SURGICAL MANAGEMENT OF PAGET’S DISEASE OF THE VULVA: A CASE REPORT

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ABSTRACT
Extra-mammary Paget disease (EMPD) is one of the rare neoplastic conditions of the skin that accounts for less than 1% of the vulvar malignancies. The condition typically presents as a red, velvety, pruritic skin rash of the vulva region which mimics a multitude of other, more common conditions in postmenopausal women. Well-established guidelines for diagnosis and management are not available for this rare condition. As a result, vulvar Paget's disease is frequently misdiagnosed, and could be associated with multifocal neoplasms. The current gold standard for the treatment of vulvar EMPD is surgical excision. Our patient is a 64-year-old postmenopausal woman with the complaint of itching of two years duration. She was diagnosed with EMPD on incisional biopsy and treated with only surgery at our centre. No recurrence was seen during two years after treatment with disappearance of pain and improved quality of life.

KEYWORDS: Paget’s disease, Vulva, Surgical treatment.

INTRODUCTION
Vulvar Paget’s disease is very rare malignancy originating in vulvar apocrine-gland bearing skin cells or as a manifestation of adjacent primary anal, rectal or bladder adenocarcinoma.[1] The most common site of involvement is the vulva, although perineal, perianal, scrotal and penile skin may also be affected. In most cases it is an intraepidermal adenocarcinoma in which tumor cells involve the epidermis and sometimes the underlying skin appendage, but sometimes there is focal dermal invasion.[2] Extra-mammary Paget disease (EMPD) is an extremely rare clinical entity, accounting for only 1% of vulvar malignancies, and most
commonly affects post-menopausal Caucasian women. Although rare, it should be considered in the differential diagnosis of any chronic dermatitis of the perineum.[3,4] While the current gold standard for the treatment of vulvar EMPD is surgical excision, recent scientific publications have proposed the use of imiquimod 5%.[5,6] However, such case reports typically have limited follow-ups compared to classical surgical resection studies.[7] This paper reports the case of a 64-year-old postmenopausal woman with noninvasive Paget’s disease of vulva.

CASE REPORT
A 64-year-old Moroccan woman was suffering from erythematous rash and itching of the genitalia for about two years, felt embarrassed to consult a doctor, but was forced by her immense feeling of itching to consult a gynaecologist. She presented with an eczematosus lesion of the left outer lip extending to the posterior fourchette (fig.1A). On physical examination, the vaginal wall was intact and the per-speculum examination was normal. There was no significant inguinal lymphadenopathy. There were no other similar lesions noted elsewhere. The biopsy of the vulvar lesion was then performed, resulting in a diagnosis of Paget’s disease based on haematoxylin-eosin staining and the immunohistochemical profile (negative Melan-A and positive cytokeratin 7). Upon the result of Paget disease, other systems were examined. A breast examination and mammography were unremarkable. Colonoscopy, cystoscopy, an abdominal and pelvic CT scan were performed and no abnormality could be found. The serum carcinoembryonic antigen (CEA), serum carbohydrate antigen 125 (CA-125) and squamous cell carcinoma antigen (SCC-Ag) levels were normal. The proposed treatment was a partial vulvectomy with 2-5 cm safety margin, performed by an experienced gynecologic surgeon. The area of the vulva to be excised was first delimited, taking into account surgical margins (fig.1B). The partial vulvectomy was then performed using a monopolar electrosurgical device. The skin closure was completed in two layers. The final result showed no open defects (fig. 2). The patient presented no complications post-surgery and was discharged a week later. A follow-up session took place three weeks later for a post-operative examination and suture removal. The final pathologic analysis revealed a noninvasive Paget’s disease of vulva, with surgical margins free of tumor. No recurrence was seen during two years after treatment with disappearance of pain and improved quality of life.
Figures

Fig.1. (A) Macroscopic appearance of Paget’s disease of the vulva. A thick vulvar skin, leading to the impression of leukoplakia. (B) Preoperative marking of the resection margins.

Fig.2. Skin closure performed in two layers.

DISCUSSION
Paget’s disease of the vulva is a rare neoplasm that tends to recur locally. It is most commonly seen in postmenopausal Caucasian women, although there has been a report involving a premenopausal woman. The precise pathogenesis and cell origin of EMPD
remains controversial. Apocrine and eccrine ductal and glandular cells, pluripotent keratinocyte stem cells, and Toker cells have all been considered as possible cells of origin of EMPD.\textsuperscript{[9,10]} Paget’s disease of the vulva has recently been subclassified based on the origin of the neoplastic cells. Type 1: is primary vulvar cutaneous origin. Type 2: is a manifestation of an associated adjacent primary anal or rectal adenocarcinoma. Type 3: is a manifestation of bladder (urothelial) neoplasia.\textsuperscript{[11]} The clinical diagnosis of EMPD is difficult. The most common presenting symptoms of EMPD are pruritus and a pink eczematoid lesion with hyperkeratosis.\textsuperscript{[12]} The thick vulvar skin, leading to the impression of leukoplakia with the cake icing effect is pathognomonic for Paget’s disease. The clinical differential diagnosis for EMPD includes psoriasis, contact dermatitis, fungal infections, lichen sclerosus, intraepithelial neoplasia and melanoma. The nonspecific clinical findings often lead to misdiagnosis and an average of one year can pass before a biopsy is taken and definitive diagnosis is made. An associated underlying malignancy may appear in 12–33\% of the cases, therefore all patients should be thoroughly investigated for occult metastases.\textsuperscript{[13]} In addition to an abdominal and pelvic CT scan, as well as a skin biopsy, appropriate evaluations which include Papanicolaou smear, breast examination are required. Further examinations such as colonoscopy and cystoscopy are required if the aforementioned analyses are not satisfactory.\textsuperscript{[14]} Standard therapy is complete surgical excision with 2–5 cm safety margin, with Mohs micrographic surgery being the preferred technique. It offers the most reliable margin control, adequate tissue preservation, and has the lowest recurrence rates (16\% – 28\%).\textsuperscript{[14,15]} However, it is not as highly effective when the disease is clinically asymptomatic and has a skin texture of normal appearance.\textsuperscript{[4]} Topical creams, radiotherapy and surgery are used in combination for the management of EMPD. Topical treatment using imiquimod 5\% has been reported in the past few years with varying results, occasionally yielding remissions in small tumors and in recurrent cases.\textsuperscript{[5,6]} Other options include 3.5\% bleomycin, 5-flurouracil, CO2 laser ablation and radiotherapy. Systemic therapy also has been used to treat advanced EMPD when surgery and radiation are contraindicated.\textsuperscript{[12]} The recurrence rate is high; therefore patients should be examined every three months after the surgery for the next two years, after which annual follow-ups are recommended. The prognosis for primary EMPD confined to the epidermis is excellent. The challenge for these patients is symptom control and the early detection of local recurrence. By contrast, invasive primary EMPD carries a poor prognosis, particularly if lymphovascular invasion is present. Lengthy follow up is advocated in all cases of primary EMPD and each patient should be thoroughly investigated to rule out an underlying malignancy.
CONCLUSION
Vulvar Paget’s disease is an extremely rare clinical entity and can be successfully treated with surgery. The high frequency of recurrence remains the most challenging feature in the management of vulvar intraepithelial Paget’s disease. Long-term monitoring of patients is recommended, and repeat surgical excision is often necessary. The optimum treatment regimen needs to be defined in prospective studies to determine the best combination of greatest efficacy with least morbidity.

CONSENT
Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing Interests
The authors declare that they have no competing interests.

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