

Paget's Disease: The importance of the specialist

Doença de Paget: a importância do especialista

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Abstract: A twenty-six-year-old woman with a two-year history of an erythematous, scaly lesion on the left nipple was being followed up by her gynecologist and treated using a topical corticoid for chronic eczema albeit with no improvement. She was referred to this department where a diagnosis of Paget's disease of the breast associated with a ductal carcinoma in situ was made. Paget's disease is uncommon prior to the fourth decade of life and the great majority of cases are associated with breast carcinomas. Differential diagnosis must be made between this condition and nipple eczema. As shown in the present case report, late diagnosis results in poor prognosis and higher morbidity since mutilating procedures then become necessary.

Keywords: Breast tumors; Paget's disease, breast; pathology.

Resumo: Mulher, 26 anos, com história de lesão eritemato-escamosa no mamilo esquerdo, há dois anos. Era acompanhada pelo seu ginecologista como eczema crônico em uso de corticoide tópico, sem melhora. Encaminhada ao nosso serviço, realizou-se o diagnóstico de doença de Paget mamária associada ao carcinoma intraductal. Antes da quarta década de vida, a doença de Paget é rara, e, na grande maioria dos casos, está associada ao carcinoma mamário. Essa enfermidade constitui diagnóstico diferencial obrigatório do eczema do mamilo. O diagnóstico tardio, como no caso relatado, implica em pior prognóstico e aumento da morbidade, já que terapêutica mutilante é necessária.

Palavras-chave: Doença de Paget mamária; Neoplasias da mama; Patologia

INTRODUCTION

Paget's disease of the breast presents as an erythematous, scaly lesion affecting the nipple and the areola and extending to the periareolar region. Nipple retraction may occur, a signal that is highly suggestive of the disease. In the great majority of cases, Paget's disease is associated with ductal carcinoma of the breast, as occurred in the case presented here. ¹

This condition has been documented in patients of 26 to 82 years of age; however, it occurs predominantly in patients of 40-60 years of age and is rarely found in younger patients, highlighting the uncommonness of the present case. ² The occurrence

of this disease in males is rare. ³ The treatment of Paget's disease associated with ductal carcinoma in situ is segmental resection followed by radiotherapy or total mastectomy ⁴, this latter therapeutical option being used in the current case due to the delay incurred in reaching diagnosis.

CASE REPORT

A 26-year-old, white female patient presented with a two-year history of a pruriginous lesion on her left breast. She was in treatment with her gynecologist for chronic eczema. Topical corticoids were used

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albeit without improvement.

She was referred to this department, where examination revealed an erythematous, crusted, scaly lesion on her left nipple, extending into the areola, with no sign of any palpable swelling in the lymph nodes of the axilla (Figures 1 and 2). With a clinical hypothesis of Paget's disease, histopathology of the areolar lesion was performed, the results of which showed an intraepidermal proliferation of round cells with large clear cytoplasm and large nuclei, with no intercellular bridges (Figures 3 and 4). Immunohistochemistry showed these cells to be negative for S-100, eliminating the possibility of melanoma. They were positive for C-erb2, an immunohistochemical marker of poor prognosis in breast cancer.⁵

The patient reported no family history of Paget's disease or any other breast carcinoma. Mammography showed grouped microcalcifications on the left breast, classified as BI-RADS IV. Chest x-ray and breast ultrasonography revealed no abnormalities. Investigation of the sentinel lymph node was negative. The patient was submitted to a total mastectomy. Pathology revealed Paget's disease of the nipple associated with multiple foci of ductal carcinoma in situ, the largest measuring 2.5 cm in diameter and consisting of the solid comedo type, nuclear grade 3, in the principal ducts. Microsurgical reconstruction of the left breast was performed using tissue removed from the abdomen. The patient has been followed up for 10 months and shows no signs of recurrence or metastases.

