Austin Journal of Dermatology

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Austin Publishing Group

Case Report

Lipschütz Ulcer in an Adolescent with Acute Lymphoblastic Leukemia: A Diagnostic Challenge between Infection, Autoimmunity, and Immunosuppression

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Received: December 29, 2025
Accepted: January 27, 2026
Published: January 30, 2026

Abstract

Lipschütz ulcer is an uncommon entity characterized by the acute onset of painful genital ulcers, generally occurring in adolescents without a history of sexual activity, whose timely recognition is essential to avoid misdiagnosis and unnecessary treatments. We present the case of a 13-year-old adolescent with acute lymphoblastic leukemia undergoing chemotherapy who developed fever and bilateral vulvar ulcers that were confluent, fibrinous-based, and with violaceous borders, associated with pancytopenia, markedly elevated C-reactive protein, and ferritin levels. Sexually transmitted infections and herpetic etiology were ruled out through specific testing, and the positive serology for Treponema pallidum was interpreted as a false positive. Based on the clinical context, morphological findings, and self-limited evolution, the diagnosis of Lipschütz ulcer was established. This case represents a diagnostic challenge due to the immunosuppression context, in which most classic case series exclude this condition, thereby requiring thorough clinical evaluation and consideration of this entity even in oncologic settings. Early recognition helps avoid invasive interventions, limit unnecessary treatments, and provide mainly symptomatic management with appropriate clinical monitoring. Likewise, the importance of follow-up is highlighted given the potential association with immune processes and the risk of recurrence or linkage with other systemic diseases. This report contributes to expanding knowledge regarding the presentation of Lipschütz ulcer in immunocompromised patients and emphasizes the need to include it in the differential diagnosis of acute genital ulcers in pediatric oncologic populations.

Keywords: Lipschütz ulcer; Acute genital ulcer; Adolescence; Immunosuppression; Acute lymphoblastic leukemia; Differential diagnosis

Case Presentation

We report the case of a 13-year-old adolescent diagnosed with acute lymphoblastic leukemia undergoing chemotherapy, who presented with fever of 39 °C and painful vulvar ulcers. Physical examination revealed large bilateral and symmetrical lesions on the labia minora, with a fibrinous base and violaceous borders ("mirror pattern") (Images 1 and 2). The patient denied prior sexual activity. Complementary studies revealed pancytopenia compatible with antineoplastic treatment, elevated C-reactive protein (35.7 mg/L), and markedly elevated ferritin levels (7767 ng/mL), suggesting a severe systemic inflammatory state. Serology showed positive IgG and negative IgM for Epstein–Barr virus (EBV) and cytomegalovirus (CMV), indicating past infections without evidence of acute disease.

Tzanck smear testing of the lesions (Image 3) was negative for herpes simplex virus, thus ruling out an evident herpetic etiology. Additionally, treponemal antibodies against Treponema pallidum were detected (index: 3.21) despite the absence of sexual activity. This finding was interpreted as a possible false positive due to clinical inconsistency. No other infectious etiologies were detected (HIV negative, genital exudate cultures without growth). Therefore, the case was considered an acute painful genital ulcer in an adolescent patient, negative for HSV, CMV, EBV, and common STIs, with immunosuppression secondary to chemotherapy.

Discussion

Acute Lipschütz genital ulcer is a rare entity that typically occurs in girls and adolescents without prior sexual activity [1,2]. It is characterized by the abrupt onset of one or multiple large, deep, painful vulvar ulcers with a necrotic or fibrinous base and reddish-violaceous border [2,3]. The "mirror-image" ulcer pattern is highly suggestive of this diagnosis, and patients usually present with prodromal systemic symptoms such as fever, malaise, odynophagia, and asthenia before or during the onset of lesions [2], as in this patient. Lipschütz ulcer follows a self-limited course, resolving spontaneously in 2–6 weeks, typically without scarring. Management is supportive with analgesia, local hygiene, and sitz baths; however, topical or systemic corticosteroids and antibiotics may be used in severe cases or when superinfection is suspected [2].

Citation: Fernández-Reynoso C, Maldonado-Colín G, Gómez-Picos A, Arellano-Vivero M and Achell-Nava L. Lipschütz Ulcer in an Adolescent with Acute Lymphoblastic Leukemia: A Diagnostic Challenge between Infection, Autoimmunity, and Immunosuppression. Austin J Dermatolog. 2026; 13(1): 1117.

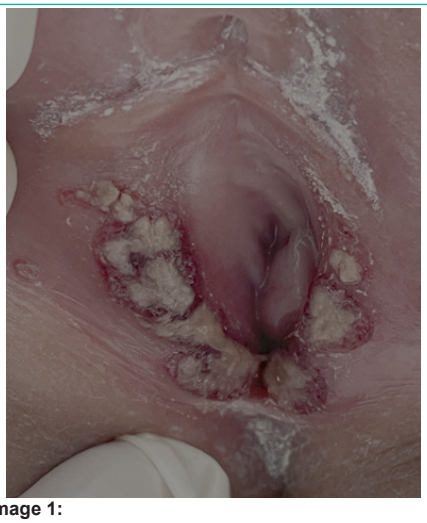

Image 1:

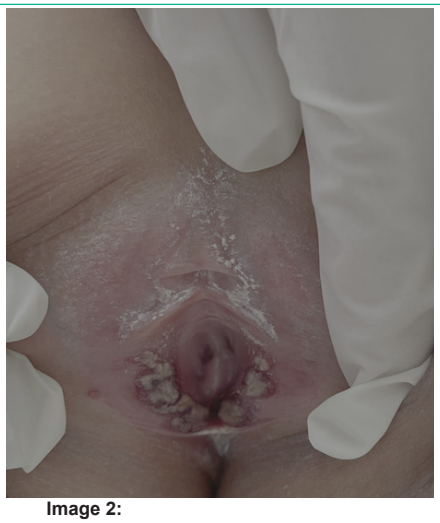

Image 2:

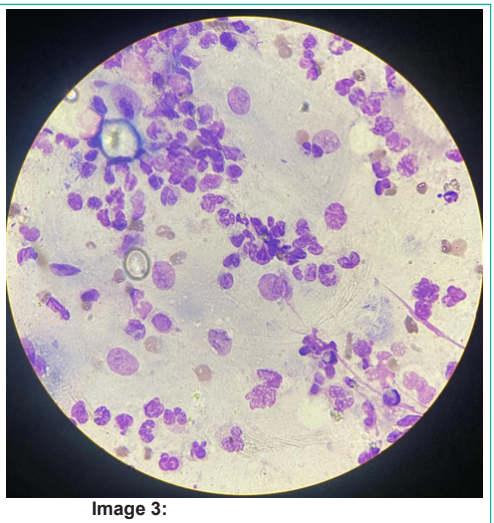

Image 3:

Etiopathogenesis and Pathogenesis

The etiology of Lipschütz ulcer is uncertain. Up to 70% of cases are considered idiopathic, although many have been associated with recent systemic infections [4]. Epstein–Barr virus is the most frequently implicated agent; however, CMV, influenza, parvovirus B19, and bacterial infections such as Mycoplasma pneumoniae, Salmonella, streptococci, and Borrelia have also been reported. The most accepted hypothesis suggests an exaggerated immune response to an infectious trigger, involving hypersensitivity reactions with immune complex deposition in dermal vessels, complement activation, and vascular microthrombi formation leading to local tissue necrosis [5]. Histopathological studies of EBV-associated ulcers have shown lymphocytic vasculitis, thrombosis, and necrosis consistent with this immunological mechanism. In our patient, the absence of positive IgM suggests no acute EBV or CMV infection, although previous exposure supports a possible distant immune trigger. Lipschütz ulcer has also been reported in specific immunodeficiency contexts, such as IgA deficiency; however, significant immunosuppression is generally excluded as a diagnostic criterion. In our case, chemotherapy-induced immunosuppression was a relevant and atypical factor [3-5].

Differential Diagnosis

Diagnosis of Lipschütz ulcer is clinical and based on exclusion of more common causes of genital ulcers. Sexually transmitted infections must be primarily ruled out. Genital herpes is the most frequent cause of vulvar ulcers; however, herpetic lesions typically present as multiple clustered vesicles evolving into superficial ulcers and can be easily identified by culture or PCR (4). In our patient, negative PCR/Tzanck testing makes herpetic etiology highly unlikely. Primary syphilis manifests as a painless ulcer with a clean base and indurated borders, differing from the painful fibrinous lesions in our case. Isolated treponemal antibody positivity was considered a false positive, a known phenomenon in autoimmune and chronic infectious contexts [6]. Other systemic infections (HIV, hepatitis) were excluded by negative serology.

Non-infectious causes such as Behçet disease, Crohn's disease, and other neutrophilic or blistering dermatoses (pemphigus, pyoderma gangrenosum) should also be considered; however, no extragenital signs or clinical history suggested these diagnoses. Behçet disease was excluded due to absence of recurrent oral ulcers or systemic manifestations, and there were no gastrointestinal or cutaneous findings suggestive of inflammatory bowel disease.

After excluding the most frequent infectious and systemic etiologies, diagnosis relied on typical clinical findings and spontaneous evolution. Diagnostic criteria proposed in the literature include first episode of acute genital ulcer, adolescent age (<20 years), absence of recent sexual activity, deep painful ulcers on the labia with necrotic base, and resolution within ≤6 weeks [1]. Our patient fulfilled most criteria, except for chemotherapy-induced immunosuppression, which traditionally excludes diagnosis in classical criteria [4]. Nevertheless, given the compatible clinical picture and lack of alternative causes, Lipschütz ulcer was considered appropriate, highlighting that although immunosuppression theoretically excludes it, it may occur in oncologic patients, representing a diagnostic challenge.

Conclusions

Lipschütz genital ulcer is a rare but relevant entity in adolescents, characterized by acute painful vulvar ulcers unrelated to sexual activity or contagion [1]. In our case of a patient with acute lymphoblastic leukemia on chemotherapy, clinical suspicion was essential given negative HSV, syphilis, and HIV results and the typical appearance of lesions. Management was supportive with analgesics and local care, and the patient showed favorable evolution with spontaneous healing within weeks. It is important to emphasize that Lipschütz ulcers may be associated with acute infections and immune mechanisms; some studies describe subsequent development of autoimmune diseases such as Sjögren syndrome. Therefore, long-term follow-up is recommended to monitor for autoimmune disease or recurrence.

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