T-cell prolymphocytic leukemia presenting with erythematous patches, plaques, and erythema gyratum–like lesions masquerading as Sézary syndrome

Leah Cohen, BA,[a] Adel Haque, MD,[b] Sophia Ma, MD,[b] Ling Zhang, MD,[c] Lubomir Sokol, MD, PhD,[d] and Lucia Seminario-Vidal, MD, PhD[b,e]
Miami and Tampa, Florida

Key words: cutaneous presentations; gyrate erythema; Sézary syndrome; T-cell prolymphocytic leukemia.

INTRODUCTION

Mature T-cell leukemias (MTCLs) are clonal proliferations of posttyhmic T cells that often exhibit systemic involvement including a variety of cutaneous manifestations.[1] Because of the morphologic and phenotypic overlap, diagnosis of MTCLs requires comprehensive assessment of clinical presentation, immunophenotypic profiles, and serologic, cytogenetic, and molecular studies.[2]

T-cell prolymphocytic leukemia (T-PLL) accounts for only 2% of small lymphocytic leukemias in adults and classically manifests with striking leukocytosis, lymphadenopathy, and marked hepatosplenomegaly.[1,3] Unlike Sézary syndrome (SS), in which cutaneous presentation is a rule, only one-third of patients with T-PLL have cutaneous manifestations.[4-7] Cutaneous manifestations of T-PLL are heterogenous.[5,7,8] We describe a patient who presented with erythematous patches and plaques, gyrate erythema, and bulky lymphadenopathy with an immunophenotype masquerading as SS. A diagnosis of T-PLL was confirmed using flow cytometry and cytogenetic analysis of the bone marrow aspirate demonstrating chromosome 14q32 rearrangement.

Abbreviations used:

MTCLs:	mature T-cell leukemias
SS:	Sèzary syndrome
TCR:	T-cell receptor
T-PLL:	T-cell prolymphocytic leukemia

CASE PRESENTATION

A 76-year-old man was referred to our institution with an 8-month history of a generalized erythematous rash and outside diagnosis of SS. The eruption was progressive in nature, becoming pruritic 1 month after it started. It was worse with exercise, with no alleviating factors. A prednisone taper was attempted with no improvement. He denied night sweats, fevers, chills or weight loss, and had no significant medical history.

On examination, the patient was afebrile and had gyrate erythematous plaques of the bilateral upper extremities showing a wood-grain pattern (Supplemental Fig 1). Erythematous patches and plaques covered the abdomen and bilateral lower extremities (Fig 1) affecting 65% of his body surface area. Lymphatics examination found diffuse and substantial peripheral lymphadenopathy of the left preauricular (3 cm), parotid (3 cm), submandibular (3 cm), right occipital (1.5 cm), bilateral supraclavicular fossa (2 cm), bilateral axilla (4-5 cm), and left groin (2 cm). No overt hepatosplenomegaly was noted.

His white blood cell count was 51.69×10^9/L with 31.53×10^9/L atypical lymphocytes. The hemoglobin concentration and platelet count were 12.2 g/dL and 273×10^9/L, respectively. Serum lactate

From Florida International University, Herbert Wertheim College of Medicine, Miami[a]; the Department of Dermatology, University of South Florida[b]; and the Departments of Hematopathology,[c] Malignant Hematology,[d] and Cutaneous Oncology,[e] Moffitt Cancer Center.

Funding sources: None.
Conflicts of interest: None disclosed.

Correspondence to: Lucia Seminario-Vidal, MD, PhD, 13330 USF Laurel Drive, 6th Floor, Tampa, FL 33612. E-mail: luciasem@health.usf.edu.

JAAD Case Reports 2019;5:686-90.
2352-5126

https://doi.org/10.1016/j.jdcr.2019.06.004

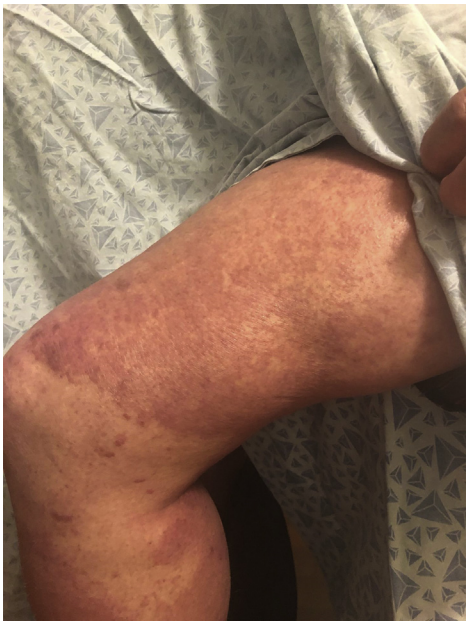


Fig 1. Erythematous patches and plaques covered the bilateral lower extremities.

