# ACUTE GENITAL ULCER (LIPSCHÜTZ ULCER): CASE SERIES

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**Summary**

*Genital aphthosis, also known as Lipschütz ulcer, first described in 1913, is a rare acute inflammatory condition, the aetiology of which remains unclear, non-sexually acquired, and predominantly affecting adolescent girls and young women, although cases have also been reported in males. It is characterised by painful ulcerations, usually associated with a viral infection, particularly Epstein-Barr virus (EBV).*

***Keywords:*** *genital ulcer, Epstein-Barr virus (EBV), genital aphthosis.*

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## Introduction

Genital aphthosis (previously known as "ulcus vulvae acutum" or "Lipschütz ulcer") is a rare acute clinical condition affecting adolescent girls and young women, described by Lipschütz in 1913 [1,2]. The disease has an abrupt onset with the appearance of transient vesicles that rupture, forming multiple genital erosions and ulcerations with a clean fibrinous base, small in size and superficial, herpetiform and well-demarcated, sometimes accompanied by areas of extremely painful necrosis, and which can cause significant emotional distress [3-6]. Patients may present a variety of systemic manifestations, resembling influenza, such as fever, headache, muscle pain, gastrointestinal disturbances such as diarrhoea, oral aphtae, lymphadenopathy, or respiratory symptoms such as odynophagia. [3-4,7].

The aetiology of aphthosis remains incompletely understood, and the diagnosis is one of exclusion. However, most studies suggest that it represents an immunological hypersensitivity reaction to an infectious agent, most frequently of viral origin [4,8-10]. Epstein-Barr virus (EBV) is most frequently implicated, being identified in a significant proportion of diagnosed female patients, followed by cytomegalovirus (CMV), adenovirus, influenza viruses, as well as bacteria such as *Mycoplasma pneumoniae* [10-15]. Other causes include fungal infections, sexually or non-sexually transmitted, and in the absence of an identifiable infectious agent, autoimmune mechanisms, hypersensitivity reactions, or idiopathic factors may be considered, particularly in recurrent forms [2,4,8,16]. Treatment is primarily symptomatic, with therapeutic measures aimed at relieving pain and inflammation. Systemic therapy includes the administration of non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics, while local therapy involves the use of epithelializing agents to reduce discomfort and promote lesion healing [2,8,17-19]. The use of systemic or topical corticosteroid therapy and antiviral treatment is controversial, but may be justified in cases with multiple or severe lesions [10,20-21].

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## Materials and methods

Four sexually active adult patients were assessed, all of them denied sexual intercourse in the previous 30 days and had no significant history of dermatological diseases or relevant systemic conditions. The differential diagnosis was established through comprehensive serological and microbiological investigations, including tests for HIV, TPHA (syphilis), herpes simplex virus (HSV), anti-Chlamydia antibodies, and mycological examination. All of the patients mentioned signed an informed consent for the collection and use of personal data for scientific research purposes, in compliance with legal provisions regarding confidentiality and data protection.

## Clinical Cases

**Case 1**

28-year-old female patient with painful, erosive, and ulcerated vulvar lesions, which appeared seven days prior to consultation. No associated systemic symptoms. Serology for Epstein-Barr virus (EBV) was negative. Under systemic and local symptomatic treatment, the patient had a favourable course, with complete healing within 14 days.

**Case 2**

25-year-old female patient with over 30 painful, erosive vulvar lesions, which appeared 10 days prior, accompanied by low-grade fever and general malaise. EBV serology was positive, with IgM and IgG antibodies. The patient received symptomatic treatment and systemic corticosteroid therapy with prednisone, at a dose of 30 mg/day for 14 days, showing a favourable clinical outcome. Three images illustrating the evolution of the lesions during treatment are available. (Figure 2-4).

**Case 3**

27-year-old female patient, with approximately 10 painful vulvar vesiculo-ulcerative lesions, without systemic manifestations. EBV serology was negative. Symptomatic treatment was instituted, with progressive remission and complete healing within 21 days. (Figure 5)

**Case 4**

26-year-old male patient, with over 30 painful, erosive, and ulcerated penile lesions, associated with malaise, fever and inguinal lymphadenopathy. EBV serology was positive for IgM and IgG antibodies. The patient received symptomatic treatment and systemic corticosteroid therapy with prednisone at 30 mg/day for 14 days, showing a favourable response to treatment. (Figure 6).

