

Extramammary Paget's Disease Presenting as a Cutaneous Lesion on the Breast

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Abstract

Extramammary Paget's Disease (EMPD) is an uncommon malignancy in apocrine rich skin commonly presenting as an irregular pruritic plaque. While EMPD has been noted to have clinical and histological features similar to Mammary Paget's disease (MPD), an important distinction is that MPD exclusively follows a progression first involving the nipple and extending to the areola with the possibility of extending further into the surrounding skin.

In order to properly diagnosis EMPD histologic features and immunophenotyping becomes very important with identification of Paget cells. We present the first case of primary EMPD of the breast.

Keywords: Extramammary, Pagets disease, Breast cancer, Cutaneous breast lesion

Introduction

A 63-year-old woman with multiple medical comorbidities was referred for consultation after screening mammography demonstrated densities in the medial aspect of both breasts. Subsequent bilateral ultrasound suggested these masses to be complex cysts and biopsy were deferred with plans for short-term follow-up. Physical examination was unremarkable with the exception of a 4 by 6 cm area of excoriation in the right upper medial quadrant, with no associated palpable masses or lymphadenopathy. The plaque noted in the upper inner aspect of the right breast was hypo pigmented with surrounding erythema. There was no involvement of the nipple or areola complex (Figure 1). No additional focal abnormalities were visualized in either breast. An MRI was suggested, but deferred due to kidney disease.

The patient underwent a punch biopsy which revealed cells with pale cytoplasm and large pleomorphic nuclei at all levels of the epidermis with scattered mitotic figures (classic Paget's cells)- (Figures 2 and 3). Paget's disease with lateral margin involvement with Pagetoid spread of breast cancer was noted despite the lack of nipple or areola involvement as seen with typical Paget's disease. The pathology report was consistent with atypical extramammary Paget's disease and immunohistochemical analysis ruled



Figure 1. A 4 by 6cm hypopigmented plaque in the right upper medial quadrant of the breast, with surrounding erythema and no involvement of the nipple and areolar complex.

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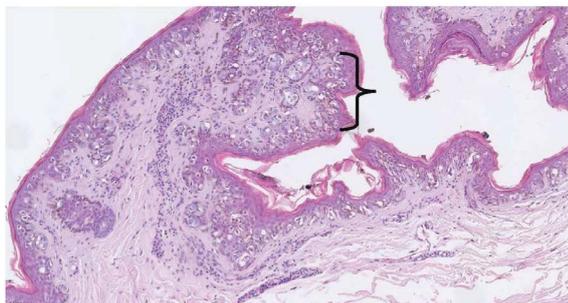


Figure 2. Extensive cutaneous involvement by Pagetoid cells (bracket). Without clinical and radiological evidence of underlying breast primary, this represents extensive cutaneous involvement by extramammary Paget's disease. (magnification 10x).

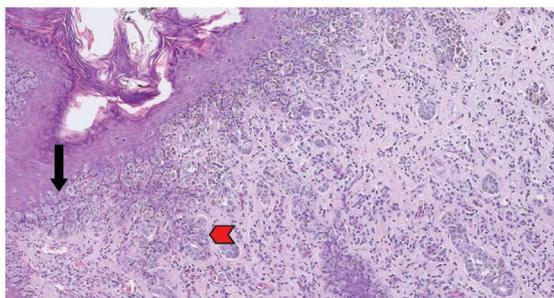


Figure 3. Involvement of epidermis (arrow, back) and epidermal appendages (arrowhead, red) by extramammary Paget's disease. The Paget's cells were immunoreactive for estrogen receptor (ER) and progesterone receptor (PR), thus supporting the diagnosis of extramammary Paget's disease. In addition, the Paget's cells were negative for melanoma markers (HMB-45, melan-A and S100) thus excluding a diagnosis of melanoma (magnification 10x).

out squamous carcinoma and melanoma. The tumor cells were strongly positive for both estrogen and progesterone receptors.

Additional staging with a PET scan showed no sites of malignancy within the breast, gastrointestinal or genitourinary tracts. However, there was increased metabolic activity within the cervix and uterus. The patient underwent wide local excision to negative margins on the right breast, and D&C hysteroscopy by gynecology. Final pathology demonstrated positivity residual Paget's disease with clear margins, and normal cervical and uterine samples. Additional immunostaining showed, ER/PR, cytokeratin-7, epithelial membrane antigen, polyclonal and monoclonal CEA and pan-keratin positivity, with no significant positivity for cytokeratin-5/6 and p63, and melanoma markers (HMB-45, melan-A and S100) in the breast tissues.

