International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Malakar A et al. Int J Reprod Contracept Obstet Gynecol. 2026 Jul;15(7):2750-2756
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20262132

Case Report

Atypical vulval cutaneous manifestation of chronic lymphocytic leukaemia following genital herpes masquerading as vulvar carcinoma: a case report

Abhishek Malakar[1]*, Fizza Javaid[1], Susanne Booth[1], Benjamin Snowden[1], Arun Manoharan[2]

[1]Department of Obstetrics and Gynecology, Hull University Teaching Hospital NHS Trust, United Kingdom
[2]York and Scarborough Teaching Hospitals, NHS Foundation Trust, United Kingdom

Received: 27 April 2026
Accepted: 02 June 2026

***Correspondence:**
Dr. Abhishek Malakar,
E-mail: drabhishekmalakar@gmail.com

ABSTRACT

Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) is the most common adult leukaemia in Western countries, characterised by monoclonal proliferation of mature B lymphocytes and accounting for approximately 1% of all new cancers in the UK. Although it primarily affects lymphoid tissues, extra nodal involvement can occur, most frequently involving the skin and central nervous system. Involvement of the female genital tract is rare and presents significant diagnostic challenges. We report an unusual case of vulval involvement by CLL mimicking vulval carcinoma. An elderly woman presented with a 6-week history of vulval ulceration. Initial biopsy demonstrated chronic inflammation without evidence of malignancy. She was subsequently diagnosed with low-level CLL and managed conservatively with active surveillance. Over time, she developed worsening vulval pain, extensive ulceration, and recurrent infections requiring multiple hospital admissions. Imaging findings and clinical progression raised strong suspicion of vulval malignancy with nodal involvement; however, repeated biopsies remained non-diagnostic. Multidisciplinary histopathological review ultimately confirmed vulval infiltration by low-grade B-cell lymphoma consistent with CLL. The clinical picture was further complicated by concurrent herpes simplex virus type 2 infection and secondary bacterial infection. This case highlights the importance of considering leukaemia cutis in non-healing vulval ulcers in patients with CLL. Early multidisciplinary involvement, repeated adequate biopsies, and appropriate viral testing are essential to avoid misdiagnosis and ensure optimal management.

Keywords: Chronic lymphocytic leukaemia, Leukaemia cutis, Genital herpes, Atypical vulval ulcer, Post herpetic cutaneous CLL

INTRODUCTION

Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) is the most common adult leukaemia in Western countries and is characterized by monoclonal proliferation and accumulation of mature B lymphocytes in the peripheral blood (PB), bone marrow (BM), lymph nodes, and spleen. In the United Kingdom, CLL accounts for approximately 1% of all newly diagnosed cancers, with an estimated 1,500 new cases occurring annually in females.[1] Although CLL predominantly affects the lymphatic system, leukemic cell infiltration may also occur in non-lymphatic organs. Extramedullary and extranodal involvement most frequently affects the skin (33%) and central nervous system (27%). Less commonly, organs such as the liver, lungs, gastrointestinal tract, bone, prostate, and heart may be involved.[2] Involvement of the female genital tract is rare as cutaneous manifestations most often occur on the head and neck (33.9%), followed by the trunk and extremities (26.8%). We report a case of vulval involvement by CLL associated with genital herpes

infection complicated by secondary bacterial infection that clinically mimicked vulval carcinoma, highlighting the diagnostic challenges, management considerations and patient experience associated with this uncommon presentation.

CASE REPORT

Case history/examination

A British woman in her eighties was referred on a '2-week wait' pathway with a 6-week history of suspected vaginal ulceration. She had three prior vaginal deliveries and a previous total abdominal hysterectomy with bilateral salpingectomy and was not on HRT. Examination showed vault prolapse and atrophic posterior fourchette changes suspicious for lichen sclerosis. Despite prior ultrapotent topical steroids, vulval biopsy was performed and showed non-specific chronic inflammation with oedema, without atypia or malignancy; topical steroids were continued. The patient was subsequently diagnosed with low-level B-cell chronic lymphocytic leukaemia on cervical lymph node biopsy. With no B symptoms, marrow impairment, or bulky/progressive disease on PET, MDT recommended active surveillance with 3-monthly monitoring rather than chemotherapy.

