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Case report

# Paget disease of de Vulva: About a rare case and a literature review

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ABSTRACT

*Introduction:* Paget disease of de Vulva (PDV) is a rare neoplastic intraepithelial pathology. In the majority of cases, neoplastic proliferation remains intraepithelial and the prognosis is favorable. The standard treatment for Paget disease is surgical excision. We report the observation of a patient with extensive and recurrent vulvar Paget's disease which we treated with surgery.

*Presentation of case:* A 39-year-old single woman presented with itchy heterogeneous erythematous vulvar lesions suggestive of Paget disease. A biopsy confirmed the diagnosis of non-invasive Paget disease. Surgical excision of the lesions was realized, with the anatomopathological examination confirming the diagnosis.

*Discussion:* MPV is often diagnosed late due to the absence of specific symptoms in its initial phase. Clinically, it manifests as an erythematous lesion or eczema. Immunohistochemistry plays a crucial role in the diagnosis of VPM, helping to distinguish the disease from other vulvar conditions. Vulvar MPV has recently been subdivided into two subtypes: type 1, which concerns primary vulvar lesions, and type 2, which concerns associated primary non-cutaneous adenocarcinomatous proliferations or pagetoid intraepithelial urothelial carcinomas. Surgery is considered the gold standard treatment for MPV.

*Conclusion:* PDV is a complex disease requiring appropriate diagnosis and management, with surgery as the main treatment, but other less invasive therapeutic options may be considered on a case-by-case basis. Prognostic factors play an important role in the choice of treatment and disease progression.

## 1. Introduction

Paget disease of de Vulva is a rare neoplastic intraepithelial pathology, accounting for approximately 1 % of vulvar cancers. It most often affects women between the ages of 50 and 80 [1]. PDV is limited and controversial due to the rarity of the disease [2]. In the majority of cases, neoplastic proliferation remains intraepithelial and the prognosis is favorable [1]. Ten to 30 % of cases are associated with locoregional carcinomas (notably bladder and colon), with a poor prognosis [3]. The standard treatment for Paget's disease is surgical excision. However, the recurrence rate is high (between 30 and 60 %) regardless of the surgical technique used (focal resection, simple or even radical vulvectomy) [4]. In order to limit the functional and aesthetic sequelae, other more conservative treatments have been proposed such as radiotherapy, $CO_2$ laser, topical dynamic phototherapy (PDT), topical application of imiquimod or 5-fluorouracil (5-FU), as first or second intention, with variable efficacy [2]. We report the observation of a patient with extensive and recurrent vulvar Paget disease which we treated with surgery. Those case reports have been reported per the SCARE 2020 criteria [5].

## 2. Presentation of case

A 39-year-old single woman of low socioeconomic status with no specific pathological history presented with pruritic heterogeneous erythematous vulvar lesions suggestive of Paget's disease. The lesions involved the labia majora and minora, with no involvement of the clitoral hood or urethral meatus (Fig. 1). A biopsy confirmed the diagnosis of non-invasive Paget's disease. Gynecological and gastrointestinal investigations revealed no significant abnormalities.

The patient underwent a right hemivulvectomy and excision of the left labia minora. Anatomopathological examination revealed a poorly

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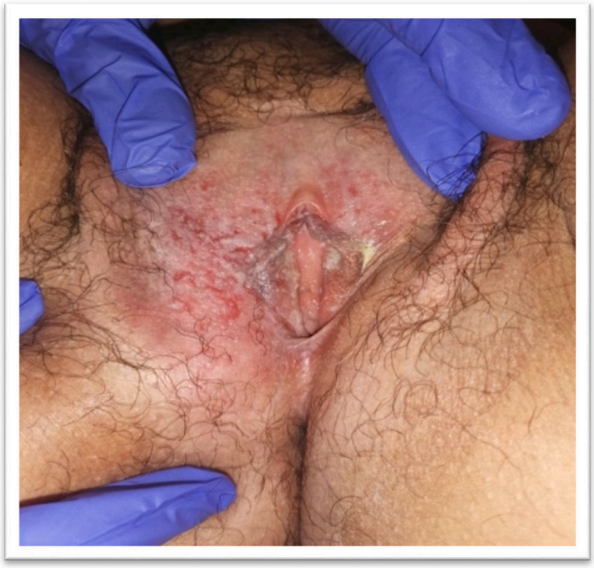

**Fig. 1.** Vulvar lesions suggestive of Paget's disease.

defined, reddish erythematous plaque at the junction of the right labia majora and minora, measuring 2 × 1 × 0.1 cm, with healthy excision margins. Microscopic examination was in favor of intraepidermal tumor proliferation, with isolated cells sometimes organized in clusters. The tumor cells had abundant pale cytoplasm and large, irregular, atypical nuclei. Immunohistochemistry showed that the tumor cells expressed cytokeratin 7 and did not express PS 100. The left labia minora was the site of tumor proliferation on a skin flap of the same appearance as that described above.

Postoperative follow-up was straightforward, with a good post-operative clinical result (Fig. 2).

