CUTANEOUS MANIFESTATIONS OF LARGE GRANULAR LYMPHOCYTIC LEUKEMIA

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1. Background

- Large granular lymphocytic leukemia (LGLL) is a rare lymphoproliferative disorder of cytotoxic T-cells or NK cells, often linked to autoimmune disorders
- Cutaneous involvement is extremely rare and may mimic other conditions, creating diagnostic challenges
- This report reviews published cases of LGLL with cutaneous involvement and their clinical features, outcomes, and management
- We report a unique case of gamma-delta T-LGLL presenting as a nodular skin ulcer, and systematically review similar reported cases in literature

2. Case presentation

A 66-year-old woman with rheumatoid arthritis presented with fatigue and a persistent right axillary ulcerated nodule. Labs showed marked lymphocytosis, neutropenia, and thrombocytopenia. Bone marrow and peripheral blood flow cytometry revealed a clonal γδ T-cell population (CD2+, CD3+, CD5+, dim CD7+, TCRγδ+), and NGS detected a STAT3 p.Y640F mutation (VAF 41%). PET/CT showed mild splenic and nodal uptake. Skin punch biopsy of the lesion confirmed clonal γδ T-LGLL. Remarkably, the ulcer resolved spontaneously post-biopsy. Final diagnosis was γδ T-LGLL. The patient was started on low-dose methotrexate with improvement in cytopenia.

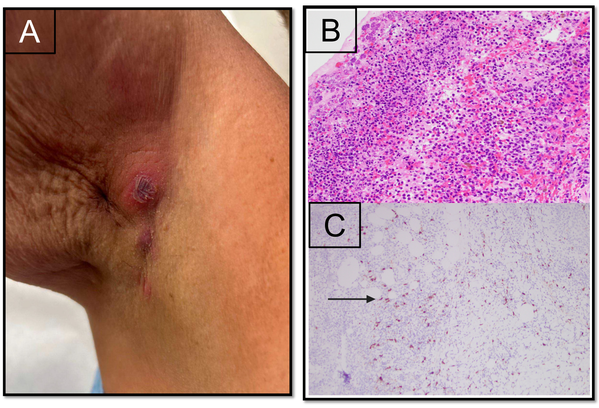


Figure 1: Gross and microscopic images of the ulcer. Skin nodular ulcer located in the right axillary region (A). Microscopic images include a Hematoxylin and eosin (H&E)-stained superficial section at 20x magnification (B) and a TCR-delta-stained sample (arrowhead) at 10x magnification (C).

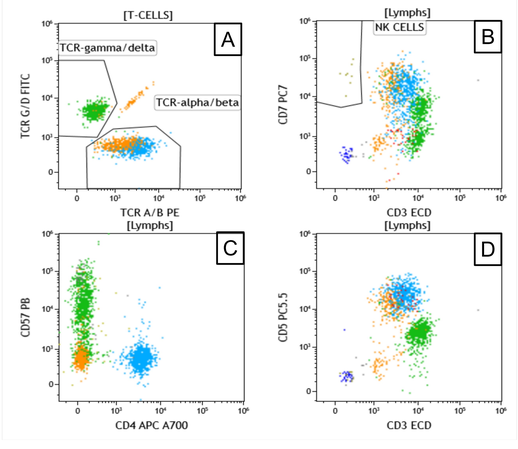


Figure 2: Flow cytometry of the ulcer biopsy. The flow cytometry plot illustrates a clonal population of TCR-gamma/delta cells (A). The γδ T-cells are characterized by CD3+ expression, dim CD7 expression (B), CD4− status, and CD57+ expression (C), along with dim CD5 expression (D).

3. Methods

- Comprehensive systematic search conducted across multiple databases (MEDLINE, CINAHL, Cochrane, Embase, Scopus) using LGLL and skin manifestation terms was conducted.
- Eligible studies were screened, extracted, and quality-assessed independently by reviewers using a modified Newcastle-Ottawa scale.

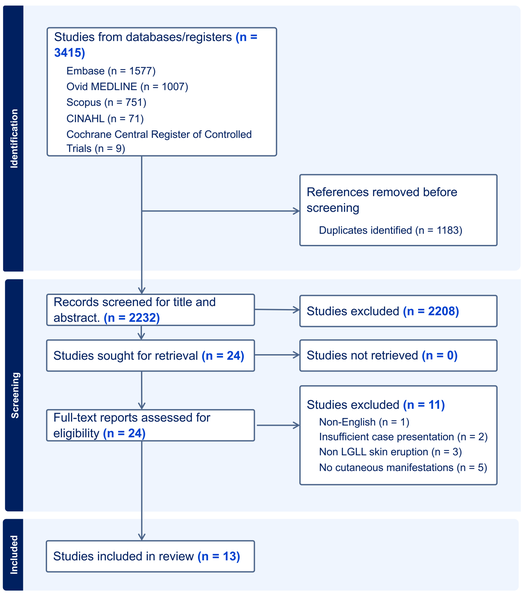


Figure 3: PRISMA Flow chart of the study

4. Results

- 3415 references screened, 13 studies met inclusion criteria, representing 24 patients including our case
- 15 females, 10 males, mean age 62 years, common comorbidities were vasculitis (42%) and rheumatoid arthritis (13%)
- Cutaneous findings included ulcers (most common, often necrotic), nodules, papules, and lesions frequently misdiagnosed as other conditions
- Diagnosis confirmed by skin biopsy showing dermal or dermal-epidermal infiltrates of large granular lymphocytes
- Treatments included methotrexate, steroids, cyclosporine, or CHOP.
- 16 of 24 patients were alive at follow-up, with mixed responses of improvement or progression

5. Conclusion

- Cutaneous involvement in LGLL is exceptionally rare, most often presenting with ulcers, nodules, or papules, and frequently misdiagnosed
- Accurate diagnosis requires integration of clinical features with immunohistopathologic and molecular analyses from blood, skin, and bone marrow
- Skin involvement may indicate a poorer prognosis, with nearly one-third of patients progressing or dying from LGLL

6. References

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