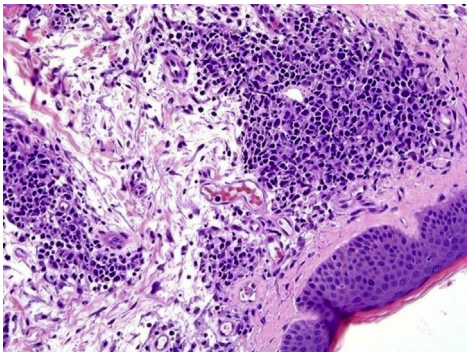


Fig 2. Biopsies found an atypical small to intermediate sized lymphoid infiltrate in the dermis, mostly in perivascular distribution, and vaguely nodular proliferation to diffuse pattern, without epidermotropism.

dehydrogenase was 614 U/L (normal range, 225-250 IU/L). Serum human T-cell lymphotropic virus panel was negative. Biopsies of a plaque and an erythema gyratum—like lesion showed an atypical small to intermediate sized lymphoid infiltrate in the dermis, mostly in perivascular distribution, and vaguely nodular proliferation to diffuse pattern, without epidermotropism (Fig 2). Immunohistochemical studies found a predominance of $CD3^+$ $CD4^+$ T cells with CD7 expression and aberrant coexpression of B-cell marker, CD20. The CD4/CD8 ratio was significantly increased (Fig 3). CD30 highlighted rare cells. CD20 also highlighted scattered small B cells in the background. Axillary lymph node biopsy found atypical small to intermediate sized lymphoid cells immunoreactive for CD2, CD3, CD5, CD4, and CD20 and intact but heterogenous expression of CD7. Monoclonal T-cell receptor (TCR) γ and β gene rearrangements were identified per polymerase chain reaction study. Peripheral blood smear identified large atypical T cells with round, oval, or irregular nuclei with or without a single prominent nucleous and intensely basophilic nongranular cytoplasm. Sézary cells were not identified. Flow cytometry found a $CD2^+$ $CD3^+$ $CD4^+$ $CD5^+$ $CD7^+$ $CD52^+$ HLA-DR^+ TCR$\alpha\beta^+$ immunophenotype with PD-1 and CCR4 expression and dim CD25 positivity. CD26 was negative. Terminal deoxynucleotidyl transferase and CD1a were not tested.

Positron emission tomography/computed axial tomography (PET/CT) scan showed extensive hypermetabolic lymphadenopathy above and below the diaphragm with bulky disease in axillary and inguinal regions, multiple hypermetabolic subcutaneous nodules, and mild nonhypermetabolic splenomegaly of 14.1 × 7.2 cm. The staging bone marrow biopsy was normocellular with trilineage hematopoiesis and 15% involvement by neoplastic T cells coexpressing $CD3^+$ $CD4^+$ $CD8^-$ $CD52^+$ markers. TCR gene rearrangement was positive for clonal rearrangement of both γ and β genes.

Cytogenetic studies of the bone marrow aspirate found complex abnormalities in multiple chromosomes: 85, XXY, -1,t(1;11)(q21;p15),add(2)(p11.1),-9,-10, der(10)t(2;10)(p11.2;q11.2),-11,del(13)(q12q22)x2,inv(14)(q11q32.1),-22[3]/46,XY[18]. Inversion of 14q32, in conjunction with clinical and laboratory features, such as bulky lymphadenopathy and mild organomegaly, and marked leukocytosis with lack of eosinophilia but with atypical $CD7^+$ mature T-cell lymphocytosis, favored the diagnosis of T-PLL. Initial treatment included topical triamcinolone for pruritus and palliative radiation therapy to the symptomatic left axillary bulky mass. After the diagnosis of T-PLL was made at our institution, therapy was changed to intravenous administration of alemtuzumab (anti-CD52). We discuss the heterogeneity of cutaneous manifestations in T-PLL and reinforce the importance of a comprehensive clinical and laboratory assessment of every patient with MTCLs.