DISCUSSION

There are two forms of Paget's disease: Paget's disease of the breast and extramammary Paget's disease. The breast form of the disease is associated with



FIGURE 2: Erythematous, scaly, crusted lesion on the left breast

ductal carcinoma in situ, which extends to the epidermis by means of a milk duct.¹⁻³ In the extramammary form, Paget's cells are believed to originate in the apocrine gland, the disease affecting the vulvar, anal, genital and axillary regions.³

Two theories have been formulated to explain Paget's disease of the breast:

The epidermotropic theory: Paget's cells originating in the apocrine duct are transformed into a ductal carcinoma and migrate to the epithelium of the nipple. This would explain the cases of Paget's disease with an underlying intraductal carcinoma.²

The transformation theory: Paget's cell is a transformed malignant keratinocyte, which suggests that Paget's disease is an independent carcinoma in situ. This would explain the cases of the disease in which no identifiable breast carcinoma is present, as is



FIGURE 1: Erythematous, scaly lesion on the left breast

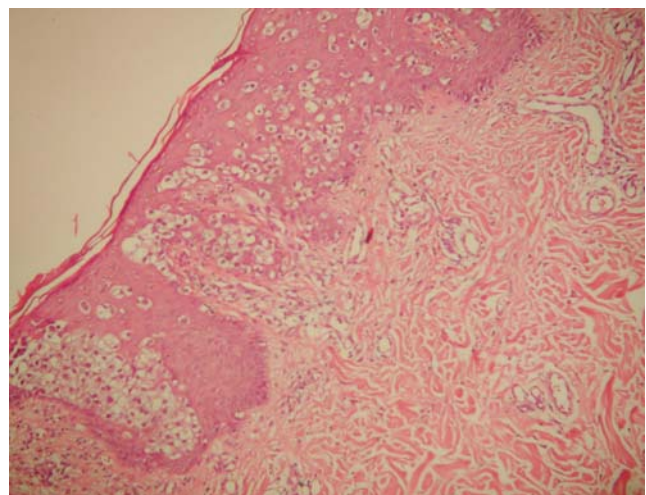


FIGURE 3: Large cells, clear cytoplasm, singly or in groups between squamous cells. (H&E, 40x)

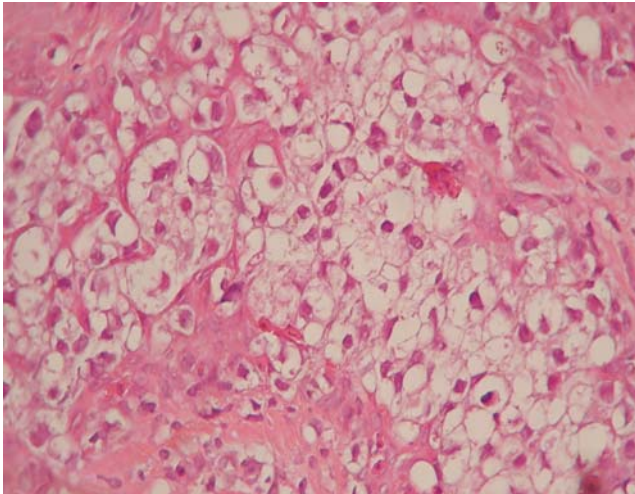


FIGURE 4: Round cells with clear cytoplasm and large nuclei. (H&E, 400x)

found in some rare cases.²

Since Paget's disease presents with eczematous lesions, the principal differential diagnosis is with eczema. It differs from eczema because it is unilateral, with less intense pruritus, showing progression and an inadequate response to corticotherapy, as in the present case. Other differential diagnoses are psoriasis and superficial basal cell carcinoma. When the lesion is pigmented, differential diagnosis is made with melanoma.^{2,6} Experience shows that delayed diagnosis in Paget's

disease of the breast is due to diagnostic error.³

When Paget's disease is suspected, mammography should be carried out in addition to histopathology of the nipples. In such cases, histopathology shows large, round cell intraepidermal neoplasia, with no intercellular bridges. The cells present clear cytoplasm and large nuclei, and are either arranged singly or in groups. Hyperkeratosis may occur accompanied by parakeratosis, papillomatosis and proliferation of epidermal ridge. In more advanced stages, the epidermis becomes atrophic.^{1-3,7} Paget's cells are PAS-positive and dopa-negative. In cases of uncertainty with respect to diagnosis, immunohistochemistry may be performed with positivity for the AE1, AE3, CEA and EMA markers.⁶

Early diagnosis reduces morbidity and improves prognosis. Segmental resection followed by supplementary radiotherapy is preferred in cases of ductal carcinomas in situ of less than 2 cm in diameter and clear surgical margins. Total mastectomy is indicated in cases of Paget's disease associated with an extensive ductal carcinoma in situ, i.e. tumors of more than 2 cm in diameter or when it is impossible to be certain that the margins are clear because of the extent of the tumor or its multicentricity,⁴ this having been the indication for total mastectomy in the current case. Early diagnosis might have avoided this mutilating therapy.⁴ □

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