## 3. Discussion

Sir James Paget (1814–1899), a British surgeon and pathologist, gave his name to three diseases: Paget's disease of the bone, Paget's disease of the nipple, and Paget's disease of the genitals. James Paget first described "Paget's disease" in 1874 in its breast location, but it was not until 1889 that Crocker described the extra-mammary location [6]. It is a malignant tumor, the diagnosis is often delayed or erroneous because in the initial phase, does not present specific symptoms [2–7]. The time from onset of symptoms to diagnosis can be several months [1–7]. Clinically, it is an erythematous or eczema lesion, pruritus is present in more than half of cases [8]. Differential diagnoses may include cutaneous candidiasis, ringworm cruris, seborrheic dermatitis, psoriasis, Bowen's disease, or melanoma, explaining the multiple topical treatments before taking biopsies, and for this reason, PDV should be diagnosed only by vulvar biopsy [9].

The importance of immunohistochemistry for the diagnosis of MPV has now been cited in all studies, it is important for the differential diagnosis with other diseases of the vulva. Finally, with immunohistochemistry, we can highlight the secondary forms of Paget's disease underlying the urinary tract and carcinomas of the gastrointestinal tract [9]. Microscopically, it is an intraepithelial proliferation of atypical large clear cells, forming islets and glands [10].

According to its origin, vulvar Paget's disease has recently been subdivided into two subtypes [1,3,7]:

- type 1 (90 to 95 % of Paget's diseases of the vulva [8]) concerns primary vulvar lesions. Its cellular origin is controversial. It would arise from the intraepidermal portion of the apocrine glands or from totipotent keratinocyte cells [1]. A recent study confirms the apocrine glandular origin [8]. This type is subdivided into Paget's disease without (1a) or with (1b) invasion, making this intraepithelial neoplasia considered potentially invasive [8]. Paget's disease associated with primary vulvar adenocarcinoma (adenocarcinoma of Bartholin's gland or other vulvar glandular structure, vulvar squamous cell carcinoma) is subtype 1c. According to studies, 10 to 20 % of women with vulvar Paget's disease present with an invasive component or associated adenocarcinoma [1,7].
- type 2 (5 to 10 % of Paget's diseases of the vulva) concerns the associated primary non-cutaneous adenocarcinomatous proliferations (rectal carcinoma in situ or invasive or cervical adenocarcinoma), or pagetoid intraepithelial urothelial carcinomas (pseudo-Paget) [8].

Surgery is still considered the gold standard for treating VPD [11], and it is a factor that increases overall survival [12]. It is extensive vulvar surgery, removing the clitoris, due to the local aggressiveness of these lesions. Clinically healthy margins of 2 cm are necessary, because the limits of the lesion, very poorly defined, are difficult to assess pre-operatively. Inguinofemoral dissection is associated in the event of invasion with a sentinel node technique currently being evaluated [12].

In order to limit the functional and aesthetic sequelae, other more conservative treatments have been proposed such as radiotherapy, $CO_2$ laser, topical dynamic phototherapy (PDT), topical application of imiquimod or 5-fluorouracil (5- FU), as first or second intention, with variable efficacy [2,6].

The prognostic factors to be taken into consideration are: a diagnosis of intraepithelial Paget's disease with underlying adenocarcinoma,

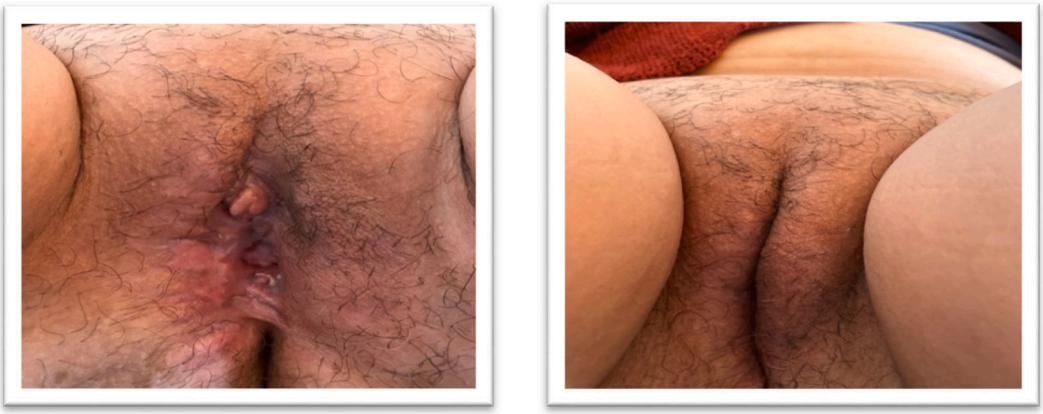

**Fig. 2.** Post-operative results after vulvectomy.

invasive Paget's disease, or intraepithelial Paget's disease with a coexisting cancer predicted poor survival. Patients who had received chemotherapy or radiation as treatment had poor survival, and patients with clitoral Paget's disease had a higher incidence of death from the disease. When death from all causes was considered, patients treated with wide local excision had a significantly longer survival than patients treated with other more radical treatments [1,2].

## 4. Conclusion

Whatever the clinical aspect of Paget's disease, the histological diagnosis is usually easy and the histochemical and immunohistochemical techniques confirm the diagnosis. The treatment of this condition is based on limited excision of visible lesions. The prognosis of PDV is linked to the evolution of a possible associated neoplasia.

## Patient's consent

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

## Ethical approval

I declare on my honor that my establishment has exempted the ethical approval.

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None.

## CRediT authorship contribution statement

All authors have read and approved the final version of the manuscript.

## Declaration of competing interest

The authors declare having no conflicts of interest in this article.

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