

Primary Cutaneous Diffuse Large B-cell Lymphoma Presenting as a Non-healing Axillary Ulcer

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Abstract

Primary cutaneous diffuse large B-cell lymphoma (PCDLBCL) is a rare, aggressive lymphoma primarily affecting the skin. We report an unusual case of a female patient in her late 50s with a persistent non-healing ulcer in the left axilla, initially misdiagnosed as cutaneous tuberculosis. Despite empirical treatment, the ulcer worsened, leading to further investigation and a revised diagnosis of germinal centre-type PCDLBCL through biopsy and immunohistochemistry. The patient showed significant improvement in the wound following chemotherapy, but succumbed to complications of severe neutropenia and acute respiratory distress syndrome (ARDS). This case underscores the importance of early biopsy and histopathological evaluation in atypical, rapidly progressing cutaneous lesions to avoid misdiagnosis and ensure timely treatment, ultimately significantly improving patient outcomes in cases of primary cutaneous diffuse large B-cell lymphoma if managed and diagnosed early.

Categories: General Surgery, Oncology, Dermatology

Keywords: anti-tuberculosis therapy, chemo markers, general surgery, nonhealing ulcer, non-hodgkin's lymphoma, skin cancers

Introduction

Diffuse large B-cell lymphoma (DLBCL) represents one of the most common subtypes of non-Hodgkin lymphoma (NHL), comprising over one-third of all NHL cases. These are very aggressive tumours arising from mature B cells and can involve both nodal and extranodal sites. The extra-nodal involvement in DLBCL can affect various organs, including the stomach, spleen, Waldeyer's ring, central nervous system (CNS), lungs, bone, and skin. Skin and the gastrointestinal tract are the frequent extra-nodal sites, accounting for approximately 18% of cases [1]. Cutaneous involvement in DLBCL can be categorised into two primary types: primary cutaneous DLBCL (PCDLBCL), which is confined to the skin and secondary cutaneous involvement resulting from systemic DLBCL with secondary cutaneous involvement. Primary cutaneous lymphomas are further classified into primary cutaneous follicle centre lymphoma (PCFCL), primary cutaneous DLBCL-leg type (PCDLBCL-LT), and primary cutaneous marginal zone lymphoma (PCMZL) [2,3]. Here, we report a case of PCDLBCL involving the left axillary skin (a very rare site of presentation), which progressed to a large axillary ulcer but showed significant improvement following the initiation of chemotherapy.

This case report describes a rare presentation of non-Hodgkin lymphoma, initially mimicking a non-healing ulcer at a very rare and atypical site with an insidious onset. Despite multiple evaluations, the diagnosis was delayed due to the unusual clinical presentation and rarity of the condition. Unfortunately, the patient succumbed to the disease before definitive treatment could yield full benefit. We present this case to raise awareness among healthcare professionals, emphasising the importance of considering malignancy in atypical, non-resolving ulcers. Early recognition and timely intervention can significantly improve patient outcomes and quality of care.

Case Presentation

Case presentation

A female in her late 50s with no known comorbidities presented to our outpatient department with complaints of a non-healing ulcer in the left axillary region for six months. The ulcer had an insidious onset and showed significant progression over the past three months. The patient denied any history of trauma. She had undergone wound debridement at an outside hospital one month before, in view of worsening of the wound condition, and was referred to our tertiary care centre for further management. On examination, a 6 × 4 cm ulcer was noted in the left axilla, extending from the level of the third to the seventh rib along the mid-axillary line. The ulcer had irregular margins, with a floor covered in necrotic tissue, slough, and minimal purulent discharge (Figure 1).

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FIGURE 1: Patient image at presentation

The image shows the initial presentation in our outpatient department, status post wound debridement done in an outside hospital.

Given the ulcer's atypical location and the absence of risk factors such as trauma or diabetes, and despite debridement, dressings, and multiple courses of antibiotics, its persistence for over six months raised suspicion of an underlying malignant/autoimmune/tubercular pathology.