DISCUSSION

The heterogeneity of cutaneous manifestations in T-PLL and the degree of clinical and morphologic overlap with SS and a rare leukemic variant of PTCL, NOS, often necessitates a comprehensive immunophenotypic, cytogenetic, and molecular analysis to render a definitive diagnosis. In this case, the skin eruption was the first sign of T-PLL,

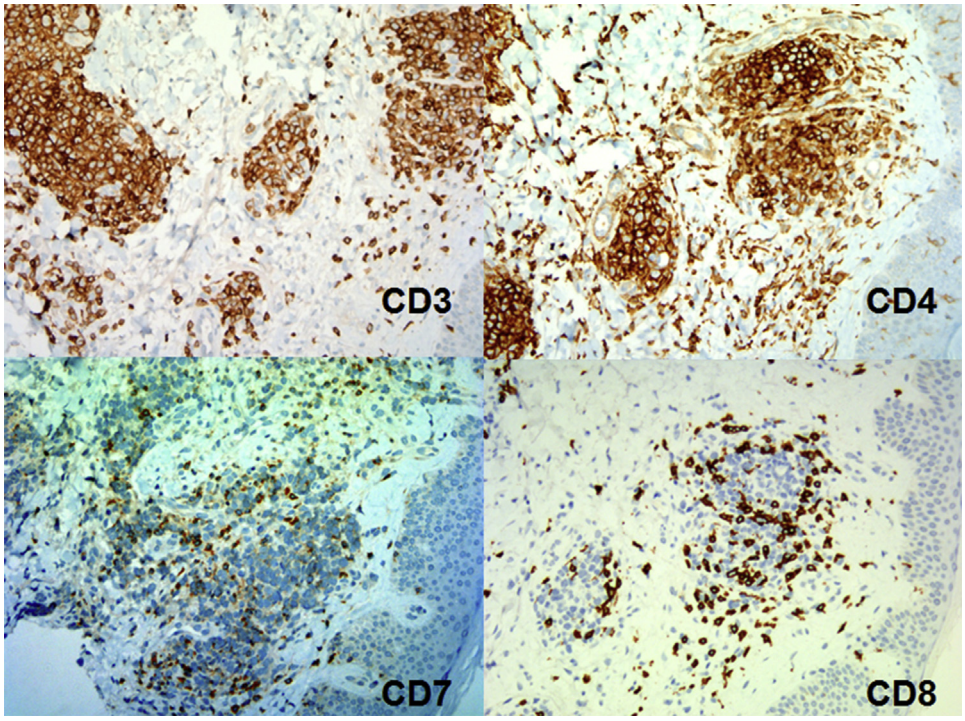


Fig 3. Immunohistochemistry shows $CD3^+$, $CD4^+$ greater than $CD8^+$ and $CD7^+$.

with the erythematous lesions suggesting a possibility of cutaneous T-cell lymphoma, such as SS. The initial cutaneous manifestations of SS are variable and include nonspecific dermatitis in 49%, erythroderma in 25.1%, patches and plaques of mycosis fungoides in 10.6%, and atopic dermatitis—like eruptions in 4.9%.[6] Erythroderma presents in 86.3% of all patients with SS at some point of disease.[6] Cutaneous manifestations of T-PLL, which are seen in up to 34% of patients, span a wide spectrum of disease including generalized or local erythema, and erythematous nodules and papules.[4,5,7,8] The largest series describing skin involvement in T-PLL includes 26 patients, 23 of which had involvement at the time of diagnosis, and reports a predilection for facial involvement, including facial swelling, plethora, and diffuse infiltrated erythema.[5]

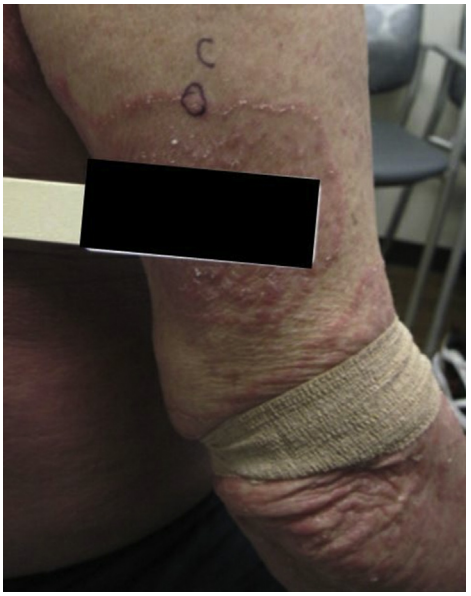
Despite a spectrum of cutaneous manifestations, lesional histology consistently corroborates a perivascular and periadnexal dermal infiltrate of small to medium sized lymphoid cells without epidermotropism.[2,7,9] Corresponding immunophenotype can be helpful for differentiation as well. Although variable, the presence of epidermotropism and the absence of CD7 expression are more characteristic for SS, the opposite of which is frequently true for T-PLL.[1,2,6-8] Our case, with CD7 expression on immunohistochemistry and on flow cytometry, and CD26 negativity, created a confusing picture, which required further study. The demonstration of abnormalities at chromosome 14 on cytogenetic studies of bone marrow, with break points at q11 and q32, were suggestive of T-PLL, as alterations at this region are seen in 76% of T-PLL cases, 63% of which are inv(14)(q11;q32).[8] Chromosomal abnormalities of SS, observed in greater than 40% of cases are gain of 17p11.2-q25.3 and 8q24.1-8q24.3 and loss of 17p13.2-p11.2 and 10p12.1-q26.3; additionally, complex cytogenetic abnormalities such as hyperploidy are less likely seen.[9-11]

