PERINATAL JOURNAL

Original Article

Perinatal Journal 2025; 33(2):528-530

https://doi.org/10.57239/prn.25.03320056

# A diagnostic odyssey: Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder mimicking inflammatory and infectious dermatoses in a young woman

**Hendarto Arif Budiman[1]*, Awalia Awalia[2], Putu Niken Ayu Amrita[3]**

*Universitas Airlangga, Indonesia*

**Abstract**

This report presents a rare case of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCS-TCLPD) in a young woman, highlighting its role as a master mimicker of inflammatory and infectious dermatoses. It addresses critical gaps in recognizing this entity in atypical demographics and anatomic locations. A 22-year-old woman presented with a 3-year history of a firm, erythematous right leg plaque and bilateral hyperpigmented macules worsening with sun exposure. Physical examination revealed livedo reticularis and tender induration without systemic symptoms. Diagnosis required two biopsies and comprehensive immunohistochemistry (CD3+/CD4+/CD5+, Ki67). Treatment with oral methylprednisolone (16 mg TID), hydroxychloroquine (200 mg OD), and topical desoximetasone resulted in significant improvement within 2 weeks.

**Keywords:** Primary cutaneous CD4+ T-cell lymphoproliferative disorder, Diagnostic mimicry, Cutaneous lymphoma, Case report, Indolent T-cell disorder.

## 1.Introduction

Primary Cutaneous CD4+ Small/Medium T-Cell Lymphoproliferative Disorder (PCS-TCLPD) is a low-grade T-cell lymphoproliferative disorder primarily affecting the skin, characterized by T cells with a follicular T-helper phenotype [1]. Initial lesions often present as asymptomatic purplish-pink papules, plaques, or nodules, lacking distinct clinical features, which complicates differentiation from inflammatory or infectious dermatoses [2]. Diagnosis is challenging due to symptom overlap with conditions like eczema, psoriasis, or fungal infections, necessitating biopsy and immunohistochemistry for confirmation [3]. We report a 22-year-old woman with a chronic leg lesion ultimately diagnosed as PCS-TCLPD.

## 3. Method

A 22-year-old woman of Manggarai ethnicity from East Nusa Tenggara Province, Indonesia, presented to our Rheumatology clinic on December 30, 2024, referred by a dermatovenerologist from Dr. Soetomo Hospital with suspected subacute cutaneous lupus erythematosus profundus. Her primary complaint were progressive swelling and erythema on her right leg, persisting since 2021, characterized by a firm, non-pruritic, and non-painful plaque. Additionally, she reported recurrent hyperpigmented macules on both legs since adolescence (initially erythematous, later turning hyperpigmented) that worsened with sun exposure. The patient denied systemic symptoms, including fever, oral ulcers, alopecia, arthralgia, or weight loss. Her diagnostic odyssey spanned four years, beginning in February 2020 when she first noted right leg swelling treated unsuccessfully at multiple institutions with repeated radiographs (all unremarkable) and wound care. By 2024, the lesion expanded with new erythema, and in October 2024, a biopsy at a regional hospital suggested cutaneous leprosy, prompting referral to our tertiary center (Fig. 1). Subsequent investigations at Dr. Soetomo Hospital included a punch biopsy (December 27, 2024) and comprehensive laboratory testing, which revealed an elevated erythrocyte sedimentation rate (32 mm/h) but normal autoimmune markers (negative ANA test, negative anti-dsDNA), normal complement levels, and microbiological studies. Physical examination demonstrated livedo reticularis with telangiectasia on both feet and a tender, indurated erythematous plaque on the right crural region without joint involvement. Histopathology ultimately revealed a dense dermal lymphocytic infiltrate (Fig. 2A-B) with

**Correspondence:** Hendarto Arif Budiman, Universitas Airlangga, Indonesia, **e-mail:** hendartoarifb@gmail.com, **Received:** September 16, 2025 **Accepted:** October 29, 2025

immunohistochemical staining confirming CD3+/CD4+/CD5+ T-cells with partial CD7/CD8 loss, CD30 negativity, and a Ki67 proliferation index of 20% (Fig. 2C-G), establishing the diagnosis of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder. Ultrasound showed soft tissue inflammation with normal X-rays.

## 4.Results and Discussion

Primary Cutaneous CD4+ Small/Medium T-Cell Lymphoproliferative Disorder (PCS-TCLPD) represents a diagnostic enigma in dermatopathology, epitomizing the critical intersection of clinical mimicry and histopathological specificity. This case underscores the disorder's propensity to masquerade as inflammatory or infectious entities, exemplified by our patient's initial misdiagnoses of cutaneous leprosy and lupus profundus, a phenomenon attributable to its polymorphic clinical presentations. The protracted diagnostic odyssey spanning four years highlights a well-documented challenge: PCS-TCLPD's non-specific erythematous plaques or nodules frequently imitate common dermatoses like psoriasis, eczema, or granulomatous infections, delaying definitive diagnosis by a median of 1–3 years in reported series [5,9]. Such delays carry significant psychosocial and therapeutic implications, particularly in young patients like ours, where malignant etiologies are rarely suspected.