Differential diagnosis, investigations and treatment

Nine months after her first biopsy, the patient presented with vulval pain and soreness. Examination of the vulva discovered a 3x3 cm excoriated purulent lesion to the right lower vulva and ulceration of the posterior vaginal wall, swabs were obtained during examination but were reported negative. The patient received IV flucloxacillin, was discharged on cefalexin and metronidazole, and scheduled for repeat biopsy.

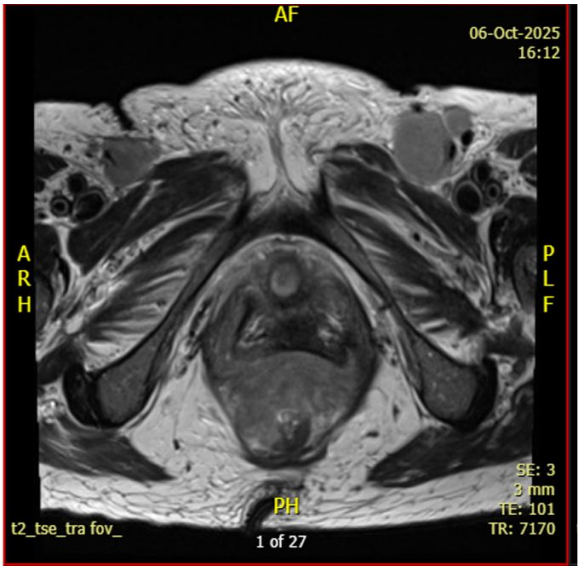

Figure 1: MRI axial view showing enlarged inguinal nodes (left and right).

Three weeks later, she had markedly swollen labia with extensive bilateral ulceration and severe pain impairing mobility.

Repeat swabs and punch biopsies were taken, and the patient was readmitted for for IV antibiotics and analgesia. Histology showed ulcerated dermatitis with superimposed infection, without atypia or malignancy; swabs showed no growth. The patient was treated with IV Flucloxacillin and Metronidazole and was discharged on oral Co-Trimoxazole and Metronidazole following microbiological advice.

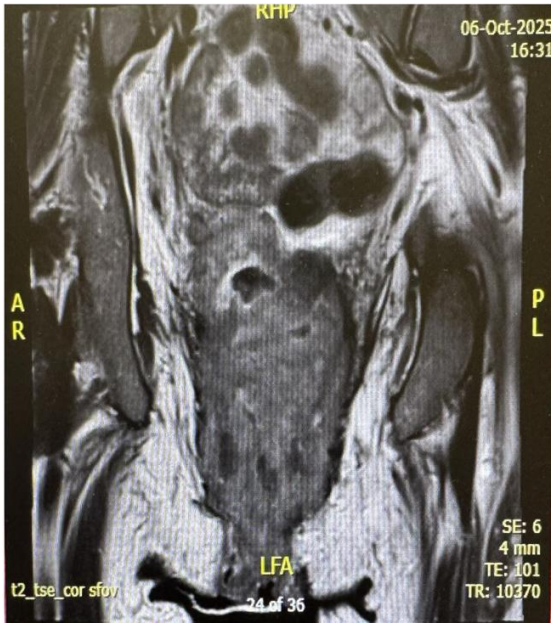

Figure 2: MRI coronal view showing extensive abnormal soft tissue.

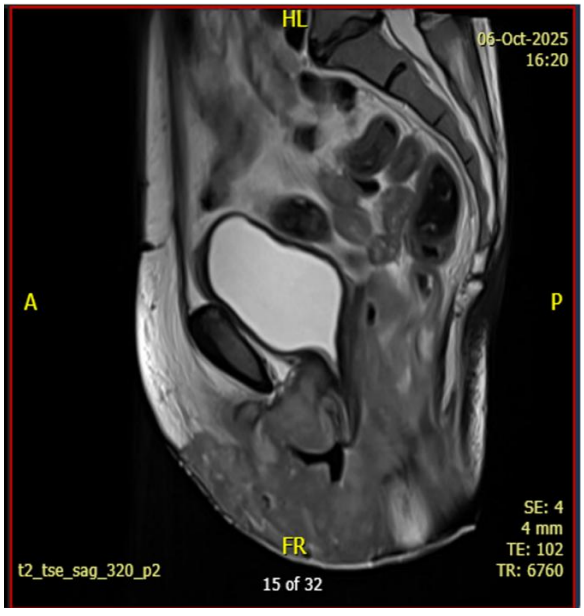

Figure 3: MRI sagittal view showing extensive abnormal soft tissue.

