DOD Clinical Case Report
2018; 2: 17-22 ***doi:***

Case Report

PAGET'S DISEASE OF VULVA: A CASE REPORT

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ABSTRACT
Extramammary Paget's disease (EMPD) is a rare clinical entity which can be associated with other malignancies. The vulva is the mostly seen presentation in women. Lesions frequently presents in adnexal structures and clinically demonstrate as erythematous, well-demarcated plaques. Early detection is mandatory because the diagnosis is frequently delayed and there is a high incidence of associated invasive disease. With this case, we discuss the management of vulvar Paget's disease which is rarely seen and importance of investigating the accompanying secondary malignancies.

Key words: Extrammammary Paget's disease, vulva

ÖZET
Meme dışı Paget hastalığı (MDPH) nadir bir klinik antitedir ve diğer malignansilerle birlikte görülebilir. Kadınlarda en sık vulvada görülür. Lezyonlar sıklıkla adneksal yapılarda ortaya çıkar ve eritematöz iyi sınırlı plaklar olarak görülürler. Erkenden tespit edilmesi önemlidir, çünkü tanı sıklıkla gecikir ve yüksek oranda invazif hastalık vardır. Bu olguyla nadir görülen vulvar Paget hastalığının takibini ve eşlik eden malignansilerin önemini tartışıyoruz.
Anahtar kelimeler: Meme dışı Paget hastalığı, vulva

INTRODUCTION

Paget's disease of the vulva (VPD) is a rare dermatologic condition most commonly seen in post-menopausal women.[1] The origin of VPD is not fully understood. It is hypothesized that VPD is originated from epidermis or apocrin sweat glands or mammary-like glands or Toker cells.[2-4] The incidence of underlying adenocarcinoma has been reported %4-17.[2,5,6] EMPD is classified as primary (cutaneous) or secondary according to the origin of the neoplastic Paget cells. Primary EMPD derived from epidermis and epithelium of skin appendages while secondary EMPD originates from a noncutaneous internal malignancy.[7] By this case, we discuss the management of extramammary Paget's disease and highlight the importance of investigating secondary malignancies.

CASE REPORT

A 70-year-old woman referred to our clinic with a 13 years history of vulvar erythema and pruritus which did not respond to topical corticosteroid and antifungal ointments. For these complaints, she had received systemic corticosteroids, acitretin and topical imiquimod treatment within the last 6 months, but erythema and pruritus did not regress. She had hypertension, chronic obstructive pulmonary disease, xerophthalmia, chronic hepatitis B infection, coronary artery disease and 35 pack / year smoking in her history. Her family history was nonsignificant.

Dermatological examination revealed white hyperkeratotic plaque with small superficial erosions and hyperpigmentated areas on the right inguinal region, bilateral labium minors, majors and clitoris (Figure 1).

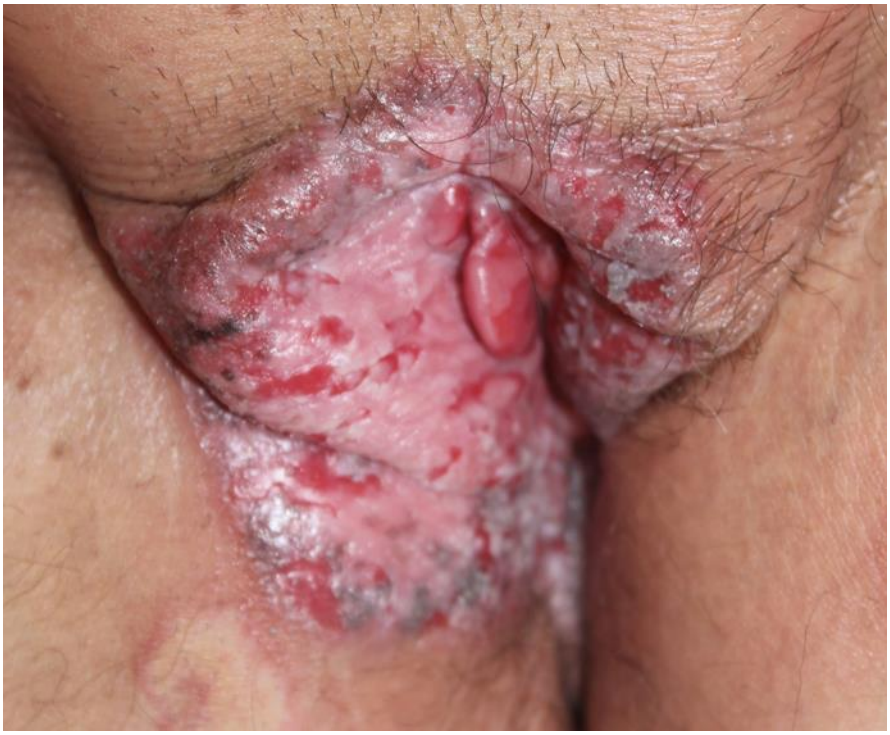

Figure 1. White hyperkeratotic plaque with small superficial erosions and hyperpigmentated areas on the right inguinal region, bilateral labium minors, majors and clitoris