Initial investigations

On admission, the baseline investigations were unremarkable. An edge wedge biopsy of the lesion was performed, which was reported as T-cell-rich atypical lymphoid proliferation, with positive staining for CD20, CD3, CD5, and CD7, but negative for CD10 and CD30. The Ki-67 proliferation index was noted to be 30%. Based on the presence of scattered pleomorphic cells with atypical mitoses, a T-cell clonality test was performed to rule out a neoplastic process, which was negative for clonal T-cell receptor gamma chain gene rearrangements. Pus culture from the axillary ulcer revealed *Enterococcus faecium* and *Proteus mirabilis* growth. The patient was managed conservatively with intravenous (IV) antibiotics based on culture sensitivity and daily bedside dressing and debridement. Laboratory tests for autoimmune testing were sent, revealing the following: C3 - 204.5, C4 - 63.3, PR3-ANCA, and MPO-P ANCA were negative. ANA by immunofluorescence (IF) for antinuclear antibodies and anti-ds-DNA was also negative, effectively ruling out an autoimmune cause. Given suspicion for cutaneous tuberculosis (TB), samples were sent for GeneXpert, acid-fast bacillus (AFB) testing, and Gram stain, all of which were negative for tuberculosis. However, considering the high endemicity of TB in India and after ruling out other causes, the patient was empirically started on anti-tuberculosis treatment (ATT).

Initial treatment

Despite aggressive empirical anti-tuberculosis treatment, the ulcer continued to worsen very rapidly (Figure 2).



FIGURE 2: Patient image during the treatment

Figure showing the rapid worsening of the ulcer despite conservative management of the wound.

The patient subsequently developed features of sepsis and underwent wound debridement of the left axillary ulcer under general anaesthesia. Intraoperatively, the muscle fibres of the latissimus dorsi and serratus anterior muscles appeared pale, with early features suggestive of necrosis and sloughing noted. Aggressive wound debridement was performed until fresh bleeding was noted with healthy tissue. Postoperatively, the wound continued to worsen, with progressive necrosis despite twice-daily bedside dressings (Figure 3).

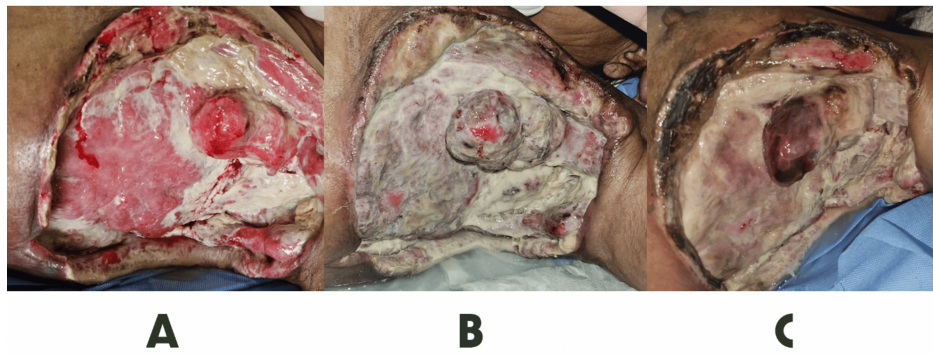


FIGURE 3: Patient images after wound debridement

The images show rapid worsening of the wound post-wound debridement and aggressive bedside dressing with culture-sensitive intravenous (IV) antibiotics. (A) picture of the ulcer taken on postoperative day (POD) 2, (B) picture of the ulcer taken on POD 5, (C) picture of the ulcer taken on POD 10.

