An unusual presentation of mammary Paget's disease with a 12-year duration and no palpable mass

Reza Yaghoobi, MD [1]
Nestaran Ranjbari, MD [2]
Farzaneh Alamshahi, MD [1]

1. Department of Dermatology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Department of Pathology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Corresponding author:
Reza Yaghoobi, MD
Department of Dermatology, Imam Hospital, Ahvaz, Iran
Tel: 00989161186021
Fax: 00986132222114
E-mail: yaghoobi_rz@yahoo.com

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Paget's disease of the nipple is an unusual manifestation of breast cancer. Most cases of mammary Paget`s disease are associated with an invasive or in situ breast tumor, even with no mass observed in mammography imaging. Very rarely does Paget's disease occur in the absence of any underlying neoplasia .Herein, we report an 82-year-old woman with an unusual presentation of mammary Paget's disease with a 12-year duration, and no palpable mass, density or calcification in imaging assessments. Immunohistochemistry showed that the tumor cells stained positive for cytokeratin-7, and Her-2-neu, yet negative for S-100, HMB-45, CEA, and P63. Skin biopsy and immunohistochemistry findings corresponded with Paget's disease.

Keywords: Breast, mammary, Paget's disease

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INTRODUCTION

Paget's disease of the nipple is an unusual appearance of breast cancer, accounting for 1-4% of breast malignancies [1,2]. This disease is almost always a presentation of underlying breast carcinoma with a prevalence rate of 67-100% [1-4]. Recent investigations have reveal that Paget's disease of the nipple may be associated with poor prognosis in breast cancer patients [2]. Paget's disease alone (without a lump) encompasses nearly 2% of all cases of breast malignancy [5].

It is not frequent to have invasive mammary Paget's disease without an underlying intraductal carcinoma in situ (DCIS) or invasive breast carcinoma. Hanna *et al*. cited only three cases of invasive mammary Paget's disease with no underlying breast malignancy [6].

Paget's disease is generally associated with eczematous crusted or excoriated gray white plaques [7]. We report an unusual presentation of a 12-year-old mammary Paget's disease, without underlying breast carcinoma on clinical and imaging examination.

CASE PRESENTATION

An 82-year-old woman was referred to our dermatology clinic with a right breast discoloration which she had had for 12 years. The lesion appeared in the right nipple and extended to the entire parts of the breast, yet nipple discharge and itching were not present. Familiar anamnesis was negative for breast cancer. No therapeutic responses were observed with topical steroids, antibiotics, and antifungal agents. On examination, an extensive violaceous scaling patch with atrophy, and no ulcer or discharge, was observed on the entire surface of the right breast (Figure 1). In addition, areole and nipple complex had been completely destroyed without any breast lump. Bilateral axillary lymph node enlargement was not observed, and the left breast and other organs were normal. Breast lesion biopsy specimen indicated the underlying foci of

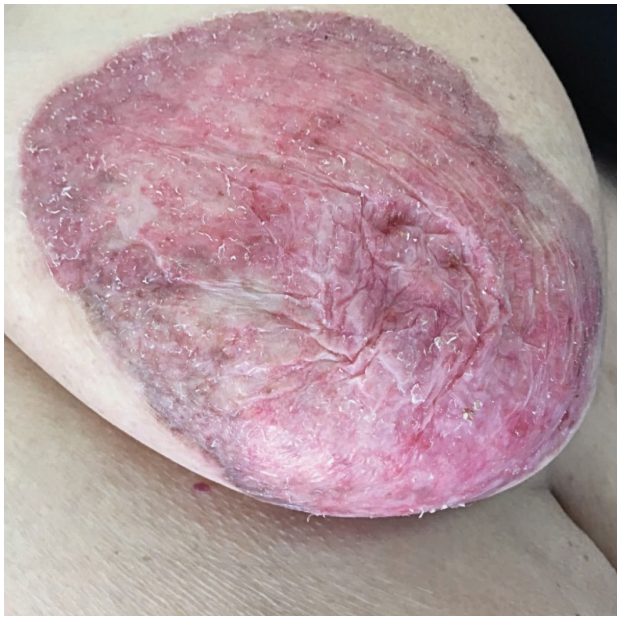

Figure 1. An extensive violaceous scaly patch with atrophy on the whole surface of the right breast.

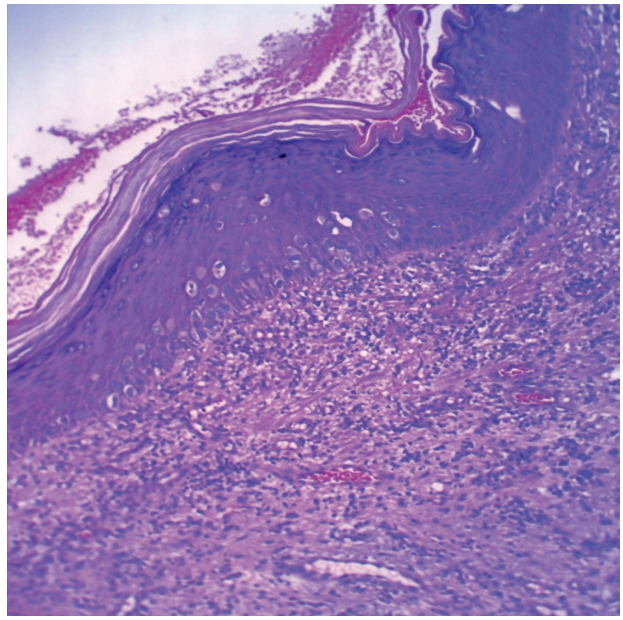

Figure 3. Paget`s cells with abundant pale cytoplasm and large pleomorphic nuclei arranged singly and in small groups in the lower and middle parts of epidermis (H&E ×200).

