Case Report

Vulvar Paget’s disease associated with squamous cell carcinoma: A case report

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1. Introduction

Extramammary Paget’s disease (EMPD) of the vulva is a rare vulvar intraepithelial neoplasm and accounts for less than 1% of all vulvar malignancies [1]. It usually affects postmenopausal women, more frequently between the ages of 50 and 80 years [2]. Paget’s disease of the vulva is often limited to the epidermis and mucosa without invasion. Very rarely, Paget’s disease may be associated with squamous proliferation. A series of 35 cases of Paget’s disease of the vulva and perianal areas were studied by Brainard et al. and only two patients were found to have malignant squamous cell carcinoma with Paget’s disease in their study [3].

Herein, we report one such rare case and treated in the same manner as a squamous vulvar carcinoma. This case has been reported in line with SCARE guidelines [4].

2. Presentation of case

A 70-year-old para 5 postmenopausal lady, hypertensive under medication, non-diabetic, and non-smoker, presented with a history of vulvar itching and a gradually progressive reddish lesion on genitals for one year. She was treated with topical steroids at the nearby local health facility, however, there was no improvement with it and she came to our hospital for further management. There was no history of such lesions in the family.

On examination, there was a well-defined, moist erythematous plaque of 15cm × 10cm with multiple erosions involving bilateral labia majora and clitoris. Per speculum examination revealed a cervix with apparently normal epithelium and external os without any pathological discharge. Manual examination revealed a closed, mobile, and painless cervix. The inguinal lymph nodes were not palpable. Additionally, all other physical examinations including a digital rectal examination were normal.

Keywords:
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Introduction: and Importance: Extra Mammary Paget’s disease (EMPD) of the vulva, a rare postmenopausal entity, is responsible for less than 1% of all vulvar neoplasms. Invasive EMPD of the vulva with underlying squamous cell carcinoma is even rare.

Case presentation: A 70-year-old para 5 postmenopausal lady presented with a history of vulvar itching and a gradually progressive reddish lesion on genitals unresolved by topical therapies for one year. Vulvar biopsy confirmed the presence of pagetoid cells with a focus of squamous invasion.

Discussion: The clinical presentation is often non-specific and typically presents as a pruritic skin rash in the vulva. Optimal management of EMPD of the vulva is unclear, but wide surgical excision is considered the standard therapeutic approach. Local recurrence in EMPD is common even with aggressive radical procedures. Constant follow-up is required to ensure early diagnosis of recurrences.

Conclusion: Early biopsy of the suspicious eczematous lesion can help in definitive diagnosis and timely treatment of EMPD.

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Vulvar biopsy was taken which showed the presence of dysplastic epithelium composed of Paget’s cells and focal area of superficial invasion into the stroma. The tumor cells were positive for p40 and negative for p16 with a high Ki67 index (Figs. 1 and 2). The histomorphological and immunohistochemistry were suggestive of Paget’s disease with a focal invasion of squamous cell carcinoma. Complete gynecological and staging workup including a Pap smear, mammogram, and cystoscopy was done and were normal. Magnetic resonance imaging (MRI) of the abdomen and pelvis showed diffuse heterogeneous moderate enhancement in the vulva confined to cutaneous/subcutaneous and submucosal area along with a sub-centimeter diameter of bilateral iliac and right inguinal lymphadenopathy. With all the work-up, she underwent radical vulvectomy with bilateral groin dissection with bilateral gracilis pedicles flap with urethral and introitus reconstruction by a team of experienced gynecologists and plastic surgeons (Figs. 3 and 4). The post-operative period was uneventful and was discharged after five days of surgery. Histopathological examination of the resected specimen showed Paget’s disease of the vulva with a focus of moderately differentiated squamous invasion along with margin free of tumor infiltration. All the superficial inguinal lymph nodes were free of tumor (pT1bN0).

She was given adjuvant radiation therapy considering the large size of the tumor and close margin. The patient is on close follow for two years, satisfied with the treatment and there is no evidence of recurrence observed till this period (Fig. 4).

3. Discussion

Paget’s disease of the vulva was first described by Dubreuilh in 1901 and the pathogenesis remains unclear [5]. The clinical presentation is often non-specific and typically presents as a red, velvety, pruritic skin rash in the vulva and perianal region with the clinical differential diagnosis as psoriasis, contact dermatitis, fungal infections, lichen sclerosis, intraepithelial neoplasia, and melanoma. For this reason, as pertinent with this case, the diagnosis is often delayed up to two years of disease onset when a definitive diagnosis is made on histological examination for chronic dermatosis not responding to treatments like antifungals and corticosteroids [6].

Vulvar EMPD is predominantly an intraepithelial lesion. However, it has been associated with an underlying adenocarcinoma reflecting its potential for dermal invasion [7]. A 13-year long Dutch epidemiology study with 226 cases of EMPD found that 178 (79%) cases were invasive and 48 (21%) non-invasive. Also, when the data were interpreted by location, invasive Vulvar Paget’s disease (VPD) (n = 59) was reported twice as often as non-invasive VPD (n = 32) [8]. However, no consensus has been established on how to distinguish between invasive VPD, VPD with an underlying associated intestinal/urological malignancy, or vulvar adenocarcinoma. As most cases of invasive VPD have an underlying adenocarcinoma, SCC represents an uncommon finding [9]. The patient in our case had underlying SCC of the vulva with EMPD.

