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Paget disease of the male breast

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Abstract

Paget disease of the breast is an uncommon tumor of the nipple-areola complex that usually presents as an erythematous and erosive lesion. We report the case of a 61-year-old man that presented with a three-year history of an erythematous lesion of the right areola, first treated with topical corticosteroids without benefit. He was then referred to our dermatology department and the clinical suspicion of Paget disease was considered. The diagnosis was later confirmed by biopsy. This case report highlights the importance of clinical recognition of this entity along with other diseases that mimic these skin changes in order to allow earlier diagnosis and proper follow-up.

axillary nodes or other tangible swellings.

Mammography showed thickening of the right nipple and a diffuse retromamillary density of 8 mm in depth with no differentiated nodules. Ultrasonography only evidenced thickening of the right nipple.

Given the clinical suspicion of Paget disease, we performed a skin biopsy that confirmed the clinical diagnosis. Immunohistochemical analysis showed expression of cytokeratin 7 (CK7), gross cystic disease fluid protein 15 (GCDFFP-15), and mammaglobin in the neoplastic cells. The patient underwent right mastectomy with sentinel node biopsy. Histopathological examination of the surgical specimen showed Paget disease with foci of invasion of the superficial dermis and high-grade ductal carcinoma in the milk ducts. There was overexpression of Her-2 and absence of lymph node involvement. Testing for BRCA2 gene mutation was negative.

Keywords: Paget disease, breast, male

Introduction

Paget disease is a rare type of cancer that affects the nipple-areola complex and usually occurs with an underlying in situ or invasive carcinoma of the breast [1, 2]. It is clinically similar to other pathologies with skin involvement, which often delays the diagnosis [1].

Case Synopsis

We describe the clinical case of a 61-year-old man with a right areolar plaque, initially diagnosed as eczema. It was treated with topical corticosteroids without evident benefit. Since he had no improvement with previous therapies, he was referred to our dermatology department 3 years later. The patient had no personal or family history of malignancies. Clinically, there was an erythematous and erosive plaque of the right areola with nipple destruction and gynecomastia (**Figures 1, 2**). There were no palpable



Figure 1. Erythematous and erosive plaque of the right areola with nipple destruction



Figure 2. Ulcerated area in the lower right quadrant of the right areola after removal of surface crusting

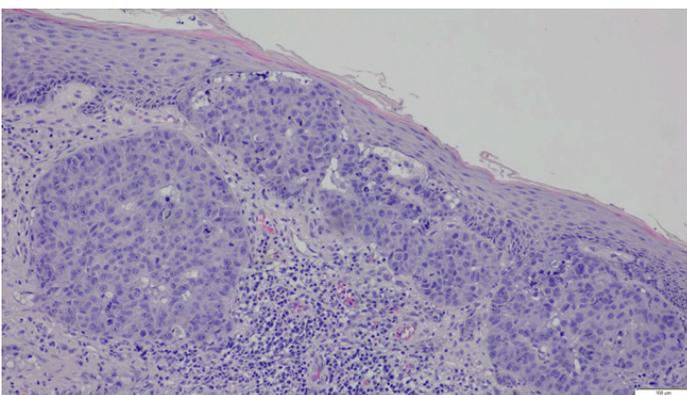
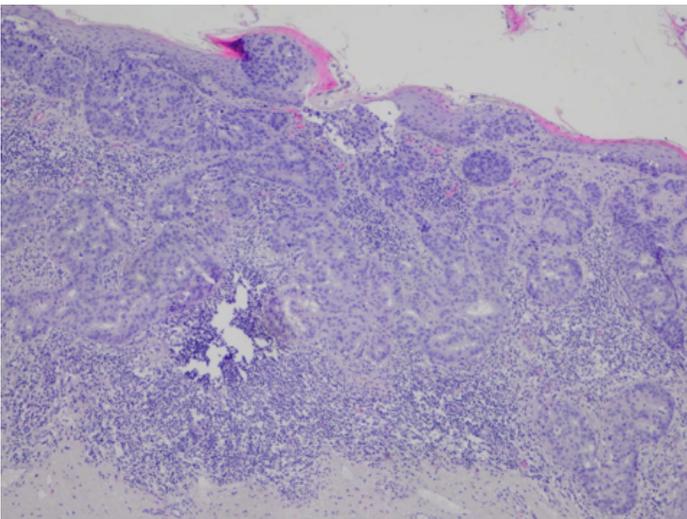


Figure 3. Histologically there is involvement of the epidermis by Paget cells and the presence of high-grade ductal carcinoma in the dermis. A, 100x; B, 200x; H&E.

