# Complications in Surgical Management of Recurrent Vulvar Paget's Disease: Treatment and Follow-up

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Arch Oncol 2025;31(1):34-38

https://doi.org/10.2298/AOO241023001S

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Received: **2024-10-23**
Accepted: **2024-12-11**
Published online: **2025-01-20**

## SUMMARY

**Introduction:** *Paget's disease of the vulva is an intraepithelial adenocarcinoma, primarily arising from vulvar skin glands, with or without an underlying invasive adenocarcinoma. It brings low mortality and a high local recurrence rate and mainly affects postmenopausal women.*

**Case outline:** *This is a case report of a 57-year-old postmenopausal woman, who had histopathological (HP) verified Extramammary Vulvar Paget's disease (EVPD) in 2014, and underwent a radical vulvectomy with a right-sided inguinofemoral lymphadenectomy and V-Y flap at the Oncology Institute of Vojvodina. Nine years later, in 2023, the patient was presented with a biopsy HP proven EVPD recurrence. The recurrence was surgically treated with vulvectomy and bilateral fasciocutaneous V-Y flaps reconstruction. The operative HP specimen proved the EVPD recurrence with atypical cells on one edge of the specimen. Due to the infection-complicated healing and wound dehiscence, the first reoperation was performed, which included wound debridement and left-sided rotational flap. We carried out the wound care and toileting in the postoperative course, with antibiotic treatment. Due to infection-complicated healing, tissue necrosis and consequent dehiscence, the second reoperation was performed, which included wound debridement with granulation tissue excochleation and Tiersch-type skin graft.*

**Conclusion:** *The patient was discharged 21 days after the second reoperation in good condition. A regular oncological postsurgical follow-up on the 3th and 6th month revealed no recurrence or deterioration of the general condition or local findings. The patient subjectively feels well and has no complaints or unwanted effects of the applied treatment.*

**Keywords:** *vulvar extramammary Paget's disease, EMPD, V-Y flap, Tiersch-type skin graft*

## INTRODUCTION

Paget's disease of the vulva (VPD) is a rare intraepithelial malignant neoplasm originating from glandular cells, typically developing in the apocrine sweat glands. It represents approximately 1-2% of vulvar neoplasms with metastatic potential and represents the most prevalent form (60%) of extramammary Paget's disease (EMPD) (1). VPD primarily affects postmenopausal women over 60 years old, characterized by a high local recurrence rate and low mortality.

EMPD manifests in two forms: primary, as intraepithelial adenocarcinoma with invasive potential, and secondary from metastatic spread to the skin. Although primarily localized within the epithelium, approximately 10% of cases may progress to an invasive disease, spreading to regional lymph nodes and distant organs (1,2).

Primary VPD lesions typically present as well-defined erythematous or eczematous plaques with multifocal hyperkeratotic and dyschromatic changes, often described as "strawberries and cream" appearance. They are predominantly multifocal and can occur anywhere on the vulva, commonly affecting the labia majora and potentially extending to the perineum, thighs, and pubic mons. Symptoms include long-term itching, burning sensations, and vulvar pain. They develop asymptomatically, leading to delayed diagnosis (1).

The diagnosis of VPD requires biopsy and subsequent histopathological analysis. Additional diagnostics are crucial for excluding other neoplasms, including breast examination, ileocolonoscopy, cystoscopy and analysis of tumor markers (Ca 125, CEA, CA 19.9), alongside CT scans of the chest, abdomen, and pelvis (1).

The primary treatment for EMPD is surgical excision, often necessitating repeated procedures due to high recurrence rates. Wide local excision with margins up to 1-2 cm is standard, although disease recurrence remains common even with negative margins. In cases of suspected invasive disease, a partial radical vulvectomy involving deep resection to the perineal membrane and inguinofemoral lymphadenectomy is needed. Radical surgeries can result in extensive defects, requiring a multidisciplinary approach involving gynecologists and plastic surgeons to balance oncological efficacy with reduced treatment-associated morbidity. In such cases, reconstructive skin flaps offer advantages over secondary healing.