The patient was then referred back by her GP the following day, complaining of severe vulval pain, reporting loss of appetite and significant weight loss. She was admitted for the third time, with further examination findings reporting a broken down vulva with 10x5 cm bilateral ulcers and purulent discharge throughout. At this point, she also complained of loss of appetite and significant weight loss.

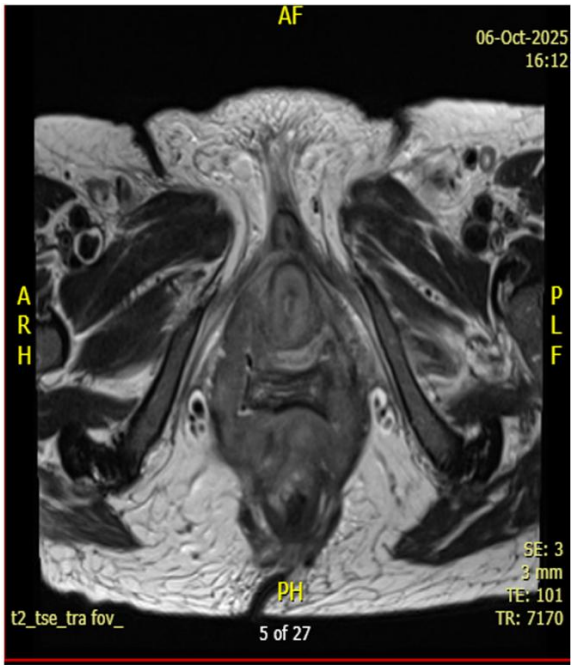

Figure 4: MRI axial view showing extensive abnormal soft tissue.

Following a review performed on the ward by the Consultant Gynae Oncologist, there was a clinical suspicion of vulval malignancy with involvement of the bilateral inguinal lymph nodes therefore, staging imaging was requested including MRI pelvis and abdomen and a CT scan of the chest. MRI showed extensive abnormal soft tissue around vulva, vagina, urethra, perineum and Ano rectum with part centrally necrotic tissue and enhancement of the solid tissue mostly peripherally, appearance highly suggestive of malignancy; with bulky bilateral inguinal nodes (around 3 cm on left and 2 cm on the left) and enlarged pelvic/external iliac nodes measuring 17 mm. (Figure 1,2,3,4). CT chest did not show any lung involvement.

A third vulval biopsy was performed as an inpatient by the Consultant Gynae Oncologist which revealed chronic inflammation, however the small tissue sample may not accurately represent the observed lesion. Therefore, the decision was made to perform multiple biopsies.

The fourth vulval biopsy with cystoscopy was scheduled under a senior Consultant Gynae Oncologist. Examination under anaesthesia revealed extensive oedematous, ulcerated vulval disease involving the entire vulva, most marked posteriorly, extending anteriorly and into the vagina (predominantly the right wall), with profuse exudate including the periurethral region. A 5 mm right mons pubis lesion was suspicious for a satellite deposit.

Cystoscopy showed no bladder tumour; ureteric orifices were visualised. Bladder erythema, trabeculation, and likely instrumentation-related intravesical exudate were noted. Rectal examination suggested anterior and right-sided mucosal involvement without a discrete mass. Perianal skin tags were present and possibly malignant. Multiple biopsies were taken from the vulva and perianal areas, with haemostasis achieved using 2-0 Vicryl sutures and diathermy.