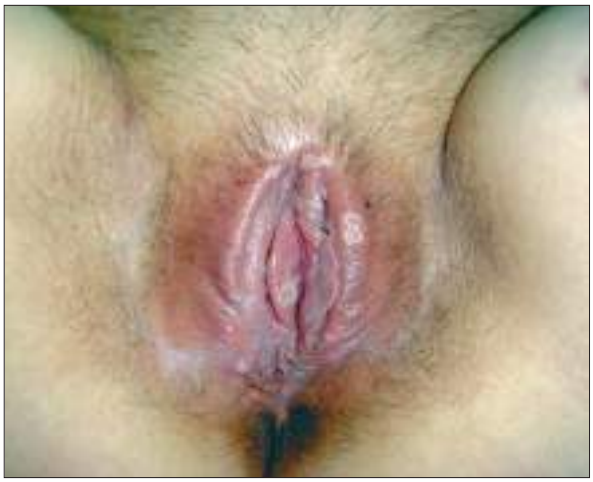

*Figure 1. Genital aphthous lesion located on the labia minora and majora, partially covered by whitish deposits.*

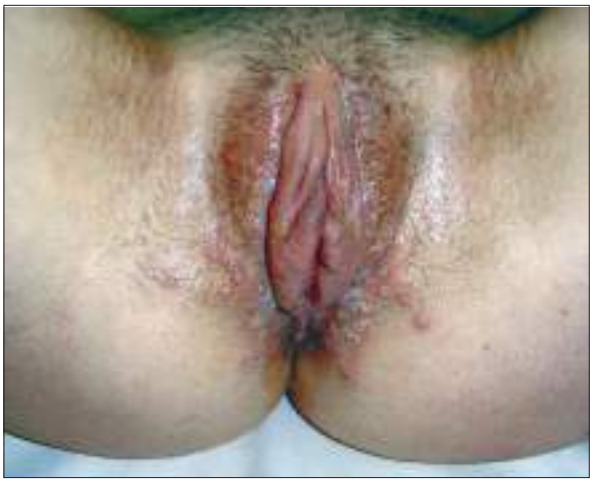

*Figure 2. Multiple ulcerated lesions, centimetric in size, fibrinous and necrotic, with erythematous margins, arranged in a "mirror-like" pattern on the labia majora, labia minora, and perianal region.*

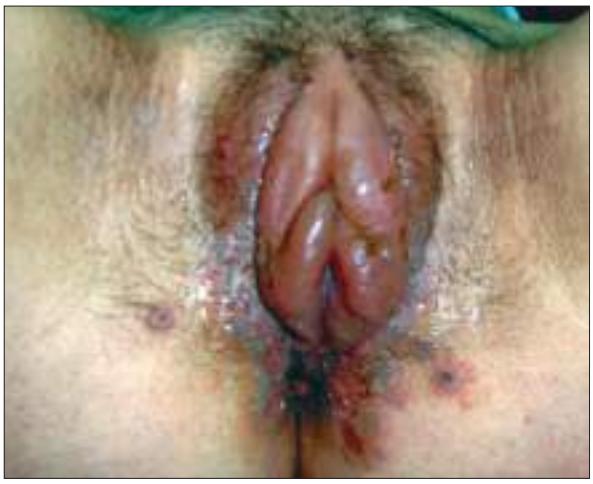

*Figure 3. Four 4 days after presentation, multiple lesions with fibrinous exudate, and associated oedema of the labia minora, perilesional erythema, and signs of local superinfection.*

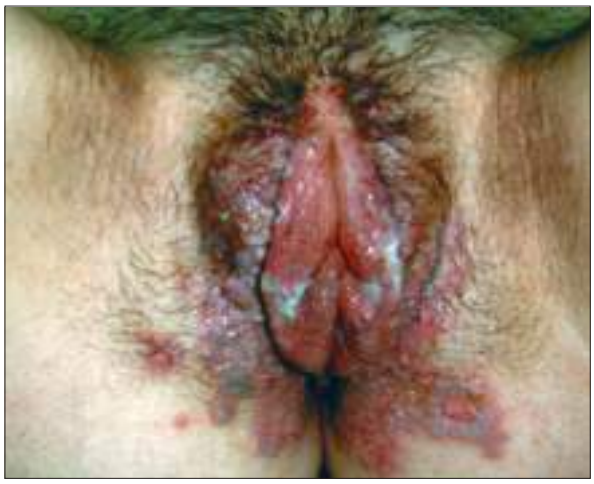

*Figure 4. Ten days after presentation, a reduction in labial oedema was observed.*