Local tissue flaps are an optimal method for defect reconstruction, utilizing adjacent tissues with their neurovascular supply. They are classified based on localization (local, regional, remote), vascular supply (random, axial, pediculated), and tissue type (skin, dermal, fascial, muscular), and include various types as sliding (advancing), rotational, and island flaps. Fasciocutaneous flaps, like the V-Y flap, are preferred for vulvoperineal reconstruction due to excellent vascularization and mobility, often performed by gynecologic oncologists. The application of a V-Y flap involves precise assessment and marking of triangular flap edges, ensuring optimal tissue coverage while preserving neural sensitivity and identifying superficial branches of the pudendal and posterior cutaneous femoral nerves. Flap elevation proceeds medially to distally, above or below deep fascia, depending on the required advancement (3).

Alternatively, skin grafts (transplants) are widely used

for defect reconstruction, involving tangential removal of skin layers from donor and transfer to recipient sites. They vary in thickness (partial, thin-Tiersch, intermediate-Blair I/II, full-Wolf), with survival dependent on the recipient site vascularization. Although surgical excision remains the primary treatment, alternative modalities include laser ablation, topical chemotherapeutics, and radiotherapy, while chemotherapy is reserved for advanced metastatic disease (1,2).

## CASE REPORT

This is a case report of a 57-year-old postmenopausal woman diagnosed with recurrent VPD.

The patient's medical history includes hypertension, chronic bronchitis and obesity (BMI 35.23 kg/m2). She used beta blockers as a regular therapy. She had laparoscopic cholecystectomy in 1996. Gynecological anamnesis showed that her last menstrual period occurred at the age of 47. She had four pregnancies, two ended by caesarean sections in 1994 and 2008, and two ended in spontaneous abortion. The patient's family history is positive for cardiovascular diseases and lung cancer.

The patient was treated in 2014 due to histopathologically proved VPD, when radical vulvectomy with a right-sided inguinofemoral lymphadenectomy and V-Y flap creation were performed at the Gynecology Department of the Surgical Oncology Clinic, Oncology Institute of Vojvodina.

Nine years later, in 2023, she was presented to our institution with a vulvar skin change, highly suspicious for Paget's disease recurrence (Figure 1). The change was biopsied, and histopathological analysis confirmed the recurrence of VPD. Further assessment with ultrasonography of both groins revealed several lymph nodes with correct morphological characteristics left-sided, alongside a single 6 mm calcified lymph node in the right inguinum. Based on these findings and clinical presentation, a decision was made for operative treatment.

**Figure 1.** Macroscopic appearance recurrent VPD before the first operation.

### The first operation

After clinical examination, laboratory analysis and preoperative preparation, the patient was operated under general anesthesia with the participation of a plastic surgeon. A vulvectomy and reconstruction using bilateral fasciocutaneous V-Y flaps were performed. The surgery and immediate postoperative course went without complications.

### Intraoperative findings and procedure course

The vulvar tissue with altered skin was removed (Figure 2-A), followed by the fasciocutaneous V-Y flaps creation bilaterally, with additional undermining and mobilization of the pubic skin. The procedure is completed after subcutaneous tissue suturing with interrupted stitches and skin stapling (Figure 2-B).