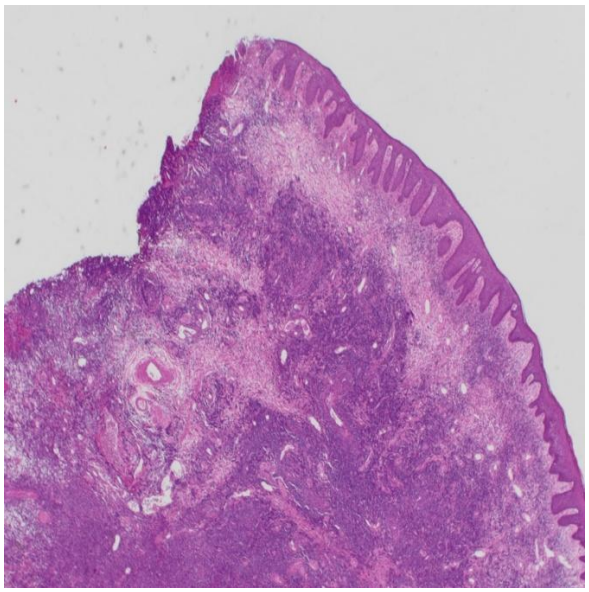

Figure 5: Haematoxylin and eosin stain.

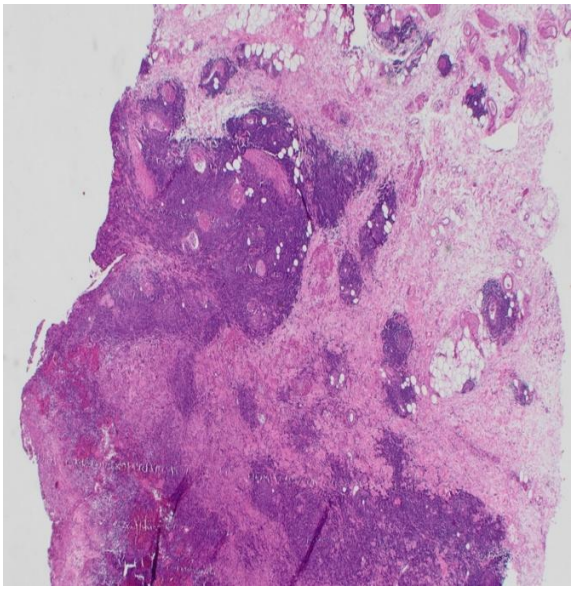

Figure 6: Skin with surface ulceration and diffuse lymphoid infiltration

Microbiology was re-consulted due to persistently negative wound swabs. Full septic screening, including blood cultures, HIV, Hepatitis B/C, Syphallis and HSV testing were all performed; all providing negative results.

Histopathology from the fourth biopsy showed chronic deep inflammation with focal necrosis, surface ulceration, exudate and adjacent vasculitis (Figure 5). There was no malignancy. Special stains for fungi, spirochetes, actinomyces, mycobacteria, and other bacteria were negative and no viral cytopathic changes were seen. Differentials included sexually transmitted infections (syphilis, donovanosis, Chlamydia trachomatis), cat scratch disease and autoimmune conditions such as Behçet's disease.

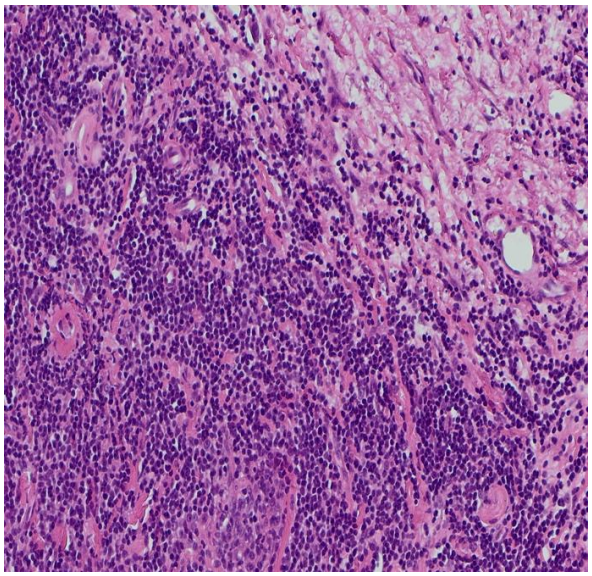

Figure 7: Surface epidermis with diffuse monomorphic lymphoid collection in the dermis.

