Original Article
Concurrent Paget’s disease and basal cell carcinoma of the vulva; a case report

Maisoun Abdelbaqi¹, Rodney E Shackelford², Brian C Quigley¹, Ardeshir Hakam¹

¹Department of Anatomic Pathology, H. Lee Moffitt Cancer Center & Research Institute, 12902 Magnolia Drive, Tampa, FL, USA; ²Department of Pathology and Laboratory Medicine, Tulane University School of Medicine 1430 Tulane Avenue, SL-79, New Orleans, LA 70112, USA

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Abstract: An 82-year-old Caucasian woman had a long-standing history of recurrent Paget’s disease of the right perianal region that was documented by multiple skin biopsies. Histological examination of a skin biopsy from an erythematous raised right perianal area revealed large rounded cells with ample pale staining cytoplasm scattered throughout the epidermis in multifocal nests and a flattened basal layer. A second lesion showed tongues of basaloid cells with peripheral palisading in continuity with the undersurface of the epidermis at multiple points. The individual tumor nests had cytoplasmic melanization and slit-like stromal separation. The tumor cells in the epidermis showed positive immunoreactivity for carcinoembryonic antigen while the basaloid cells were negative. A diagnosis of combined vulvar Paget’s disease and basal cell carcinoma of an infundibulocystic type was rendered. Concurrent involvement of the same area by Paget’s disease and Basal cell carcinoma (BCC) has been reported only once. Here we report a second case of BCC concurrent with vulvar Paget’s disease.

Keywords: Basal cell carcinoma, infundibulocystic, biology, Paget’s disease, vulva, carcinoembryonic antigen

Introduction

Paget’s disease is classified into mammary and extramammary types, with the latter usually located in the vulva, penis, scrotum, perineum, axilla, and rarely the perianal region [1-3]. Extramammary Paget’s disease is rare and can mimic various dermatoses types. A high index of suspicion is required, combined with biopsy and immunohistochemical staining in order to make the correct diagnosis. In 1986 the International Society for the Study of Vulvar Disease classified vulvar Paget’s disease (VPD) as a non-squamous intraepithelial lesion of the vulva. Underlying adenocarcinomas or stromal invasion is present in about 10% of intraepithelial VPD [4]. Patients with VPD are at risk for a second synchronous or metachronous neoplasia; colorectal adenocarcinoma (especially in the perianal areas of the VPD), cervical adenocarcinoma, transitional cell epithelium carcinoma from the renal pelvis to urethra, and mammary carcinoma. Therapy for intraepithelial VPD is a wide and deep surgical resection, including all the skin appendages. However, despite this radical treatment approach, the VPD recurrence rate is reported as 15-62% [5]. Recurrences or progression of intraepithelial VPD are reported more than 10 years following first surgical resection, making long term follow-up mandatory [5]. Basal cell carcinoma (BCC) can develop in sun protected areas, but genital involvement is very rare accounting for 2-3% of all vulvar cancers and occurring most commonly in post-menopausal women. Since its first description by Temesvary in 1926, 200 cases of vulvar BCC have been listed in the literature [6]. The etiology of vulvar BCC remains unknown, but it may include factors such as syphilis, chronic pruritus vulvae or ani, chronic irritation, chronic infection, trauma (such as burns and scars), arsenicals, pelvic region radiotherapy with subsequent p53 gene mutations, and advanced age [5, 7-10]. Clinically, vulvar BCC is an indolent and destructive tumor that rarely metastasizes, but has a high local recurrence (20%) in some series, [11].
Concurrent Paget’s disease and basal cell carcinoma of the vulva

Material and method

Case Report: We report an unusual case of a concurrent Paget’s disease and vulvar BCC. The patient is an 82-year-old white female with a longstanding history of recurrent right perianal Paget’s disease who was followed at Moffitt Cancer Center. In 2007 the patient underwent partial vulvectomy and the histological examination revealed incompletely excised infundibulocystic BCC. She was subsequently lost to follow-up. In April 2011 the patient appeared in the clinic seeking medical attention for the same lesion. Physical examination revealed a heaped up erythematous area with irregular margins involving the right posterior lateral perianal region that extended approximately 5 cm superiorly to involve the labia minus. A histological examination of a vulvar skin biopsy revealed the presence of combined lesion of Paget’s disease and BCC. Consequently, the patient underwent a modified radical vulvectomy.