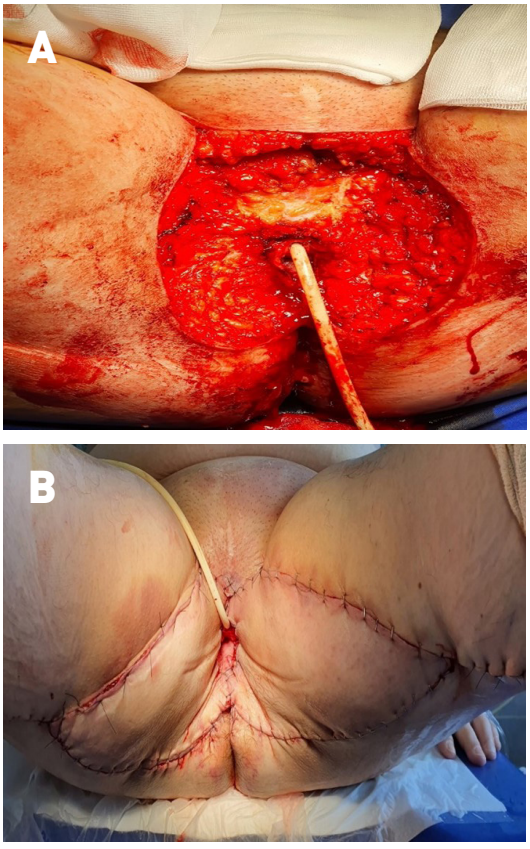


**Figure 2.** A-Operative field (during the first operation). B- Surgical wound immediately after the first operation.

### Histopathological findings in surgical specimens

The macroscopic finding describes a vulva specimen measuring 105x105x25 mm, characterized by atrophic and hyperkeratotic skin. Notably, a flattened area measuring 14x7 mm with a 1 mm margin was identified on the right labia towards the labia minora. On the left labia, an eroded skin zone measuring 13x15 mm was observed.

Histological examination reveals hyperkeratotic epidermis with focal papillomatosis. In the basal and parabasal layers, atypical epithelial cells with abundant bright cytoplasm and central large nuclei with prominent nucleoli were found. These cells within individual hair follicles and the absence of invasive tumor growth were noted. A sparse inflammatory lymphocyte infiltrate surrounded deeper dermal invaginations, without lymphovascular invasion. Atypical cells were detected at one resection margin (left labia towards the vaginal introitus). These histopathological findings confirmed the recurrence of the vulvar Paget's disease.

### Further treatment decision and its implementation

On the eighth postoperative day since the first operation, the patient developed high-grade fever (39.4°C). Gynecological examination revealed wound dehiscence. Continued wound care and antibiogram-guided parenteral antimicrobial therapy were conducted, targeting swab isolated Proteus mirabilis and Escherichia Coli (Figure 3).

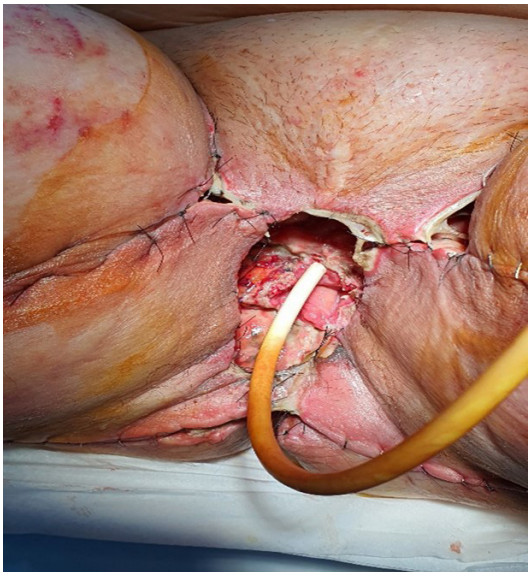

**Figure 3.** Surgical wound appearance 7-10 days after the first operation.

Despite the initial challenges, the patient's condition improved and the fever was resolved by the thirteenth postoperative day (Figure 4). Clinical assessment including the plastic surgeon facilitated decision-making regarding the need for subsequent reoperation 21 days after the first surgery.

### First reoperation

With the participation of a plastic surgeon, wound debridement was followed by rotational flap creation on the left side. The surgery and immediate postoperative course went without complications.

### Further treatment decision and its implementation

The wound care was conducted regularly, along with parenteral antibiotic therapy. In cooperation with the plastic surgeon, according to the infection-complicated healing with consequent tissue necrosis and dehiscence (Figure 5), a decision was made to have the second reoperation 9 days after the first reoperation and 30 days after the first operation.

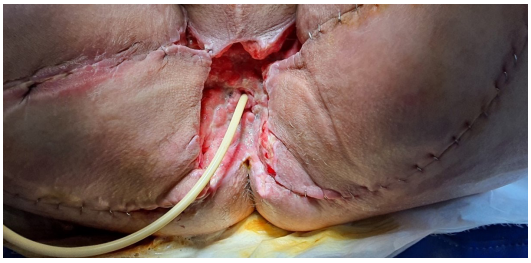

**Figure 4.** Surgical wound appearance 13-15 days after the first operation.

### First reoperation

With the participation of a plastic surgeon, wound debridement was followed by rotational flap creation on the left side. The surgery and immediate postoperative course went without complications.