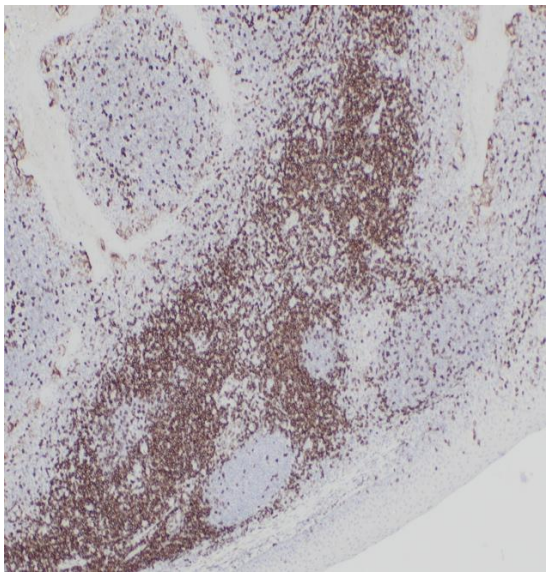

Figure 8: CD5 stained B cells indicative of CLL.

The case was subsequently discussed at a histopathology multidisciplinary review meeting, where the possibility of a low-grade lymphoma was raised, prompting referral to the hematopathology department for further evaluation.

Hematopathology review showed diffuse lymphoid population (Figure 6,7) comprising of small to medium sized lymphoid cells (prominent B cells) expressing BCL2, CD5, BCL6 (patchy) and CD23 (patchy) with low proliferation fraction on MIB1 staining; features of low-grade B cell non-Hodgkin Lymphoma and consistent with CLL without any evidence of high-grade transformation. (Figure 8,9).

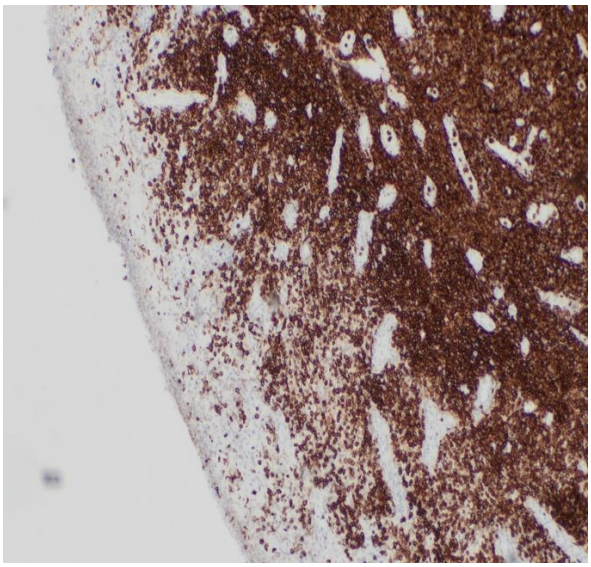

Figure 9: Lymphoid groups highlighted with CD45 immunohistochemistry.

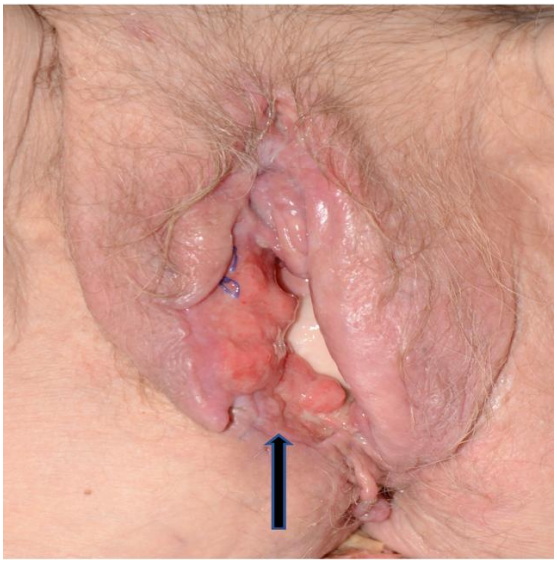

Figure 10: Right labial ulcer (healing); left labial ulcer completely healed.

