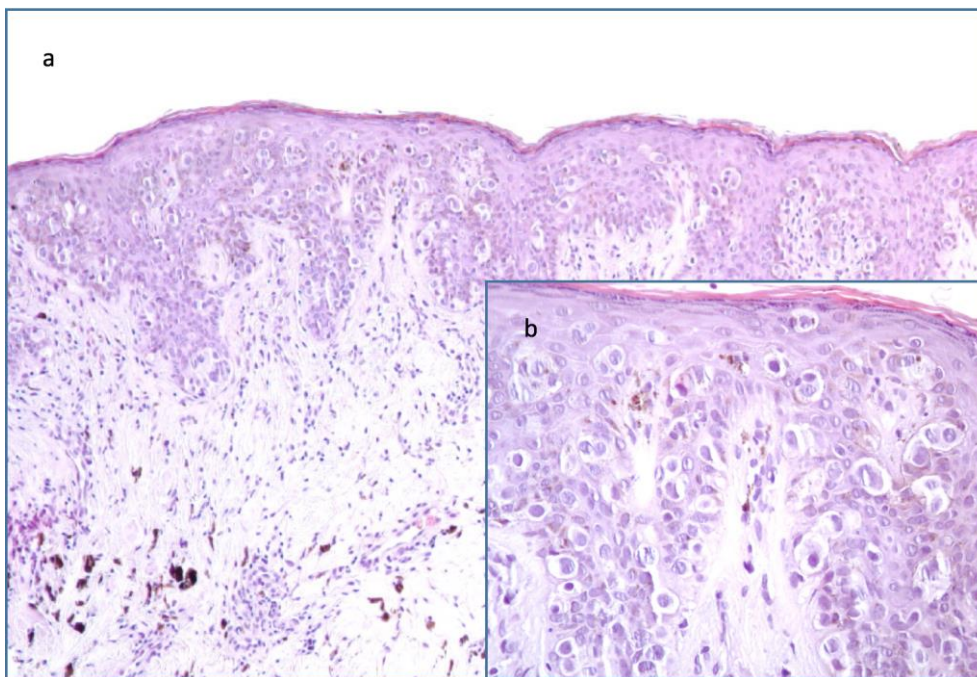


Figure 3. A, Discrete lympho-plasmocytic infiltrate and disperse melanophages. Hematoxylin-eosin, original magnification $\times 100$, and **B,** $\times 200$.

Immunohistochemically, tumor cells were positive for cytokeratin-7, HMB-45, and S-100 (Figure 4). These confirmed pigmented mammary Paget disease. Mammary imaging was performed (ultrasound, mammography and magnetic resonance imaging), showing no suspected nodules or calcifications.

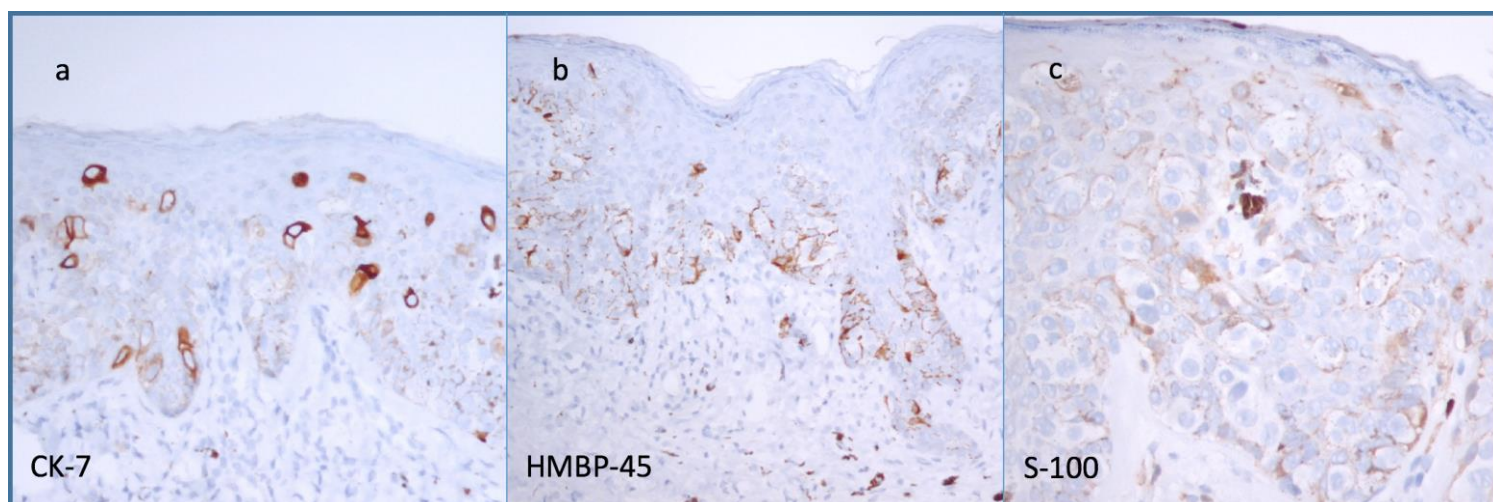


Figure 4. A, Immunohistochemistry positive for CK-7. **B,** Immunohistochemistry positive for HMBP-45, and **C,** Immunohistochemistry positive for S-100.