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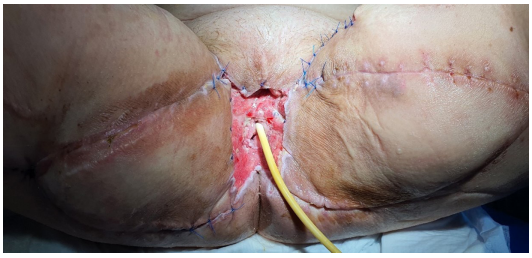

**Figure 5.** Surgical wound appearance 6 days after the first reoperation.

### Second reoperation

With the plastic surgeon's participation, wound debridement was performed with granulation tissue excochleation and the creation of a Tiersch-type skin graft. The surgery and immediate postoperative course went without complications.

### Intraoperative findings and procedure course

Partial-thickness Tiersch-type skin grafts were harvested from the right femoral region, which were meshed in a ratio of 1:1.5 and prepared for transplantation. The examination of the recipient region revealed the absence of infection. Following the debridement and curettage of granulation tissue, adequate capillary bleeding was achieved. Transplants were placed on the defect and fixed with the "tie-over" technique over vaseline gauze and flavin cotton wool. The operative procedure was completed by the adequate bandaging of the donor region of the right upper leg.

### Further treatment decision and its implementation

Regular wound care along with parenteral antibiotics supported the patient's recovery. She was afebrile, without postoperative complications. The wound was showing signs of healing per secundam intentionem in the vaginal introitus region, with a partially accepted Tiersch-skin graft (Figure 6). The patient was discharged in good condition, 21 days after the second reoperation, following advice on wound care.

### Follow-up

The patient was regularly monitored and controlled by a gynecologist-oncologist and plastic surgeon. The last control preceded this report, 6 months post-surgery.
A regular oncological follow-up in the first, third and sixth month showed no disease recurrence or worsening of the general condition or local findings (Figures 7,

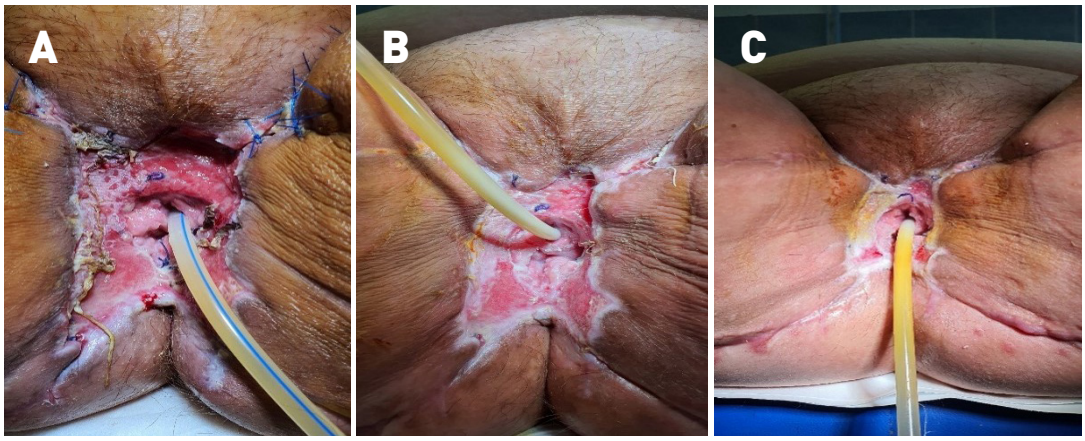


**Figure 6.** . Surgical wound appearance 6 days (A), 14 days (B) and 18 days (C) after the second reoperation.

8, 9). The patient feels well, with no health complaints or adverse effects of the applied therapy.

**Figure 7.** Surgical wound appearance 1 month after the second reoperation.

**Figure 8.** Surgical wound appearance 3 months after the second reoperation.

**Figure 9.** Surgical wound appearance at the last gynecological check-up, 6 months after the second reoperation.

This detailed narrative highlights the complexities in managing recurrent VPD through a multidisciplinary approach, emphasizing surgical expertise, wound care and collaboration in achieving favorable outcomes in challenging VPD recurrence.