Postoperatively, further infection was developed, further swabs were obtained which showed growth of *Escherichia*

coli and *Proteus mirabilis*. A Herpes simplex virus PCR was taken from the ulcer which detected the presence of Herpes simplex type 2 nucleic acid. Subsequently the patient was commenced on IV Gentamycin (as per the culture report) and IV acyclovir 10 mg/kg TDS (for herpes simplex) after discussion with Microbiology, later discharged on oral acyclovir 400 mg five times a day for 10 days. She also received a two unit blood transfusion which was indicated by the fall in Hb from 90 to 72 gm/l and clinically symptomatic.

The patient was later reviewed after 2 weeks in a joint Gynae Oncology and Haematology MDT clinic were it was noted she was recovering well clinically with healing of the vulval ulcer (figure 10), the patient reported herself to be feeling stronger with an overall improvement to her health. She was discharged from Gynaecological Services, with her care being transferred to the Haematology team where regular follow-up appointments were advised with no active treatment required at this stage.

DISCUSSION

This was a case of dermatological manifestation of chronic lymphoid leukaemia (leukaemia cutis) developing at a site of genital Herpes simplex infection with superadded secondary bacterial infection. To our knowledge this is the fourth case of vulval involvement of CLL reported so far but the first following genital herpes infection.

Gynaecological involvement in chronic lymphocytic leukaemia (CLL) is rare. Limited literature exists on lymphoid infiltration of gynaecological organs, with only one case series reporting CLL involvement in ovarian mucinous cystadenoma, ovarian fibrothecoma, and pelvic lymph nodes in patients with established disease.[3] Involvement of the external genitalia is even less common. To date, only three case reports have described labial involvement by CLL, presenting as a labial mass in one case and labial ulceration in two cases.[4-6] Notably, CLL was the initial presentation in one patient, while the remaining two were already receiving treatment for known CLL.

Cutaneous involvement of CLL (leukaemia cutis) can be in two forms, firstly as metastatic infiltration by a malignant, clonal population of leukemic cells, a direct sign of extramedullary leukaemia, and a poor prognostic sign with shorter survival; secondly as leukemic cell accumulation at a herpes infection site secondary to body's physiological, reactive immune response to an antigenic/infectious stimulus (the Herpes virus). The latter does not indicate disease progression and may not worsen the overall prognosis, provided the underlying leukaemia is stable. Cutaneous infection with Herpes viruses, including Herpes simplex and Herpes zoster, represents a common non-specific skin manifestation in patients with B-cell chronic lymphocytic leukaemia (B-CLL), largely attributable to underlying immune dysfunction. Previous reports have described the development of cutaneous CLL at sites of healed or active herpetic lesions.[7] In a study by Cerroni et al, leukaemia cutis–type lesions were identified at sites of post-herpetic scarring in 6 of 42 patients with CLL.[8] Similar leukemic infiltrates arising within scars following herpes virus eruptions have also been reported by Zimmer et al and Kakadia et al.[7,9] The predilection for leukaemia cutis to localise within areas of inflammation, scarring, or pre-existing skin neoplasms is thought to be mediated by local inflammatory mechanisms. Release of interleukin-1 (IL-1) from damaged keratinocytes and tumour necrosis factor (TNF) from skin cancer cells can induce activation of intercellular adhesion molecule-1 (ICAM-1), promoting recruitment of B lymphocytes into the skin through pathways analogous to T-lymphocyte skin homing. This phenomenon is therefore considered a reactive process rather than a manifestation of metastatic spread.[10,11]

In some cases, the cutaneous involvement has been the initial presentation leading to the diagnosis of B-CLL, while in others it has occurred months after the diagnosis, with a reported mean interval of 39 months (range 0-142 months).[12] All the previous reports of CLL skin infiltration arising at sites of Herpes simplex infection have involved non-gynaecological sites, including the upper lip, trunk, and forehead. To our knowledge, this is the first reported case of cutaneous CLL associated with genital Herpes infection and the interval in this case between the diagnosis of B-CLL and the LC was 23 months.