Further investigations

Given the worsening condition, a repeat edge wedge biopsy was performed due to increasing suspicion of malignant aetiology. The second biopsy revealed features consistent with diffuse large B-cell lymphoma, germinal centre type. Immunohistochemistry (IHC) showed positivity for CD20, CD68 (scattered positivity), Kappa and Lambda (patchy positivity), and PAX5. The tumour was negative for Cyclin D1, CD5, CD23, CD3, and CD15. Ki-67 positivity was high (70-80%), while MUM-1, C-MYC, BCL-2, and BCL-6 were expressed in the following percentages: MUM-1 (10-15%), C-MYC (10-15%), BCL-2 (5-10%), and BCL-6 (45-50%) (Figures 4-6).

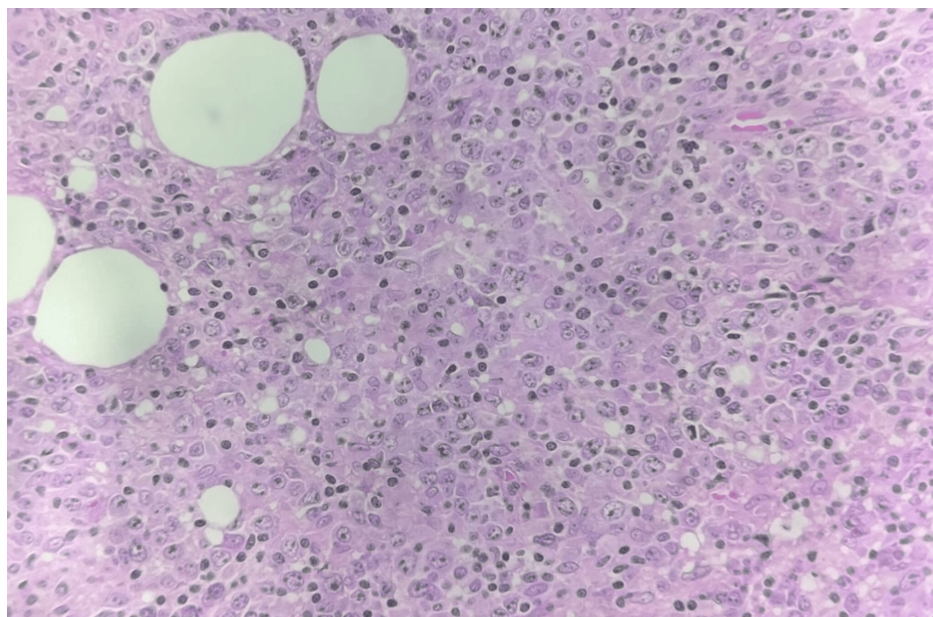


FIGURE 4: Histopathology image at 40X

The image is a histopathological examination (HPE) at 40X, showing large, pleomorphic B cells.