Results

Pathology: Macroscopically, a 10 x 5 cm erythematous raised area with irregular right perianal region margins extended superiorly to the labia minus was. Microscopically, a diagnosis of Paget’s disease was rendered. The lesion consisted of large rounded cells with ample pale staining cytoplasm scattered along the epidermis, forming nests with a flattened basal layer extending down into the dermis (Figure 1A and 1B). A second lesion was also identified, diagnosed as infundibulocystic BCC, that consisted of proliferating basaloid cells in continuity with the overlying epidermis, proliferating as oblong and rounded nests surrounding keratin-filled structures lined by stratified epithelium that shows a granular cell layer (H&E 200x).

Discussion

The etiology of Paget’s disease and BCC remains unknown, however Helwing and Graham [12] suggested that perianal and vulvar Paget’s disease results from unknown multicentric carcinogenic stimuli on rectal and urethral epidermal apocrine and glandular structures. BCC is likely the outcome of several predisposing factors discussed previously [5, 7, 8, 9, 10]. Thirty three percent of perianal Paget’s disease is associated with an anorectal carcinoma, similarly vulvar Paget’s disease can also be associated with an underlying adenocarcinoma [13]. In the present case, clinical and gynecological examination revealed no abnormal findings. Vulvar BCCs may have a variety of clinical manifestations, usually presenting as a nodule or ulcer. Here we address the principal point of contention concerning the reported neoplasm whether it is truly infundibulocystic BCC. The histological
Concurrent Paget’s disease and basal cell carcinoma of the vulva

examination of the lesion reported revealed several key morphological features including: first multiple cystic structures containing corneocytes that are lined by follicular infundibular epithelium with small amount of keratohyalin granules which are usually seen in an infundibular type epithelium. Additionally some of the orthokeratotic corneocytes are arranged in basket-weaven configuration, and the wall of the cysts showed a transition from outer basaloid cells to inner squamous-infundibular cells. Second bud-like structures simulating the follicular germs throughout the neoplasm is detected as well. These two features considered together are worth emphasizing since that a combination of follicular differentiation toward infundibula and follicular germ cells is unique in the infundibulocystic type BCC. [14, 15] Usually in infundibulocytic basal cell carcinoma the epithelial component of the tumor that is composed of anatomizing patterns of cords of neoplastic basaloid cells predominate over the stromal component. However, the present patient had undergone multiple surgical procedures which might have contributed to the cellular stroma as part of a reparative process inducing fibroblastic proliferation that is observed in the reported neoplasm. Immunohistochemical studies for MIB-1 to assess proliferation and the status of oncogene product p53, revealed high proliferative index with more than 50% of the cells staining at the BCC component of the combined lesion, and strong positivity for p53. These findings support the malignant nature of the reported neoplasm as opposed to a benign lesion such as fibroepithelioma of pinkus which usually shows a low level of staining for p53 and MIB-1 [16].

We do believe that vulvar Paget’s disease plays a contributing role in genital BCC development. The present patient had several suggested predisposing factors for BCC, including advanced age, a long history of chronic irritation, pruritus, and trauma due to repeated perianal biopsies. We agree with Ishizawa et al.’s [17] speculation regarding the pathogenesis of a similar lesion in their case report; BCC develops in the background of Paget’s disease, rather than the two lesions developing independently, or BCC developing prior to Paget’s disease.

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Address correspondence to: Ardeshir Hakam, MD, Senior Faculty Member, Department of Anatomic Pathology, H. Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, FL 33625, USA Tel: 813-745-1874; Fax: 1-813-745-1708; E-mail: Ardeshir.Hakam@moffitt.org

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Concurrent Paget’s disease and basal cell carcinoma of the vulva