A vulvar punch biopsy was performed in two different areas. Histopathological evaluation revealed numerous Paget's cells with large eosinophilic cytoplasm and prominent nucleus in the epidermis and hair follicle epithelium. Dermal invasion was not observed. The tumor cells were immunohistochemically positive with

cytokeratin 7 and EMA. The skin biopsy was consistent with VPD (Figure 2A, B, C, D).

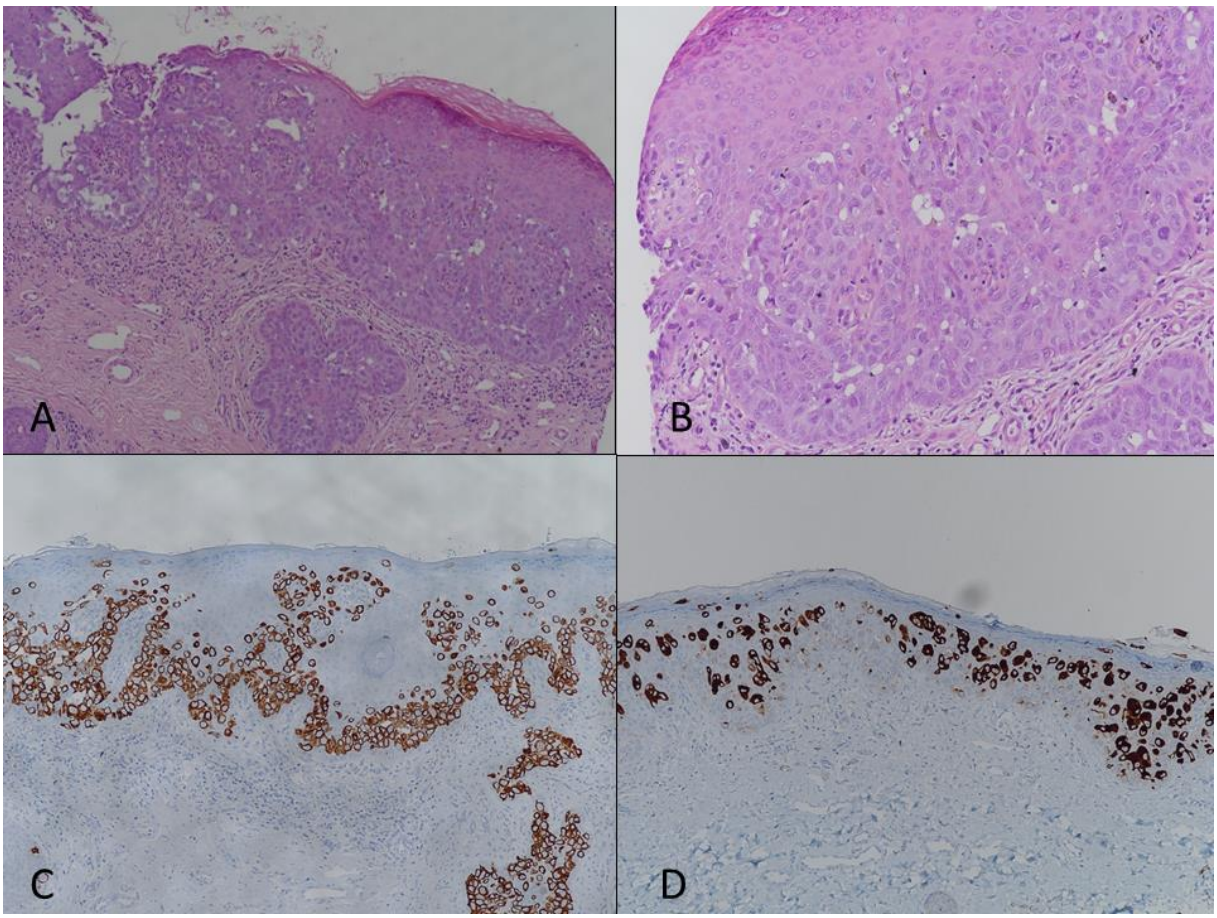

Figure 2. **A)** A large number of Paget cells in the intraepidermis and hair follicle epithelium (H&E x100) **B)** H&E x200 **C)** Positivity of cytokeratin 7 in paget cells (x40) **D)** EMA positivity (x40).