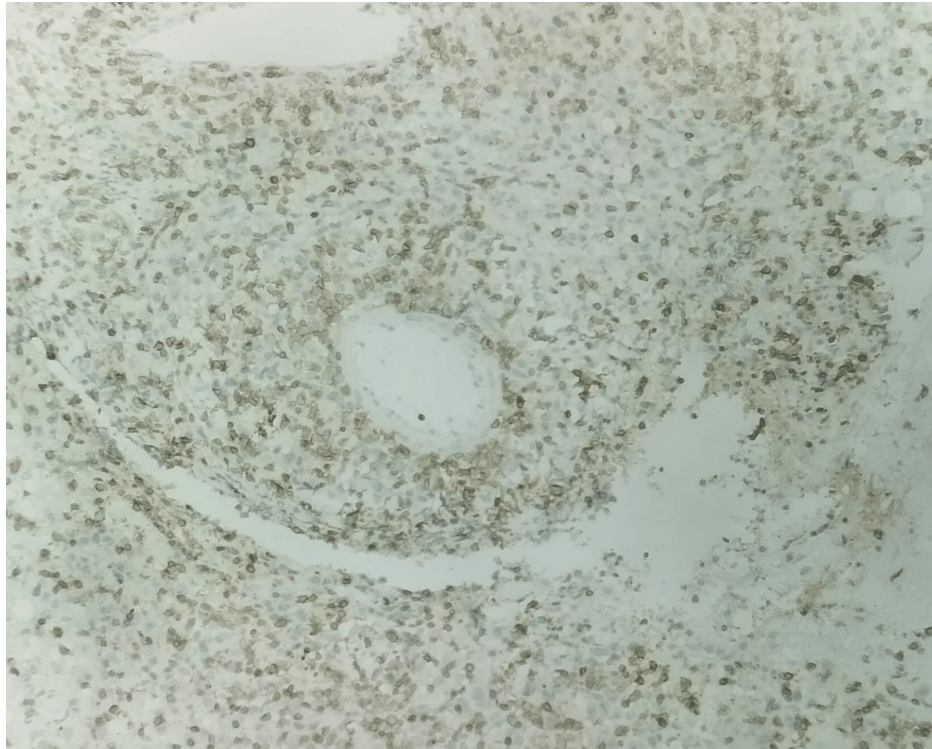


FIGURE 5: Immunohistochemistry image 1

Immunohistochemistry results showed that the sample was CD3 negative.

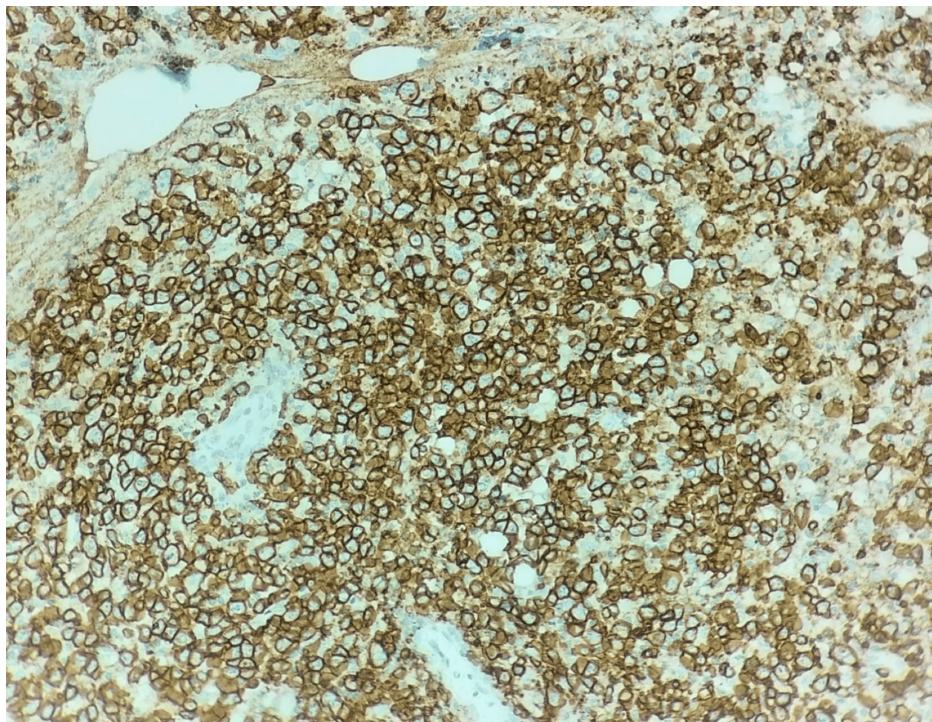


FIGURE 6: Immunohistochemistry image 2

Immunohistochemistry results showed CD20 positivity.

A Positron Emission Tomography-Computed Tomography (PET-CT) was performed, showing a large infiltrative FDG-avid lesion with multiple areas of necrosis in the left chest wall and axilla with no other

areas of any significant abnormal metabolic activity (Figures 7, 8).