Histopathologically, PCS-TCLPD demonstrates a distinctive yet deceptive architecture. The dense dermal infiltrates of small-to-medium-sized pleomorphic T-cells—often with admixed B lymphocytes, histiocytes, and eosinophils may initially resemble reactive lymphoid hyperplasia or pseudolymphoma [6,16]. Our case exhibited classic features: monotonous CD4+ T-cell predominance (CD3+/CD4+/CD5+), partial loss of pan-T-cell markers (CD7−/CD8−), absence of CD30 expression, and a low Ki67 proliferative index (20%), aligning with WHO diagnostic criteria [1,4]. Critically, the absence of epidermotropism and cytotoxic markers (TIA-1, granzyme B) helps differentiate it from aggressive variants like cutaneous γδ T-cell lymphoma [7,19,20]. Recent molecular advances further refine diagnosis; clonal T-cell receptor rearrangements, though variably present, support clonality without conferring malignant behavior, while PD-1/CXCL13 co-expression suggests follicular T-helper cell origin [16,21].

Therapeutic decisions remain nuanced due to PCS-TCLPD's indolent biology. First-line modalities include localized excision, radiotherapy (8–24 Gy), or intralesional steroids—approaches achieving complete remission in >85% of solitary lesions [9,23]. Our patient's rapid response to methylprednisolone (16 mg TID) and hydroxychloroquine aligns with evidence that even extensive lesions may regress with immunomodulation alone [10,17]. Notably, spontaneous remission post-biopsy occurs in 15–20% of cases, challenging traditional oncology paradigms [11,25]. This benign trajectory underpinned the WHO's seminal reclassification from "lymphoma" to "lymphoproliferative disorder" in 2017—a shift acknowledging its 100% 5-year disease-specific survival and <5% recurrence risk [1,4]. Nevertheless, vigilance is warranted: lesions >3 cm, ulceration, or CD30+ transformations may signal atypical behavior, necessitating systemic therapies like low-dose methotrexate or doxycycline [17,18].

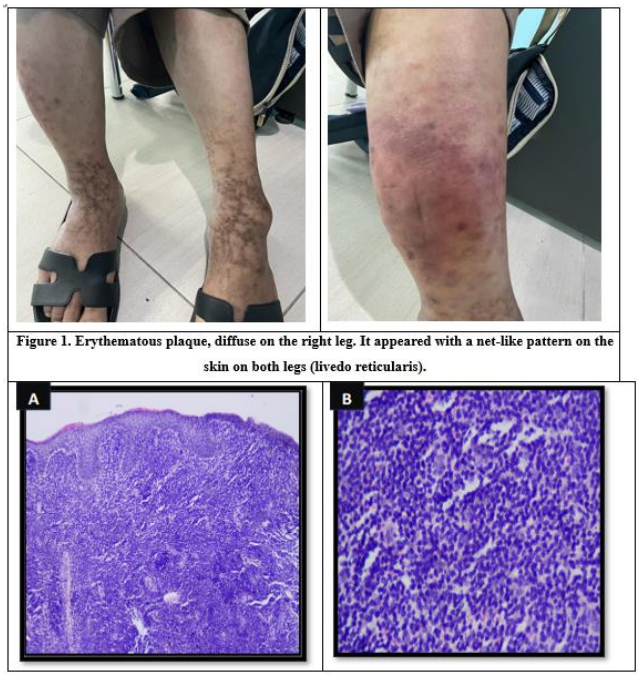


Figure 1. Erythematous plaque, diffuse on the right leg. It appeared with a net-like pattern on the skin on both legs (livedo reticularis).

In conclusion, this case illuminates PCS-TCLPD as a master of disguise within the cutaneous lymphoma spectrum. Its diagnostic complexity demands:

- High-index suspicion for persistent "inflammatory" lesions unresponsive to conventional therapy,

- Deep biopsy with immunohistochemistry to detect subtle atypical infiltrates, and

Restraint in aggressive treatment given its favorable prognosis. Future studies exploring follicular T-helper cell dynamics and PD-1 blockade may further unravel its pathogenesis.