The clinical appearances of LC are highly variable and include mainly papules, maculae, nodules, plaques and ulcers.[13] Leukaemia cutis–associated ulcers are typically solitary, a few centimetres in size, and resistant to standard treatment, with a purulent or haemorrhagic base and soft, raised margins; atypical sites may be involved. In our case, a non-healing ulcer initially confined to one labium progressively extended to both labia and the vagina, reaching 5 cm with similar characteristic features.

The histopathological diagnosis of leukaemia cutis relies on careful assessment of the distribution pattern, cytological features, and immunohistochemical profile of the infiltrating tumour cells.[14] Histological appearances can vary significantly over the course of the disease and do not always correlate with the clinical presentation.

In our case, a definitive diagnosis was only established after a haemopathology review, which demonstrated diffuse infiltration of small- to medium-sized lymphoid cells, predominantly B cells, expressing BCL2 and CD5, with patchy expression of BCL6 and CD23, and a low proliferation index on MIB1 staining. Notably, despite the clinically progressive worsening of the ulcer, the histological findings were consistent with a low-grade B-cell non-Hodgkin lymphoma in keeping with CLL, with no evidence of high-grade transformation.

The impact of leukaemia cutis–type lesions on prognosis in patients with B-CLL remains unclear. Cerroni et al

demonstrated that skin involvement does not appear to adversely affect overall prognosis. In particular when cutaneous lesions arise as a reactive phenomenon, such as at sites of herpetic infection, they may reflect an underlying immunological response and preserved immune competence rather than disease progression. Consequently, prognosis and management are primarily determined by the type, grade, and stage of the underlying leukaemia.

Similarly, in our case, the disease was low grade with a low proliferation index and no evidence of high-grade transformation; therefore, a decision was made to continue active surveillance rather than initiate immediate treatment. What further distinguishes this case is the significant diagnostic complexity encountered, which had a direct impact on the patient's clinical journey, including prolonged hospitalisation and increased physical and psychological burden. Several factors contributed to these diagnostic challenges. Herpesvirus infections classically present with a vesicular rash; however, atypical presentations are well documented in immunosuppressed patients, including those with haematological malignancies.[15] In this case, the patient did not exhibit the typical vesicular lesions associated with herpes infection, and as a result, there was no initial clinical suspicion of a herpetic aetiology.

Although the patient had a known diagnosis of CLL, the clinically stable nature of her disease, together with the rarity of leukaemia cutis, meant that it was not initially considered in the differential diagnosis. Three sequential biopsies were non-diagnostic likely due to viral changes in the first sample and focal, subtle leukemic infiltration with limited tissue in subsequent specimens. Such sampling challenges are recognised in early leukaemia cutis and can delay diagnosis. A definitive diagnosis was achieved only after multiple, more extensive biopsies. Repeated microbiological swabs were negative as testing focused only on bacterial pathogens, and a viral cause was not initially considered. Histology showed no typical viral cytopathic changes, and herpes serology was negative. Earlier viral testing of the ulcer particularly after poor response to antibiotics might have enabled a timelier diagnosis and reduced delay.

In everyday gynaecology practice, cases like this are extremely uncommon, which makes them easy to overlook. As a result, diagnosis can be delayed, especially when the presentation does not fit the usual patterns of common vulval conditions. This case highlights the importance of adopting a holistic approach, rather than focusing only on the most likely or familiar diagnoses. Clinicians should consider atypical causes when symptoms persist, worsen or do not respond to standard treatment. Early involvement of a multidisciplinary team, repeating investigations with adequate and targeted biopsies, and reconsidering the diagnosis when initial tests are inconclusive are crucial steps.