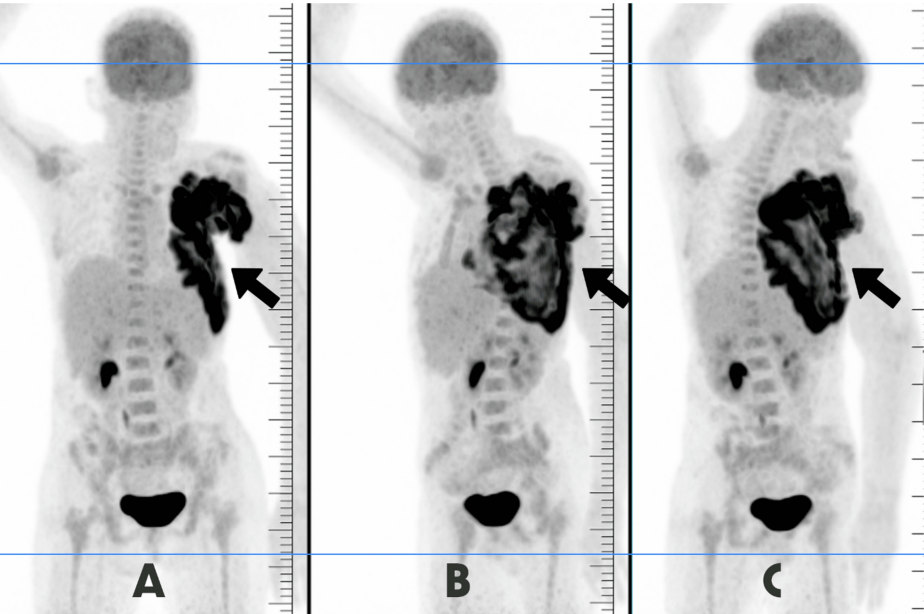


FIGURE 7: PET-CT scan images of the patient (coronal and sagittal views)

Images A (coronal view), B (sagittal), and C (sagittal) show different Positron Emission Tomography-Computed Tomography (PET-CT) views of the left axillary ulcer with significant uptake at the left axillary ulcer site.

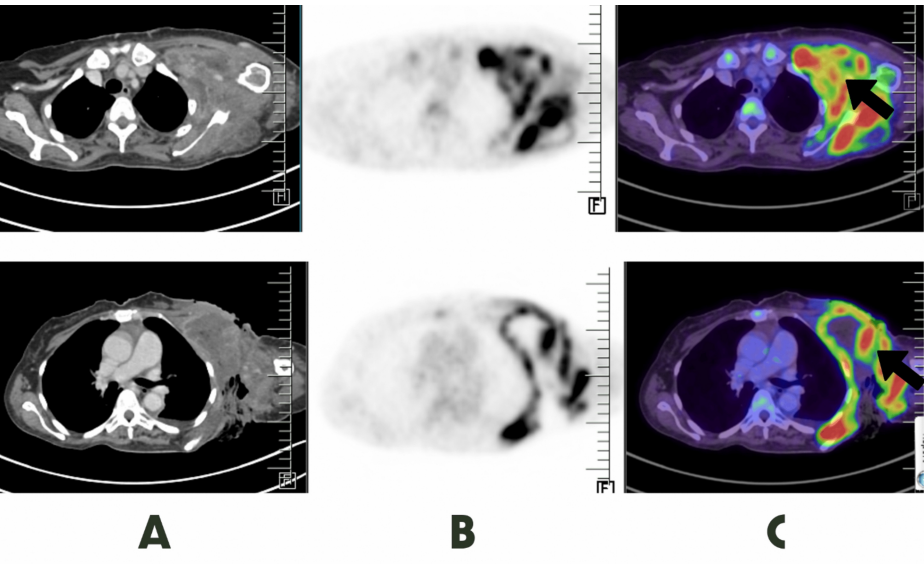


FIGURE 8: PET-CT images of the patient (axial views)

A, B and C represent Positron Emission Tomography-Computed Tomography (PET-CT) scan images of the left axillary ulcer showing uptake over the left axillary region.