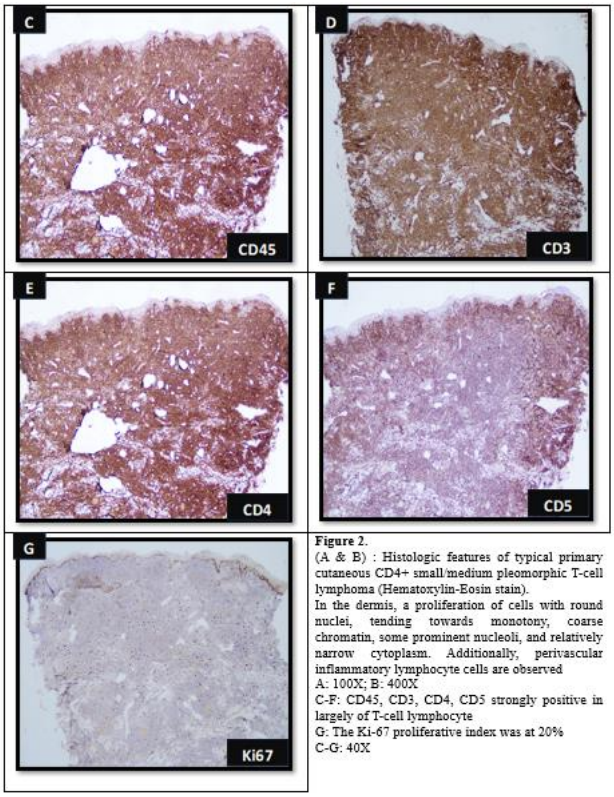


**Figure 2.**
(A & B) : Histologic features of typical primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma (Hematoxylin-Eosin stain).
In the dermis, a proliferation of cells with round nuclei, tending towards monotony, coarse chromatin, some prominent nucleoli, and relatively narrow cytoplasm. Additionally, perivascular inflammatory lymphocyte cells are observed
A: 100X; B: 400X
C-F: CD45, CD3, CD4, CD5 strongly positive in largely of T-cell lymphocyte
G: The Ki-67 proliferative index was at 20%
C-G: 40X

## 4.Conclusion

In summary, this case underscores the diagnostic complexities of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSM-TCLPD), an entity renowned for its mimicry of benign inflammatory and infectious dermatoses. The protracted diagnostic journey highlights the imperative for heightened clinical suspicion in cases of persistent, atypical cutaneous lesions refractory to conventional therapy, necessitating a deep biopsy and comprehensive immunohistochemical analysis for definitive diagnosis. The subsequent excellent response to a conservative immunomodulatory regimen reaffirms the indolent biology and favorable prognosis characteristic of this disorder, emphasizing that aggressive intervention is typically unwarranted. Ultimately, increased awareness of PCSM-TCLPD is paramount to circumvent diagnostic delays, ensure appropriate management, and alleviate the significant patient burden associated with this masquerading condition.

## 5. References

1. Gaulard P, Berti E, Willemze R, Petrella T, Jaffe ES. Primary cutaneous CD4+ small/ medium T-cell lymphoproliferative disorder. In: Swerdlow SH, ed. WHO classification of tumours of haematopoietic and lymphoid tissues. 5th ed. Lyon, France: International Agency for Research on Cancer and World Health Organization; 2017:401
2. Beltraminelli H, Leinweber B, Kerl H, Cerroni L. Primary cutaneous CD4+ small/ medium-sized pleomorphic T-cell lymphoma: a cutaneous nodular proliferation of pleomorphic T lymphocytes of undetermined significance? A study of 136 cases. Am J Dermatopathol. 2009;31(4):317-322. doi: 10.1097/DAD.0b013e31819f19bb.
3. Ardeleanu V, Moroianu LA, Sava A, Tebeica T, Jecan RC, Moroianu M, Tatu AL. Surgical, Dermatological and Morphopathological Considerations in the Diagnosis and Treatment of Cutaneous Lymphoproliferative Tumors, Primary CD4. Medicina (Kaunas). 2022 Nov 10;58(11):1618. doi: 10.3390/medicina58111618. PMID: 36363575; PMCID: PMC9692388.
4. Willemze, R.; Cerroni, L.; Kempf, W.; Berti, E.; Facchetti, F.; Swerdlow, S.H.; Jaffe, E.S. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. Blood 2019, 133, 1703–1714. [CrossRef] [PubMed]
5. Gru, A. A., Wick, M. R., & Eid, M. (2018). Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder-clinical and histopathologic features, differential diagnosis, and treatment. Seminars in Cutaneous Medicine and Surgery, 37(1), 39–48. https://doi.org/10.12788/j.sder.2018.006
6. Beljaards RC, Meijer CJ, Van der Putte SC, et al. Primary cutaneous T-cell lymphoma: clinicopathological features and prognostic parameters of 35 cases other than mycosis fungoides and CD30-positive large cell lymphoma. J Pathol. 1994;172(1):53-60. Doi:

10.1002/path 1711720110.
7. Agro CM, Olson LC, Fulmer CG. CD30+ T cell-enriched primary cutaneous CD4+ small/medium-sized pleomorphic T cell lymphoma: A distinct variant of indolent CD4+ T cell lymphoproliferative disease. Ann Diagn Pathol. 2017;30:52-58. doi: 10.1016/j.anndiagpath.2017.04.009.James E, et al. CD4+ primary cutaneous pleomorphic T-cell lymphoma. Leuk Lymphoma. 2015;56(4):951–7.
8. Besch-Stokes JG, Costello CM, Severson KJ, Bhullar P, Montoya J, Butterfield RJ, et al. Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder: Diagnosis and management. J Am Acad Dermatol. 2022;86:1167–9. [PubMed] [Google Scholar] [Ref list]
9. Virmani P, Jawed S, Myskowski PL, et al. Long-term follow-up and management of small and medium-sized CD4+ T cell lymphoma and CD8+ lymphoid proliferations of acral sites: a multicenter experience. Int J Dermatol. 2016;55(11):1248-1254. doi: 10.1111/ijd.13340
10. Ayala D, Ramón MD, Cabezas M, Jordá E. Primary Cutaneous CD4+ Small/Medium-Sized Pleomorphic T-Cell Lymphoma With Expression of Follicular T-Helper Cell Markers and Spontaneous Remission. Actas Dermosifiliogr. 2016;107(4):357- 359. doi: 10.1016/j.ad.2015.10.012.
11. Shakerian B, Razavi N, Mandegar MH. Primary Cutaneous CD4-Positive Small/ Medium-Sized Pleomorphic T-Cell Lymphoma Following Heart Transplantation. Int J Organ Transplant Med. 2017;8(3):168-169.
12. Garrido MC, Riveiro-Falkenbach E, Ruano Y, Ortiz P, Rodriguez-Peralto JL. Primary cutaneous small/medium CD4+ T-Cell lymphoma occurring during treatment with vemurafenib for advanced melanoma. Am J Dermatopathol. 2015;37(6):440- 443. doi: 10.1097/DAD.0000000000000231.
13. Ma H, Qiu S, Lu R, Feng P, Lu C. Methotrexate and etanercept-induced primary cutaneous CD4-positive small/medium-sized pleomorphic T-cell lymphoma. An Bras Dermatol. 2016;91(3):368-371. doi: 10.1590/abd1806-4841.20163875
14. Celebi Cherukuri N, Roth CG, Aggarwal N, Ho J, Gehris R, Akilov OE. Cutaneous Small/Medium CD4+ Pleomorphic T-Cell Lymphoma-Like Nodule in a Patient With Erythema Chronicum Migrans. Am J Dermatopathol. 2016;38(6):448-452. doi: 10.1097/DAD.0000000000000596.
15. Alberti-Violetti S, Torres-Cabala CA, Talpur R, Corti L, Fanoni D, Venegoni L, et al. Clinicopathological and molecular study of primary cutaneous CD4+ small/ medium-sized pleomorphic T-cell lymphoma. J Cutan Pathol. 2016;43:1121-30
16. Toberer F, Hartschuh W, Hadaschik E. Primary cutaneous CD4+ small- to medium-sized pleomorphic T-cell lymphoma: temporary remission by oral doxycycline. JAMA Dermatol. 2013;149(8):956-959. doi: 10.1001/jamadermatol.2013.4
17. Beltzung Fanny; Ortonne, Nicolas; Pelletier, Laura; Beylot-Barry, Marie; Ingen-Housz-Oro, Saskia; Franck, Frederic; Pereira, Bruno; Godfraind, Catherine; Delfau, Marie-Helene; D'Incan, Michel; Vergier, B. (2020). Primary Cutaneous CD4 + Small / Medium T-Cell A Clinical, Pathologic, and Molecular Study of 60 Cases Presenting Lymphoma Study Group. Am J Surg Pathol, 44(7), 862–872.
18. Lan TT, Brown NA, Hristov AC. Controversies and considerations in the diagnosis of primary cutaneous CD4+ small/medium T-cell lymphoma. Arch Pathol Lab Med. 2014;138(10):1307-1318. doi: 10.5858/arpa 2014-0299-CC.
19. Khader A, Vineetha M, George M, Manakkad SP, Balakrishnan S, Rajan U. Neu-Neurolymphomatosis in Primary Cutaneous CD4+ Pleomorphic Small/Medium-sized T-cell Lymphoma Mimicking Hansen's Disease. Indian J Dermatol. 2017;62(3):315- 317. doi: 10.4103/ijd.IJD_553_16.
20. Jam, F. A., Ali, I., Albishri, N., Mammadov, A., & Mohapatra, A. K. (2025). How does the adoption of digital technologies in supply chain management enhance supply chain performance? A mediated and moderated model. Technological Forecasting and Social Change, 219, 124225.