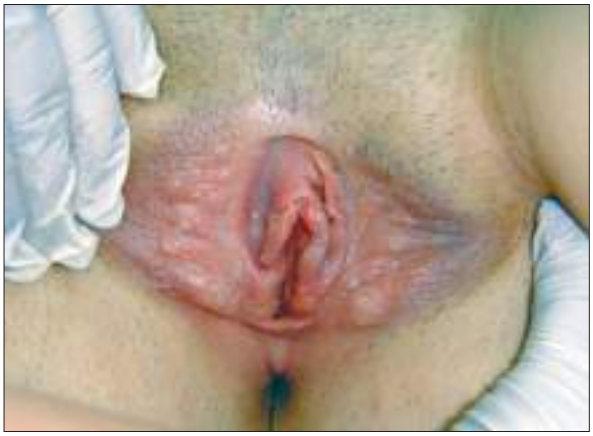

*Figure 5. Multiple ulcerated vesicular lesions on the labia majora and minora, with associated erythema.*

*Figure 6. Aphthous lesions, millimetric in size, on the anterior penile shaft, with associated perilesional erythema, right inguinal lymphadenopathy.*

## Results

Of the total of four patients, three were female (75%), and one was male (25%). The mean age was 26.5 years, ranging from 25 to 28 years. The number of lesions varied significantly, from approximately 10 to over 30, with an estimated mean of 16 lesions in vulvar cases. All patients presented with painful vesiculo-ulcerative or erosive lesions, and half of them (50%) exhibited associated systemic symptoms, such as fever and malaise (cases 2 and 4). The non-venereal nature of the condition was observed in all four cases. Serology for Epstein-Barr virus (EBV) was positive in 50% of cases (two patients) and negative in the remaining 50%. Testing for HIV and syphilis infection was negative in all patients. Systemic corticosteroid therapy (prednisone, 30 mg/day, for 14 days) was admi-

nistered in two cases (50%), both of which had positive EBV serology and systemic manifestations. The clinical course was favourable in all cases, with complete healing within 14 to 21 days.

## Discussion

Lipschütz ulcers are a rare cause of acute non-venereal vulvar ulcerations and, in most cases, affect young people without a history of sexual contact. This condition presents with the sudden onset of painful vulvar or penile ulcer, usually preceded by influenza or mononucleosis-like symptoms, such as general malaise, fever, asthenia, myalgia, pharyngotonsillitis, lymphadenopathy, and cephalalgia.[22] The exact mechanism involved in the formation of ulcers distant from the site of the primary infection is poorly understood. A hypersensitivity reaction to a viral or bacterial infection has been suggested, leading to the deposition of immune complexes in dermal vessels, which subsequently activates the complement system, resulting in microthrombus formation and consequent tissue necrosis.[23] Fahri et al. attempted to establish several diagnostic criteria (major and minor), suggesting that a diagnosis could be made if all major criteria and at least one minor criterion were present. The proposed major criteria are age <20 years, sudden onset and acute course of the ulcer, first and only episode, absence of sexual contact in the three months preceding the onset of symptoms, and absence of immunodeficiency. Furthermore, the minor criteria include one or more ulcers with a necrotic or fibrinous base and a well-demarcated, painful, symmetrical pattern. However, in a retrospective study conducted by Vieira-Baptista et al., it was concluded that the diagnostic criteria for Lipschutz ulcer should be less restrictive. Histological examination has no diagnostic value, as the findings are non-specific.[24] Analysis of the four cases highlights a common pattern of painful vesiculo-ulcerative lesions, with predominant involvement of the external genitalia in young adult patients. The presence of systemic symptoms and positive EBV serology were associated with a higher number of lesions and the need for systemic corticosteroid therapy. All patients responded favourably to symptomatic treatment, with complete healing within three weeks, suggesting a good prognosis for this condition. Although rare, genital aphthous ulcers should be considered in the presence of painful genital ulcers, especially in young patients without chronic diseases or confirmed STIs. Accurate diagnosis can prevent aggressive treatments and hospitalisations, making knowledge of possible differential diagnoses crucial.[3,4,25,26]. The differential diagnosis for this condition is broad and requires careful clinical and paraclinical approach, considering both infectious and non-infectious aetiologies. The main conditions that should be excluded are listed in Table 1.