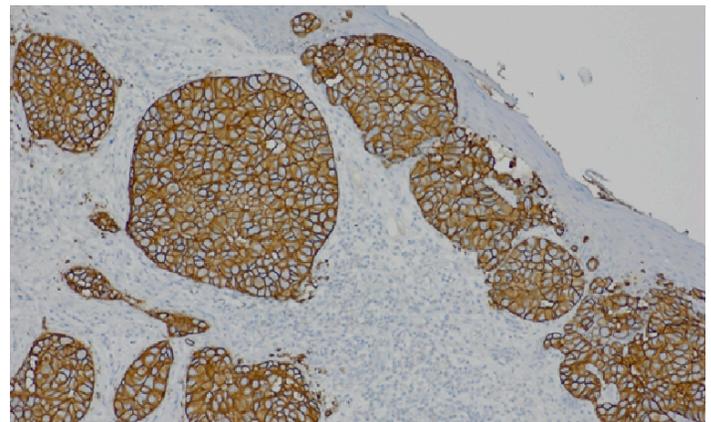
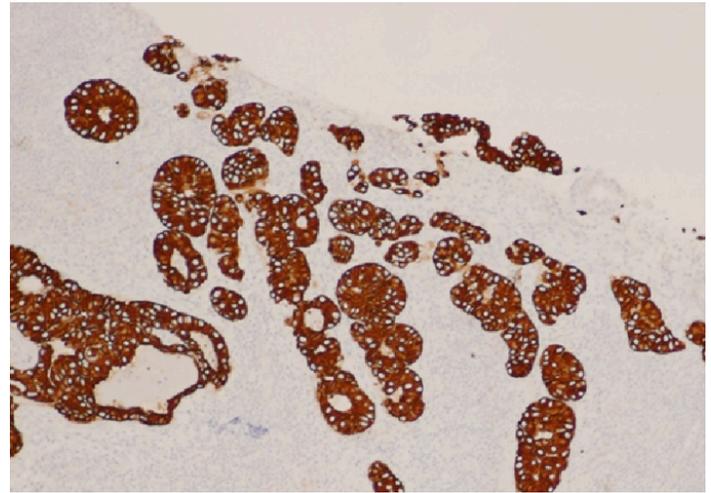


Figure 4. The immunohistochemical study showed overexpression of CK7 (A, 100x) and Her2 (B, 200x).

After 18 months, the patient had no recurrence of the disease.

Case Discussion

Paget disease was first described in 1874 by James Paget as an erosion of the areola and nipple with concomitant breast cancer [3-5]. It represents less than 5% of breast cancers and less than 1% of male cases [1, 3, 6, 7]. This is an extremely rare form of breast cancer in men whose average diagnostic age is 60-years-old [3].

Paget disease of the breast clinically presents as an erythematous lesion of the nipple with irregular edges associated with slight desquamation [2, 8-10]. It can evolve to crusting and eventually ulceration [2, 9]. In approximately half of the patients the condition has no associated symptoms [1] and is usually unilateral [2, 9]. During the course of the disease, the symptoms may include pruritus and pain [9].

The disease can be associated with invasive carcinoma, with in situ ductal carcinoma, or without any of the prior [4, 7, 11]. The prognosis is determined by the degree of invasion [4, 6, 7, 11]. In most of the cases, it presents with an in situ or invasive carcinoma [6, 8, 9, 12, 13].

Approximately 50% of patients show a palpable mass on physical examination; mammography and skin biopsy are crucial for the diagnosis [4, 6, 8]. However, a mammogram without evidence of a lesion does not exclude the presence of the disease [9]. In these situations, ultrasonography is an alternative in the detection of the tumor [2, 9]. On the other hand, magnetic resonance imaging is considered an effective diagnostic modality in the detection of clinical and mammographically occult cancers [2, 8, 9]. It is also a method to consider in the preoperative evaluation, especially if conservative surgery is an option [8]. Ninety percent of patients with a palpable swelling or radiographically identified mass have an underlying invasive carcinoma [4, 8].

Histologically, Paget disease is characterized by the presence of malignant cells, called Paget cells, in the epidermis, preferentially in the basal layer [2, 8, 12]. The underlying dermis has reactive changes [2, 9]. Ulceration may arise in later stages [2, 9]. Hyun-Woo Lee et al. suggested that the invasion of the dermis by Paget cells is possible, although it is a rare event [11] that occurred in our patient.

An immunohistochemical study is important in the diagnosis of the disease and shows overexpression of CK7 and no reactivity to other cytokeratins such as 10, 14 and 20 [2, 9]. Paget cells may express other antigens such as glandular epithelial membrane antigen, carcinoembryonic antigen, GCDFP-15, and other mucins [2, 9, 12]. Some tumors express Her-2, an oncoprotein that seems to promote the proliferation of neoplastic cells [2, 4].

The mutation of BRCA-2 gene predisposes to breast cancer in males, reaching 4% of prevalence in the absence of family history [4].

Risk factors for Paget disease in males include age, testicular disease, infertility, obesity, and cirrhosis [4]. Gynecomastia is not considered a risk factor for

breast cancer in men [4].

The similarities with inflammatory and infectious diseases as well as partial response to application of topical corticosteroids may delay the diagnosis and worsen the prognosis of these patients [3, 8, 9]. The persistence of skin changes without apparent cause should raise the suspicion of Paget disease and encourage further investigation [1, 9].

Poor prognostic factors include the presence of a palpable mass, lymph node involvement, histological type of tumor, and age below 60 years [2, 9]. Despite clinical and histological similarities in both sexes [9, 12], some authors consider that the disease has a worse prognosis in men with a survival rate between 20 and 30% at 5 years [2, 3, 9].

Mastectomy with or without lymph node biopsy was considered the standard of care in Paget disease [8]. More recently, and with early diagnosis of the disease, conservative surgery has proven to be a viable alternative to mastectomy since in most patients the malignancy is confined to the central quadrant of the breast [8, 9, 12]. After conservative surgery, monitoring of the patient is mandatory with frequent imaging controls [2].

Conclusion

This case highlights the importance of timely diagnosis of Paget disease, regardless of the gender, particularly in the presence of unilateral, inflammatory, and persistent lesions. Furthermore, an early referral to the dermatology department is essential, allowing early diagnosis and proper follow-up.

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