CONCLUSION

Persistent, non-healing vulval ulcers in patients with chronic lymphocytic leukaemia (CLL) should raise suspicion of leukaemia cutis, even when the underlying haematological disease appears clinically stable. In immunocompromised patients, atypical Herpes simplex infection may occur and may lack the classic vesicular features, leading to delayed recognition. Leukaemia cutis can closely mimic vulval malignancy both clinically and radiologically, resulting in significant diagnostic uncertainty. As initial biopsies may be non-diagnostic, repeat, deeper, and multiple biopsies may be required. Early multidisciplinary collaboration involving gynaecology, oncology, haematology, histopathology, and microbiology is essential to establish an accurate diagnosis and guide appropriate management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Cancer Research UK. Chronic lymphocytic leukaemia (CLL) incidence statistics. London: Cancer Research UK. Available at: https://www.cancerresearchuk.org/healthprofessional/cancer-statistics/statistics-by-cancer-type/leukaemia-cll/incidence. Accessed on 27 March 2026.
2. Robak T, Puła A, Braun M, Robak E. Extramedullary and extranodal manifestations in chronic lymphocytic leukemia-an update. Ann Hematol. 2024;103(9):3369-83.
3. Morell A, M. A, T. S, Z. N, M. L, A. C. Chronic lymphocytic leukemia in the female pelvis: A case series illustrating the diagnostic challenges. Curr Probl Cancer Case Rep. 2023;10:100234.
4. Udupa K, Bhat SK, Pai RS. Unusual involvement of cervix and vulva in a case of chronic lymphocytic leukemia. J Gynecol Oncol. 2012;23(3):205-6.
5. Lim WH, Mayson E, Lamaro VP. Chronic lymphocytic leukaemia masquerading as a labial lump. BMJ Case Rep. 2019 ;12(1): bcr-2018-227328.
6. Saizan A, Dean OR, Scott GA, Mannava KA, Mercurio MG. Vulvar leukemia cutis: A case report and review of the literature. JAAD Case Reports. 2023;31:97-101.
7. Kakagia D, Tamiolakis D, Lambropoulou M, Kakagia A, Grekou A, Papadopoulos N. Systemic B-cell chronic lymphocytic leukemia first presenting as a cutaneous infiltrate arising at the site of a herpes simplex scar. Minerva Stomatol. 2005;54(3):161-3.
8. Cerroni L, Zenahlik P, Kerl H. Specific cutaneous infiltrates of B-cell chronic lymphocytic leukemia arising at the site of herpes zoster and herpes simplex scars. Cancer. 1995;76(1):26-31.
9. Ziemer M, Bornkessel A, Hahnfeld S, Weyers W. 'Specific' cutaneous infiltrate of B-cell chronic

lymphocytic leukemia at the site of a florid herpes simplex infection. J Cutan Pathol. 2005;32(8):581-4.
10. Szukalski Ł, Sysakiewicz-Buda M, Męcińska-Jundziłł K, Białecka A, Czyż J, Czajkowski R. Cutaneous manifestation of chronic lymphocytic leukemia: a case report and a literature review. Postepy Dermatol Alergol. 2019;36(6):778-80.
11. Yang L, Froio RM, Sciuto TE, Darley-Usmar VM, Ma L, Sun Z, et al. ICAM-1 regulates neutrophil adhesion and transcellular migration of TNF-alpha-activated vascular endothelium under flow. Blood. 2005;106:584-92.
12. Cerroni L, Zenahlik P, Höfler G, Kaddu S, Smolle J, Kerl H. Specific cutaneous infiltrates of B-cell chronic lymphocytic leukemia: a clinicopathologic and prognostic study of 42 patients. Am J Surg Pathol. 1996;20(8):1000-10.
13. Wagner G, Fenchel K, Back W, Schulz A, Sachse MM. Leukemia cutis – epidemiology, clinical presentation, and differential diagnoses. J Dtsch Dermatol Ges. 2012;10(1):27-36.
14. Antunes J, Pacheco D, Travassos R, Filipe P. Zosteriform B-cell chronic lymphocytic leukemia infiltration. Dermatol Online J. 2011;17(9):9.
15. Khera P, Smith JRJ, Feldman SR. Atypical presentations of herpesvirus infections in patients with chronic lymphocytic leukemia. J Am Acad Dermatol. 2009;60(3):484-6.

Cite this article as: Malakar A, Javaid F, Booth S, Snowden B, Manoharan A. Atypical vulval cutaneous manifestation of chronic lymphocytic leukaemia following genital herpes masquerading as vulvar carcinoma: a case report. Int J Reprod Contracept Obstet Gynecol 2026;15:2750-6.