Beyond suggestive cytogenetic evidence, atypical lymphocytosis of 33.9×10^9/L would be unusually high for an initial diagnosis of SS but compatible with diagnosis of T-PLL. Similarly, the lack of eosinophilia and Sézary cells favored T-PLL over SS. Although lymphadenopathy is frequent at initial presentation of SS, lymphadenopathy is generally less extensive and bulky than those with T-PLL. Additionally, hepatomegaly or splenomegaly is rarely observed in patients with SS, and their presence would raise a question regarding the accuracy of the diagnosis and initiate a search for a concurrent tumor. Furthermore, although initially progressive cases of T-PLL have splenomegaly 81% of the time, initially indolent cases only have splenomegaly 11% of the time. We present a patient with diffuse erythema, some gyrate plaques, generalized lymphadenopathy, splenomegaly, and marked T-cell lymphocytosis mimicking

SS, who required comprehensive studies to render a definitive diagnosis of T-PLL over SS.

REFERENCES

1. Foucar K. Mature T-cell leukemias including T-prolymphocytic leukemia, adult T-cell leukemia/lymphoma, and Sezary syndrome. *Am J Clin Pathol*. 2007;127(4):496-510.
2. Magro CM, Morrison CD, Heerema N, Porcu P, Sroa N, Deng AC. T-cell prolymphocytic leukemia: an aggressive T cell malignancy with frequent cutaneous tropism. *J Am Acad Dermatol*. 2006;55(3):467-477.
3. Catovsky D, Ralfkiaer E, Muller-Hermelink HK. T-cell prolymphocytuc leukaemia. In: Jaffe ES, Harris NL, Stein H, eds. *Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues*. Lyon, Grance: IARC Press; 2001: 195-198.
4. Sud A, Dearden C. T-cell Prolymphocytic Leukemia. *Hematol Oncol Clin North Am*. 2017;31(2):273-283.
5. Mallett RB, Matutes E, Catovsky D, Maclennan K, Mortimer PS, Holden CA. Cutaneous infiltration in T-cell prolymphocytic leukaemia. *Br J Dermatol*. 1995;132(2): 263-266.
6. Mangold AR, Thompson AK, Davis MD, et al. Early clinical manifestations of Sezary syndrome: a multicenter retrospective cohort study. *J Am Acad Dermatol*. 2017;77(4):719-727.
7. Hsi AC, Robirds DH, Luo J, Kreisel FH, Frater JL, Nguyen TT. T-cell prolymphocytic leukemia frequently shows cutaneous involvement and is associated with gains of MYC, loss of ATM, and TCL1A rearrangement. *Am J Surg Pathol*. 2014;38(11): 1468-1483.
8. Matutes E, Brito-Babapulle V, Swansbury J, et al. Clinical and laboratory features of 78 cases of T-prolymphocytic leukemia. *Blood*. 1991;78(12):3269-3274.
9. Barba G, Matteucci C, Girolomoni G, et al. Comparative genomic hybridization identifies 17q11.2 approximately q12 duplication as an early event in cutaneous T-cell lymphomas. *Cancer Genet Cytogenet*. 2008;184(1):48-51.
10. Caprini E, Cristofoletti C, Arcelli D, et al. Identification of key regions and genes important in the pathogenesis of sezary syndrome by combining genomic and expression microarrays. *Cancer Res*. 2009;69(21):8438-8446.
11. Vermeer MH, van Doorn R, Dijkman R, et al. Novel and highly recurrent chromosomal alterations in Sezary syndrome. *Cancer Res*. 2008;68(8):2689-2698.



Supplemental Fig 1. Gyrate erythematous plaques of the upper extremities showed a wood-grain pattern.