Treatment

Following the confirmation of diagnosis of a primary cutaneous diffuse large B-cell lymphoma, the medical oncology team has been involved, and the patient was promptly started on chemotherapy (R CHOP regimen- rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) and was given one cycle.

Outcome

The wound showed significant and drastic improvement. The ulcer showed wide areas of red granulation tissue with active vascularity and significantly reduced slough (Figure 9).

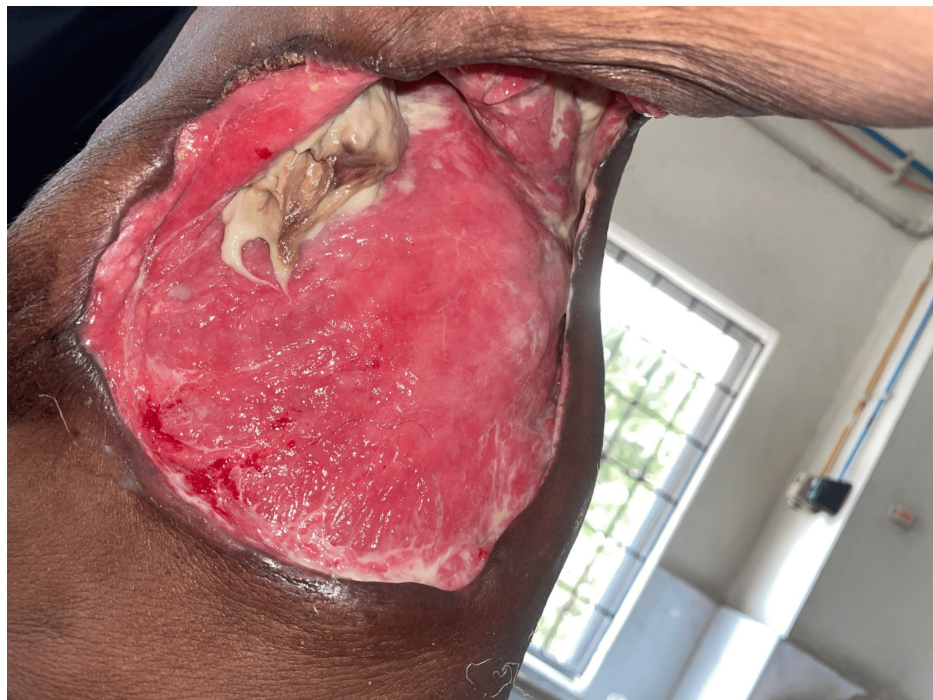


FIGURE 9: Patient image after a single cycle of chemotherapy

The image shows that a drastic improvement in the ulcer was observed after a single cycle of chemotherapy.

Despite the wound showing remarkable improvement following a single cycle of chemotherapy, the patient's general condition declined due to adverse reactions to chemotherapy and developed severe neutropenia with worsening ARDS, and the patient succumbed to the adverse reactions.

Discussion

Primary cutaneous diffuse large B-cell lymphoma (PCDLBCL) is a rare and aggressive lymphoma that predominantly affects the skin, characterised by the rapid growth of large B-cell neoplasms. It accounts for a significant proportion of cutaneous lymphomas, with the majority of cases being extranodal. PCDLBCL is known for its aggressive clinical course, often presenting as rapidly enlarging nodules, plaques, or rarely as ulcerative lesions that can cause substantial morbidity due to their rapid progression and potential for skin necrosis [3,4].

PCDLBCL is often misdiagnosed as an infectious or inflammatory condition, especially in the early stages. Conditions such as bacterial infections, tuberculosis, and fungal infections can mimic the clinical appearance of cutaneous lymphoma, leading to delays in proper diagnosis and treatment. In the above case the ulcer was at a very atypical location and did not respond to standard treatment, the initial clinical suspicion of tuberculosis prompted the administration of empirical anti-tuberculosis therapy, which did not halt disease progression. This delay in diagnosis highlights the critical need for clinicians to consider lymphoma in the differential diagnosis of rapidly progressing skin lesions, particularly in immunocompetent patients [5].