Therapeutic excision was decided, including the entire nipple areolar complex and attached subcutaneous tissue. Histologic exam revealed an *in situ* ductal breast carcinoma.

Discussion

Mammary Paget disease (MPD) represents 1-2% of all breast cancers. Most often it results from intraductal spread of ductal carcinoma cells into the skin, but it can also be caused by direct invasion of the epidermis by infiltrating carcinoma cells [1-3].

MPD usually presents as an erythematous patch or plaque, typically eczematous in appearance. An underlying mass is palpable in 45% of cases [1-3].

Infrequently, MPD can present as a pigmented lesion that may clinically, dermoscopically, and histologically simulate malignant melanoma [4, 5].

Different mechanisms can account for the occurrence of pigmented MPD (PMPD): increased number of dendritic melanocytes between carcinomatous cells, phagocytosis of melanin by atypical cells, and the presence of melanophages in the reactive dermal infiltrate [2].

Histological exam, application of a panel of antibodies, and careful analysis of the immunohistochemical findings are recommended to clarify the expression pattern of the malignant cells (epithelial or melanocytic) to achieve a correct diagnosis. MPD typically has positive epithelial markers and negative melanin markers [2, 6, 7].

Anti-cytokeratin 7 has the highest diagnostic accuracy for MPD [2, 8]. It is important to note that S-100 and HMBP-45, melanocytic markers that have been used to differentiate pigmented mammary Paget disease from malignant melanoma, are sometimes not reliable, as in our case [9, 10].

In conclusion, pigmented lesions of the nipple should be carefully examined. It is important to include PMPD in the differential diagnostics, because it can mimic pigmentation after inflammation, seborrheic keratosis, junctional nevus, pigmented basal cell carcinoma, or malignant melanoma. PMPD is an uncommon diagnosis still more usual than melanoma of the nipple. Therefore, it should always be remembered.

Our case confirms the difficulty of establishing a correct diagnosis with hematoxylin-eosin staining alone. Immunohistochemical analysis, including anti-cytokeratin 7, should be considered mandatory in lesions featuring a prominent pagetoid infiltration, to avoid mistaking PMPD for melanocytic or other tumors.

References

1. Sheen-Chen SM, Chen HS, Chen WJ, et al. Paget disease of the breast—an easily overlooked disease? *J Surg Oncol*. 2001;76:261-5. [PMID: 11320517]
2. Petersson F, et al. Pigmented Paget disease – a diagnostic pitfall mimicking melanoma. *Am J Dermatopathol*. 2009;31:223. [PMID: 19384061]
3. Requena L, et al. Pigmented mammary Paget disease and pigmented epidermotropic metastases from breast carcinoma. *Am J Dermatopathol*. 2002;24:189-98. [PMID: 12140433]
4. Pizzichetta MA, et al. Pigmented mammary Paget's disease mimicking melanoma. *Melanoma Res*. 2004;14:S13-5. [PMID: 15057051]
5. Meyer-Gonzalez T, et al. Pigmented mammary Paget disease mimicking cutaneous melanoma. *Int J Dermatol*. 2010;49:59-61. [PMID: 20465614]
6. Vani BR, et al. Pigmented Paget's disease of nipple: A diagnostic challenge on cytology. *J Cytol*. 2013;30(1):68-70. [PMID: 23661948]
7. Park JS, et al. Pigmented mammary Paget disease positive for melanocytic markers. *J Am Acad Dermatol*. 2011;65:247-9. [PMID: 21679843]
8. Smith KJ, Tuur S, Corvette D, et al. Cytokeratin 7 staining in mammary and extramammary Paget's disease. *Mod Pathol*. 1997;10:1069-74. [PMID: 9388055]
9. Bonetti F, et al. Breast carcinoma with positive results for melanoma marker (HMB-45). HMB-45 immunoreactivity in normal and neoplastic breast. *Am J Clin Pathol*. 1989;92:491-5. [PMID: 2552794]
10. Dwarakanath S, et al. S-100 protein positivity in breast carcinomas: a potential pitfall in diagnostic immunohistochemistry. *Hum Pathol*. 1987;18:1144–8. [PMID: 2824323]