Due to the rarity of the case, optimal management of EMPD of the vulva is unclear, but wide surgical excision is considered the standard therapeutic approach. However, even this approach may not always have an acceptable rate of local control, and approximately 40–75% of patients following surgical excision have involvement of microscopic margins [6]. For those with positive surgical margin, lymph node metastasis, multifocal disease, and associated adnexal adenocarcinomas, postoperative radiotherapy could be considered [10].

As in our case with squamous cell carcinoma of the vulva with EMPD, patients with an underlying invasive EMPD or adnexal adenocarcinoma over 1 mm should be treated more aggressively, considering the primary lesion and groin lymph nodes, with excision to the fascia in the involved area, and inguinofemoral lymphadenectomies bilaterally as treating lymph node metastases is very crucial [11]. Considering the radical excision, vulvoperineal reconstruction is often necessary with the use of skin grafts, local skin flaps, muscle flaps, and different fasciocutaneous flaps [12]. Various flaps used include the gracilis flap, the gluteal fold flap, the median thigh flap, and the vertical rectus abdominis myocutaneous (VRAM) flap. In Paget’s disease where reexision is common because of involved margins, large medial thigh rotation flaps and VY-advancement flaps are used as they confer well to repeat surgeries [13]. Musculocutaneous flaps such as those of the tensor fasciae latae, gracilis, gluteal thigh, and rectus abdominis are needed for extended vulvar defects depending on the reconstruction [14]. In addition, for extended vaginal defects created by pelvic exenteration, adequate reconstructive procedures with musculocutaneous flaps, bilateral pudendal thigh flaps, and sigmoid-colon flaps are required [15]. Our patient underwent radical vulvectomy with urethral and introitus reconstruction.

Radiotherapy as a primary treatment option has been used for patients with invasive and non-invasive VDP not eligible for surgery or who refused surgery, as a treatment option for patients with recurrence after surgery, and as adjuvant postoperative therapy [16]. Considering the large primary tumor and invasion, our patient received adjuvant radiotherapy.

According to a study in a large cohort of patients with invasive EMPD, the disease-specific five-year survival for malignant EMPD was 94.9% (95% CI 92.7–96.5%) for localized disease, 84.9% (95% CI 77.4–90.0%) for regional disease and 52.5% (95% CI 29.3–71.3%) for distant disease. To add, patients who had undergone surgery alone had the most favorable outcome with a mean disease-specific survival (DSS) of 346.8 months (95% CI 335.0–358.6) compared to patients who did not undergo surgery or radiation therapy (mean DSS 255.1 months, 95% CI 221.1–289.2, p = 0.002), patients who received radiation therapy alone (mean DSS 143.4 months, 95% CI 119.2–167.5, p = 0.004) and patients who underwent surgery and radiotherapy (mean DSS 120.6 months, 95% CI 93.6–147.6, p < 0.001) [17].

Other modalities of treatment for EMPD include topical agents...
including 5-fluorouracil, bleomycin, imiquimod, and photodynamic therapy. Local recurrence in EMPD is common even with aggressive radical procedures (15–61% of cases) due to microscopic invasion, positive and irregular margins, and multicentric disease [16,18]. However, it has been found that there is no correlation between disease recurrence and margin status, thus disease recurrence is common, regardless of surgical margin status [16]. Moreover, patients diagnosed with EMPD are reported to have a higher risk of developing a second primary cancer, especially the first year after diagnosis (standardized incidence ratio of 1.39 with a 95% CI of 1.11–1.73) [19]. Our patient is on regular follow up and there are no signs of recurrences up to 24 months of surgery and radiotherapy.

Since Paget’s disease does not regress spontaneously and is progressive, constant follow-up is required to ensure early diagnosis of the disease.
recurrences as no standard follow-up modalities have been established.

4. Conclusion

Vulvar Paget disease is a chronic disease with a high recurrence rate. Early diagnosis, minimal surgery with free margins, and long-term follow-up are the cornerstones of treatment. We emphasize early biopsy of the pruritic eczematous lesion that fails to resolve with appropriate anticezema therapy for early detection of EMPD.

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Ethics approval

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Availability of data and materials

All the necessary data and materials are within the manuscript.

Authors contributions

Anu Bajracharya (AB), Janith Singh (JS), and Srijana Lama (SL) = Study concept, data collection, and surgical intervention for the patient. Anu Bajracharya (AB) and Suraj Shrestha (SS) = Writing-Original draft preparation and editing. Moushami Singh (MS), Suniti Shrestha (SS) = Histopathological Examination and Interpretations. Anu Bajracharya (AB) = Senior author and manuscript reviewer. The manuscript is reviewed and approved by all the authors.

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None to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jamsu.2022.103320.

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