Primary cutaneous B-cell lymphomas are mainly classified into primary cutaneous marginal zone lymphoma, primary cutaneous follicle centre lymphoma, and primary cutaneous diffuse large B-cell lymphoma, leg-type. Rare cases may fall outside these categories and require careful clinicopathological correlation. This subtype tends to have a more favourable prognosis when treated with chemotherapy, compared to other forms of cutaneous lymphoma [6,7].

Immunohistochemical studies play a pivotal role in distinguishing PCDLBCL from other cutaneous lymphomas and inflammatory disorders. Markers such as CD20, PAX5, BCL-6, and Ki-67 are frequently used to confirm the diagnosis. High Ki-67 indices (greater than 50%) indicate high proliferative activity, a hallmark of aggressive disease [8]. The histopathological diagnosis is typically made by biopsy, where large pleomorphic B-cells are identified within the dermis or subcutaneous tissue, often with a high mitotic rate and necrosis. Immunohistochemistry (IHC) and genetic studies are then used to confirm the diagnosis [9]. In

this case, the immunohistochemical staining supported a B-cell lineage with positivity for CD20 and PAX5. The expression profile, including BCL-6 and MUM-1, was interpreted as compatible with germinal centre-type DLBCL. The high Ki-67 proliferation index (70–80%) indicated an aggressive tumour with a high risk for dissemination and poor prognosis if left untreated [10].

Chemotherapy, particularly CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or R-CHOP (with rituximab), remains the cornerstone of treatment for PCDLBCL. Chemotherapy is shown to improve overall survival rates and can lead to complete remission in many patients. Rituximab, an anti-CD20 monoclonal antibody, has revolutionised treatment by targeting B-cells and enhancing the efficacy of traditional chemotherapeutic agents [10].

In this case, the patient's positive response to chemotherapy, with significant wound healing and clinical improvement, supports the value of accurate diagnosis and treatment in managing PCDLBCL; however, careful monitoring of treatment-related toxicity was necessary. The prognosis for PCDLBCL varies depending on factors such as the histological subtype, extent of the disease at presentation, and response to treatment. The germinal centre subtype of PCDLBCL, as noted in this patient, tends to have a relatively better prognosis compared to other, more aggressive types like the leg-type. However, treatment outcomes are still heavily influenced by the timeliness of diagnosis and the extent of skin involvement at presentation [7]. Although cutaneous lymphoma may remain confined to the skin, systemic spread can occur, particularly if untreated, and it can lead to lymph node or organ involvement, further complicating management.

Conclusions

This case underscores the importance of a comprehensive diagnostic approach for rapidly progressing skin lesions. Early biopsy, coupled with immunohistochemistry, is essential to differentiate cutaneous lymphoma from other potential causes such as infections or inflammatory conditions. Molecular studies, including clonality tests and genetic profiling, can also help confirm the diagnosis and tailor therapy accordingly. Timely intervention, with a focus on initiating appropriate chemotherapy or immunotherapy (such as rituximab-based regimens), significantly improves patient outcomes, as seen in this case. Timely diagnosis may improve the chance of appropriate treatment initiation, although outcomes may still be limited by disease severity and treatment-related complications. This highlights the importance of not only recognising the clinical signs of PCDLBCL but also implementing a rapid and systematic diagnostic approach to prevent misdiagnosis and ensure the initiation of the most effective treatment regimen.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Veda Munnangi, Narayanan Cunnigaiper, Ludia John

Drafting of the manuscript: Veda Munnangi, Narayanan Cunnigaiper, Ludia John

Critical review of the manuscript for important intellectual content: Veda Munnangi, Narayanan Cunnigaiper, Ludia John

Concept and design: Narayanan Cunnigaiper, Ludia John

Supervision: Narayanan Cunnigaiper

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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