The patient has been doing well since her surgery in 2012 and is followed biannually with routine mammographic surveillance. She has not demonstrated recurrence of her disease and is currently also taking anastrozole.

Results & Discussions

Extra mammary Paget's Disease is a rare malignancy that has been described in the literature presenting on the vulva, perianal region, scrotum, penis, as well as various other locations [1,2].

Extramammary Paget's disease is found more commonly

in Caucasian postmenopausal women between 60-80 years, however, cases of EMPD in men have been reported [2,3]. Clinically EMPD can presents as multifocal, well circumscribed pruritic erythematous plaques or macules with occasional hyperpigmentation or hypopigmentation [2,4]. Due to this clinical presentation patients are often initially misdiagnosed and treated for benign dermatologic condition including; psoriasis, tinea corporis, irritant dermatitis and eczema.¹ The differential diagnosis for the clinical presentation of EMPD also includes malignant melanoma, Bowen's disease, mycosis fungoides, Langerhans cell histiocytosis and spitz nevus, due in part to all of these disease processes exhibiting Pagetoid spread [3]. Primary EMPD arising in the breast has never been described in the literature, making this case unique. An initial indication that this was not a presentation of classical Mammary Paget's disease was the absence of typical nipple and areolar involvement [3,4].

In order to properly diagnosis EMPD histologic features and immunophenotyping is very important. Both an immunophenotype of CK7+/CK20- in Paget cells, as well as, staining strongly positive for Carcinoembryonic Antigen (CEA) is suggestive of primary EMPD or cases without an associated carcinoma [5,6]. In the majority of EMPD cases the tumor cells contain cytoplasmic mucin, staining positively with mucicarmine and periodic acid Schiff reagents in comparison to MPD in which only 40% stain for intracellular mucin and are generally weaker [7].

EMPD can be divided into primary, arising directly from the epithelium with no other associated neoplasm, and secondary, arising from another primary malignancy.³ For this case, it was therefore necessary to exclude any other possible primary neoplasms. Previous studies have connected presentation of both breast and vulvar Paget's and EMPD [8]. The increased metabolic activity within the cervix and uterus noted on CT therefore required a thorough diagnostic work up to confirm whether this patient was presenting with primary or secondary EMPD. Based on the negative results of D&C hysteroscopy a conclusion of primary EMPD could be made.

Management of EMPD at any site includes wide local surgical excision with 1 cm margins [3]. Currently there is little data to determine the behavior of invasive primary EMPD and the role of adjuvant therapy is still under investigation [1]. Management of secondary EMPD, however, does include adjuvant therapy. In this case a conservative approach including the use of exemestane as adjuvant therapy and chemoprevention was deemed appropriate.

This is the first reported case of Extramammary Paget's disease of the breast to be described in the literature. While rare, it should be considered in the differential when patients present with skin lesions of the breast. Currently wide local excision, with adjuvant hormonal therapy and long term follow up is recommended.

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References

1. Chiu CS, Yang CH, Chen CH. Extramammary Paget's disease of the unilateral axilla: a review of seven cases in a 20-year experience. *Int J Dermatol.* 2011;50(2):157-160.

2. De la Garza Bravo MM, Curry JL, Torres-Cabala CA, et al. Pigmented extramammary Paget disease of the thigh mimicking a melanocytic tumor: report of a case and review of the literature. *J Cutan Pathol*. 2014;41(6):529-535.
3. Lloyd J, Flanagan AM. Mammary and extramammary Paget's disease. *J Clin Pathol*. 2000;53(10):742-749.
4. Lopes Filho LL, Soares Lopes LR, Michalany AO, et al. Mammary and extramammary Paget's disease. *An Bras Dermatol*. 2015;90(2): 225-231.
5. Ohnishi T, Watanade S. The use of cytokeratins 7 and 20 in the diagnosis of primary and secondary extramammary Paget's disease. *Br J Dermatol*. 2000;142(2): 243-247.
6. Guarnier J, Cohen C, DeRose PB. Histogenesis of extramammary and mammary Paget cells. An immunohistochemical study. *Am J Dermatopathol*. 1989;11(4):313-318.
7. Sitakalin C, Ackerman AB. Mammary and extramammary Paget's disease. *Am J Dermatopathol*. 1985;7(4):335-340.
8. Popiolek DA, Hajdu SI, Gal D. Synchronous Paget's Disease of the Vulva and Breast. *Gynecol Oncol*. 1998;71(1):137-140.