## DISCUSSION

Vulvar Paget's disease is adenocarcinoma of the vulvar skin glandular epithelium, which occurs very rarely in the general population. Considering epidemiology, there is a lack of literature about VPD diagnosis and treatment. Much of the data stems from studies of Paget's disease of the breast and other extramammary sites, and attention was paid to the vulvar disease research only in the second half of the previous century. Consequently, much of the available information comes from a limited number of studies conducted over the past three decades, underscoring the need for more comprehensive research to elucidate the diagnostic challenges, oncological behavior, and treatment outcomes crucial for clinical practice.

As with most oncological diseases, the pathogenesis and etiology are unknown, and VPD is the only lower female genital tract epithelial tumor not associated with the Human Papilloma Virus infection (4). Research exploring the connection with Herpes simplex virus infection has been inconclusive. In contrast, the extramammary Paget's disease of the bone and breast has shown evidence of the Epstein-Barr virus infection in a non-negligible percentage of cases. Similar studies in vulvar disease are scarce, leaving the question of etiology and pathogenesis unresolved. Our case report aligns the patient's characteristics, age and clinical presentation of VPD with the existing literature. But our patient exhibits a high BMI (35.4 kg/m$^2$), contributing to heightened risks of infections, wound healing problems and other complications of operative treatment.

Most individual case reports advocate initial surgical treatment, a consensus supported by Caruso et al.'s meta-analysis involving 5617 patients from 96 studies (5). Depending on lesion size and location, surgical treatment ranges from wide local excision to radical vulvectomy with skin flap reconstruction. Due to the multifocal disease appearance and irregular edges of lesions, the margins are often positive, so local disease recurrences can often be expected. Recorded recurrence rates of VPD ranged from 20 to 70%, as observed in our patient.

In cases of recurrence, the preferred clinical approach leans towards reoperations, although radiotherapy remains a legitimate alternative, particularly for invasive disease, lymph node metastases or suspicion thereof, or when extensive surgical excision is contraindicated due to the patients' age or comorbidities (6,7).

Although the literature advocates a wide excision, which can compromise the genital anatomy and functionality, impacting the quality of life, new research suggests Mohs micrographic surgery. This technique ensures clean surgical margins with a minimal removal of healthy tissue reducing the need for complex reconstructive procedures and has shown a statistically significant lower recurrence rate compared to wide local excision (8,9).

The clock mapping technique involves multiple vulvar lesion biopsies. Its surrounding healthy region in a clockwise direction and vagina accurately predicts the extent and invasiveness of VPD preoperatively (10).

Our study followed the traditional approach of wide excision to healthy skin, recommended in the literature. Mohs' micrographic surgery was not feasible due to logistical constraints for consecutive tissue analyses during surgery and clock mapping was not considered because of limited supporting studies at the time. Another intraoperative method, analyzing individual tissue frozen sections from suspicious margins, looks promising in reducing recurrence rates.

The initial treatment of our patient involved a wide excision of altered tissue confirmed through histopathological analysis, followed by V-Y flap reconstruction, consistent with established surgical practice (3,5,7). The decision to utilize advancing V-Y flaps was guided by studies demonstrating lower rates of wound dehiscence in lesions larger than 40 or 45mm, highlighting the reconstructive surgery benefits in achieving complete resection (11).

The outcome analyzing study of reconstructive interventions in oncology of the vulva supports the high complication rate, reaching 65%, with a reoperation rate of 33%. Specifically, flap surgery had complication rates of 47%, and subsequent reoperations were required in 19% (12), which is consistent with our case study experience.

In our patient, postoperative complications included wound dehiscence and infections, necessitating antibiotics and secondary surgery with partial skin autograft transplantation, consistent with research on managing such complications (12).

Currently, a consensus on the optimal surgical technique to minimize local recurrence risks remains elusive, necessitating a further definition of surgical and pathological prognostic factors. Preoperative mapping shows potential in achieving these goals, warranting validation through prospective studies.

For patients ineligible for operative treatment, radiotherapy offers an alternative, emphasizing the need for research to establish effective dosing, field volumes, and clear guidelines beneficial to clinicians in daily practice.

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