The cases presented by us are consistent with the clinical profile in the relevant literature. Two of the patients showed positive serology for EBV, with multiple painful lesions, accompanied by general malaise and lymphadenopathy. Multiple articles describe similar cases of vulvar ulcers associated with primary EBV infection, highlighting the potential aetiological role of the virus as well as a transient, self-limiting immunological mechanism with a favourable outcome [2,8]. The other two cases, with negative serology and milder symptoms, also showed a self-limiting course, suggesting a spectrum of variable severity depending on the patient's immune response. A case of genital aphthosis in a male patient is rare. According to recent literature, fewer than 1% of reported cases involve males. The symptomatology is similar to that observed in women, but the lack of awareness often results in excessive investigations and unnecessary treatments [23]. A rare case, published in Autopsy and Case Reports, described a 27-year-old man who simultaneously presented with penile genital ulcers and viral meningitis, both associated with primary EBV infection. Although far less common in men, this case suggests that males can also experience genital manifestations in the context of EBV infection.[48) In our case, the presence of EBV and the favourable response to corticosteroid therapy reinforced the hypothesis of an immune reaction secondary to a viral infection.

**Table 1.** Differential diagnoses

| Differential diagnosis | Key features | Main investigations | References |
|---|---|---|---|
| Primary syphilis | Solitary, indurated, painless chancre, regional lymphadenopathy | VDRL, TPHA, dark-field microscopy | [27] |
| Secondary syphilis | Papulo-ulcerative syphilides, generalised lymphadenopathy, systemic manifestations | VDRL, TPHA | [28] |
| Tertiary syphilis | Destructive granulomas, years after infection | Biopsy, positive serology | [27], [28] |
| Primary genital herpes | Grouped vesicles, painful ulcers, fever, local lymphadenopathy | HSV PCR, viral culture | [29], [30] |
| Recurrent genital herpes | Recurrent episodes, similar lesions, short duration (7–10 days) | HSV PCR | [29], [30] |
| Chancroid | Painful ulcers with irregular margins, suppurative lymphadenopathy | H. ducreyi culture, PCR | [31], [32] |
| Lymphogranuloma venereum (LGV) | Initially minor ulcerations, inflammatory inguinal adenitis and suppuration | Chlamydia L1–L3 PCR | [33], [34] |
| Granuloma inguinale (donovanoza) | Chronic, friable ulcerations, with Donovan bodies | Biopsy | [13] |
| Ulcerative gonorrhoea (Julien) | Superficial painful erosions, possible urogenital symptoms | Gram stain, *N. gonorrhoeae* culture | [35] |
| Chemical ulcer | Local necrosis following contact with irritant substances (ammonia, mercury) | Exposure history, pH testing | |
| Post-coital traumatic erosions | Superficial wounds, irregular margins, without systemic signs | Detailed history | |
| Dermatitis artefacta (Dieulafoy) | Self-inflicted lesions, irregular margins, psychiatric context | Psychiatric evaluation, biopsy | [36] |
| Tuberculous ulcer | Ulcer of cutaneous or haematogenous spread, foul margins | PPD test, *M. tuberculosis* culture | [37] |
| Tumoral/metastatic ulcer | Infiltrative lesions, indurated margins, associated with squamous cell carcinoma | Biopsy | [38] |
| Fixed drug eruption | Recurrent ulcerations at the same site following medication use | Drug testing, biopsy | [39] |
| Genital amebiasis | Painful ulcers in endemic areas, identification of Entamoeba histolytica | Parasitological examination, PCR | [40] |
| Behçet's disease | Bipolar aphthosis, erythema nodosum, uveitis | International criteria, HLA-B51 | [41], [42] |
| Cutaneous Crohn's disease | Painful granulomatous perineal and genital lesions | Colonoscopy, biopsy | [43], [44] |
| Erythema multiforme bullous | Bullous or ulcerative lesions, precipitated by infections/drugs | Medication history, biopsy | |
| Other rare conditions | Pemphigus vulgaris, atrophic lichen sclerosus, actinomycosis, genital diphtheria | Biopsy | [45],[46],[44] |

## Conclusion

Genital aphthosis is a rare clinical entity, often underdiagnosed or mistaken for sexually transmitted infections, particularly among sexually active young patients. The four cases presented in this study highlight a range of clinical manifestations, from mild, self-limiting forms to severe cases associated with systemic viral infection, particularly Epstein-Barr virus (EBV), which required systemic therapeutic intervention. The particularity of this case series lies in the diversity of clinical presentations, including a rare case in a male patient; the role of

laboratory tests and extensive differential diagnosis in excluding other causes and identifying EBV as a possible trigger, supporting the hypothesis of an immune-mediated viral aetiology.

The importance of this case series derives from its contribution to raising awareness of a rare, but physically impactful condition, and emphasises the need for the development of comprehensive diagnostic and treatment guidelines for this pathology, which currently remains poorly defined in the relevant literature. These cases also highlight the challenges of performing a complex differential diagnosis for genital ulcerations.

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Conflict of interest
NONE DECLARED

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