acanthosis, hyperkeratosis, and large pale cells with prominent nuclei diffusely or focally infiltrating the epidermis. The dermis showed reactive changes (plasma cell and lymphocyte infiltrations), formation of new capillaries, and hyperemia (Figures 2 and 3). Immunohistochemistry showed that the tumor cells stained positive for cytokeratin-7, and Her-2-neu, but negative for S-100, HMB-45, CEA, and P63. All these findings corresponded with Paget's disease. Mammography did not demonstrate discrete abnormalities such as mass or cystic lesion. In ultrasound imaging, bilateral breast parenchyma proved normal and cystic or solid lesions were not observed. Furthermore, right breast parenchyma was normal in the site of skin erythema, without any mass or inflammation. Laboratory tests indicated mild normochromic microcytic anemia, while other hematologic and serologic tests were normal. It is to be noted that the patient refused to undergo MRI Finally, the patient was referred to a surgeon for mastectomy, yet she did not accept it. After a one-year follow-up, the general condition of the patient was good, and the right breast skin lesion showed only a small thickness.

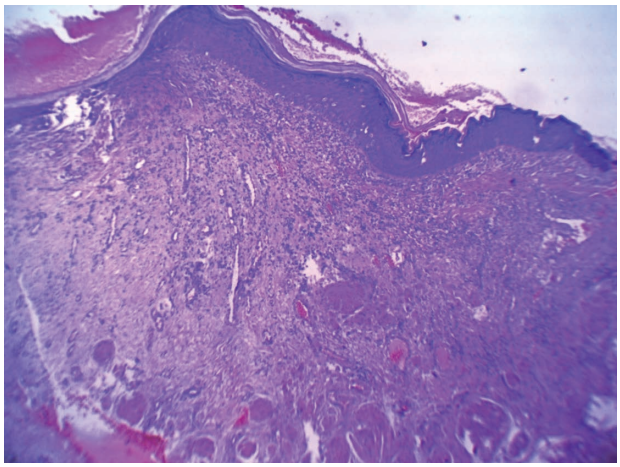

Figure 2. Paget`s cells in the epidermis. Dermis shows inflammatory cell infiltration and vascular proliferation without evidence of malignant cells (H&E ×100).

DISCUSSION

Characterized by the infiltration of neoplastic cells in the nipple epidermis [8], Paget's diseaseis divided into three categories: *(a)* Paget's disease of the nipple without DCIS; *(b)* Paget's disease of the nipple with associated DCIS in the underlying lactiferous ducts of the nipple-areolar complex; and *(c)* Paget's disease of the nipple with associated DCIS in the underlying lactiferous ducts of the nipple-areolar complex and related DCIS or invasive breast cancer in other parts of the breast, at least 2 cm away from the nipple-areolar complex [4]. Paget's disease pathogenesis is controversial and supported by two diverse theories: intraepidermal transformation hypothesis, and the most reliable

epidermotropic theory which is associated with an underlying carcinoma [8]. In very few cases of Paget's disease is there an underlying breast cancer, and if a tumor is present, it is not related with the disease in the nipple. In these cases, nipple skin cells may independently change into cancer cells, a view supported by the results of ultrastructural studies, which have revealed a desmosomal connection between Paget cells and adjacent keratinocytes in the epidermis. This finding is against the migratory nature of the epidermotropic theory which is also supported by the existence of intermediate cells with features of both keratinocytes and Paget cells [4]. Although the diagnosis of Paget's disease is usually based on clinical findings [3], imaging features can complement the confirmation of the diagnosis. Exfoliative cytology, which displays Paget cells, may be valuable, yet negative results can happen. Surgical biopsy is the diagnostic standard [4], and mammography conduces to finding the malignancy. The sensitivity of the latter seems to be considerably higher in patients with palpable mass compared to patients with a disease confined to the nipple. Ultrasound (US) should be considered as a part of the initial evaluation, particularly when the results of mammography are negative [4]. Because mammography and US may not show breast lesions even clinically suggestive for Paget's disease, MRI is employed to depict the lesions particularly in patients without palpable lump [3]. MR imaging plays a major role in the preoperative evaluation of patients with nipple-areolar complex and underlying breast cancer, specifically when the results of mammography or US are negative. MRI has a 95% sensitivity, while mammography has a 70% sensitivity in the detection of breast lesions [8].

Mastectomy, with or without axiliary dissection, is considered as the standard treatment in patients with a long-duration Paget's disease [3,4,9]. The 5-year overall survival chances of patients with palpable masses are considerably lower than those with palpable masses. A similar difference is observed between Paget's disease with DCIS and patients with invisible cancer [2].

CONCLUSION

Our patient is reportable owing to the following points: 1) a prolonged course of 12 years and a good general condition which is not very common, 2) the notable extensive dissemination to the entire right breast skin and the destruction of nipple and areole, and 3) the remarkable absence of palpable mass and underlying malignancy in clinical, histological, and radiologic examinations.It is supposed that the patient had a form of Paget's disease without DCIS, associated with a prolonged course and good prognosis.

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Conflict of Interest: None declared.

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