Because of the presumed association of VPD with locoregional and distant malignancies, patient was examined by mammography, abdominal tomography, endoscopy, colonoscopy, transvaginal ultrasonography and smear examination. No malignancy was detected. The treatment of the case was planned as surgical excision together with the gynecologist.

DISCUSSION

Primary (cutaneous) extramammary Paget's disease is defined as a intraepithelial adenocarcinoma that may spread to adjacent epithelial glandular structures.[7] The most common localization is vulva. VPD accounts for less than 1% of vulvar neoplasms (6) and predominantly seen in Caucacian elderly women.[8] In the

majority of patients, VPD causes symptoms such as pruritus, irritation, itching, and burning.[6, 9,10] Lesions are localized spread from the labium major to the pubis, inguinal region, perineum and rarely to the labia minor and vagina. In some cases, whitish or grayish islands and ulcers may be present.[11] Ulcerations and nodules are more common findings in the presence of an underlying tumor.[12] In our case, pubis, inguinal region, perineum, labia majors, labia minors and clitoris involvement, whitish-grayish islands and ulcerations were present.

Diagnosis is usually delayed by 2-3 years as a result of biopsy resulted as chronic dermatosis that does not respond to conventional treatments. The differential diagnosis includes chronic nummular dermatitis, inverse psoriasis, candidal intertrigo, lichen simplex chronicus, lichen planus, lichen sclerosis, pemphigus vegetans.[9,10,12] Lesions in the anal, perianal, and perineal regions should be distinguished from other premalign and malign diseases, such as squamous cell carcinoma, basal cell carcinoma, Bowen's disease.[12] Our case was diagnosed with candidial intertrigo and lichen sim-plex chronicus previously. It was diagnosed as delayed vulvar Paget as a result of the biopsy on not responding to the treatments applied.

VPD's histopathological examination reveals oval or polyhedral shaped paget cells in the epidermis and epithelium of hair follicle which have large pale cytoplasm and large nucleus. Acanthosis, hyperkeratosis, papillomatosis can be seen due to reactive changes.[9] The Paget's cells are diagnostic but the differential diagnosis with the melanoma or Bowen disease may be difficult. Immunohistochemistry is important in this regard. Paget cells are positive with cytokeratin 7 or EMA, whereas they were negative with the melanocytic markers such as HMB-45, MelanA or p63. In our case, a large number of intraepidermal Paget cells were seen in histopathological examination, and they were positive with cytokeratin 7 and EMA.

Paget's disease is almost always spreads locally and regionally. The prognosis varies according to accompanying underlying adenocarsinoma or associated malignancies. It has been reported that 11-20% of vulvar EMPD may be associated by vagina, cervix, uterus, ovary, bladder, rectum, colon, breast, gallbladder, liver or skin carcinoma.[13-15] Primary Extramammary Paget's disease usually has good prognosis when there is no invasion.

The overall mortality rate is 26%. In patients with cutaneous lesions, mortality rate is reported as 18%, whereas in the presence of a coexisting tumor, this rate increases up to 46% .[13]

Patients diagnosed with extramammarian Paget's disease are at increased risk for secondary malignancies especially within the first year after diagnosis.[16] For this reason, the cases should be investigated in terms of colorectal carcinoma, cervical adenocarcinoma and ureteral carcinoma.[17] Our case was also investigated in terms of secondary malignancies and no accompanying carcinoma was found.

Traditionally, the primary treatment approach for vulvar Paget's disease is primary excision. However, is highly focused and has broad microscopic and subclinical spread beyond clinically visible surgical margins. Because of this, disease recurrence is common regardless of the surgical border status.[18] Chemotherapy, radiotherapy, laser, photodynamic therapy, topical imiquimod, topical 5-fluorouracil treatments are applied to patients who can not undergo surgery due to tumor size, localization or patient preference.[2,10] Our case was treated surgically and monitored for recurrence.

CONCLUSION

Vulvar Paget's disease is a rare neoplasm with poor prognosis. Recurrence risk and mortality are high. Today, the optimal treatment option is accepted as surgical. Because of the high risk of recurrence, long-term follow-up in disease management is of great importance. The cases diagnosed with extramammary Paget disease should be investigated in terms of colorectal carcinoma, cervical adenocarcinoma and urethelial carcinoma.

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