γδ lymphomatoid papulosis type D: A histologic mimic of primary cutaneous γδ T-cell lymphoma

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INTRODUCTION

Gamma-delta T cells represent a small subset of normal human T cells that possess a distinct T-cell receptor (TCR) on their surface. Their exact function has not yet been determined, but these cells are known to play a role in both the adaptive and innate immune system.[1] The World Health Organization currently recognizes 2 subtypes of γδ T-cell lymphoma, primary cutaneous γδ T-cell lymphoma and hepatosplenic γδ T-cell lymphoma,[2] both of which are rare. Primary cutaneous γδ T-cell lymphoma has an aggressive clinical behavior and poor prognosis, with a meager response to multiagent chemotherapy. However, with the advent of detecting TCR-γδ in paraffin-embedded sections, a few reports have shown examples of indolent γδ T-cell proliferations within the skin, namely in pityriasis lichenoides (PL) and lymphomatoid papulosis (LyP).[3-5] In contrast to primary cutaneous γδ T-cell lymphoma, a retrospective study of TCR-γδ expression in cases of PL and LyP found that such cases have a benign clinical course, with most patients achieving eventual resolution of the lesions and none having lymphoma.[4] Here we describe such an example, with a rare case of γδ LyP type D histopathologically mimicking primary cutaneous γδ T-cell lymphoma but having an indolent clinical course. This case further highlights the expanding classification scheme of LyP and aims to bring awareness to this newly described entity to allow distinction from primary cutaneous γδ T-cell lymphoma.

Abbreviations used:

TCR: T-cell receptor
PL: pityriasis lichenoides
LyP: lymphomatoid papulosis

CASE REPORT

An otherwise healthy 46-year-old white woman presented with a 3-month history of a rash, primarily on the extremities. The lesions began as erythematous papules, which eventually ulcerated and then self-resolved. The patient denied pruritus or tenderness associated with the lesions and had no systemic symptoms. She was initially treated with a 3-week course of prednisone with mild improvement. Outside biopsy found a markedly atypical lymphoid infiltrate composed of T cells that were weakly $CD8^+$, positive for granzyme and TIA-1, and TCR-βF^-. The cells also expressed TCR-γ and TCR-δ, leading to a diagnosis of primary cutaneous γδ T-cell lymphoma. The patient was subsequently referred to our institution for further workup. At the time of presentation to our clinic, most of her lesions had resolved with only a few erythematous papules remaining on the forearms and lower legs (Fig 1).

Repeat biopsy of the left forearm found an atypical epidermotropic lymphoid infiltrate expressing CD2, CD3, CD7, CD8, TIA-1, CD30, diminished CD5, TCR-γ, TCR-δ, and lack of CD4 and βF1 (Fig 2, *A-C*). Complete blood count,

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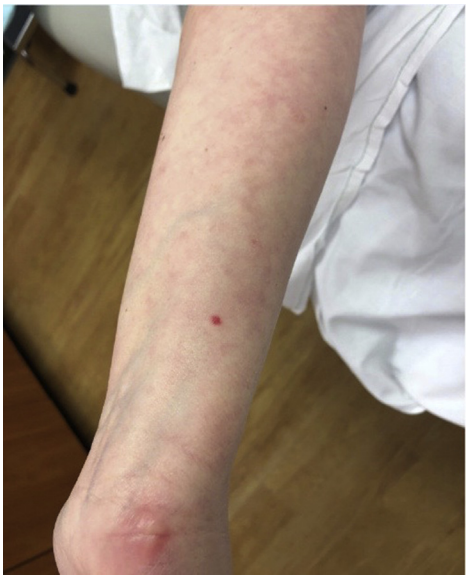

Fig 1. Clinical presentation of a patient with γδ lymphomatoid papulosis type D. Small erythematous papules involving the extremities. The lesions are asymptomatic, last approximately 1 month and then self-resolve.

metabolic panel, and lactate dehydrogenase were significant only for mildly elevated liver function. Flow cytometry showed 17% of the total T-cell population expressing TCR-γδ, with an absolute count of 221 cell/μL. The immunophenotype of the γδ TCR expressing cells was not aberrant: $CD2^+$, $CD3^+$, $CD5^+$ (diminished), $CD7^+$, $CD8^+$ (diminished minor subset), $CD16^+$ (diminished), $CD45^+$, $CD56^+$ (diminished), $CD57^+$ (subset), and TCR-γδ. They were $CD4^-$, $CD19^-$, $CD26^-$, $CD38^-$, and negative for TCR-αβ. After review with the hematology/oncology department, this minor increase in γδ T cells was deemed physiologic. Peripheral blood smear showed only rare atypical large granular lymphocytes. Polymerase chain reaction for T-cell receptor gene rearrangement performed on the peripheral blood was negative for any clonal *TRG* gene rearrangement or T-cell clones. Put together, these findings ruled out peripheral involvement of a lymphoproliferative process. The patient declined systemic treatment. She continues to get intermittent, small, erythematous papules that last approximately 1 month and then self-resolve without treatment. She follows regularly with the hematology/oncology and dermatology departments and will have repeat testing for complete blood count with differential, metabolic panel, lactate dehydrogenase and leukemia/lymphoma immunophenotyping annually. At 10-month follow-up, the patient had no evidence of systemic disease.

DISCUSSION

Primary cutaneous γδ T-cell lymphoma accounts for less than 1% of all cutaneous T-cell lymphomas. Patients typically experience extranodal and nodal dissemination, with 5-year overall survival rates ranging from 11% to 15%. This lymphoma typically presents with plaques, tumors, ulcers, or panniculitis. Histologically, the lesions are typically composed of atypical medium-to-large sized lymphocytes expressing CD3 and CD2, with variable expression of C7 and CD56, and strong positivity for cytotoxic proteins such as granzyme B, perforin, and TIA-1. CD8 positivity is seen rarely, but most cases are negative for both CD4 and CD8. The T cells express the γδ receptor by definition and are negative for TCR-βF1.[6-8] Our patient showed these histopathologic features; however, the atypical lymphocytes showed epidermotropism and were $CD30^+$ and $CD8^+$. Epidermotropism and CD30 positivity are common in LyP type D but would typically not occur in γδ T-cell lymphoma. The complete histologic picture as well as the clinical course of relapsing and remitting erythematous papules and lack of systemic symptoms led to the ultimate diagnosis of LyP, specifically LyP type D.

LyP is a chronic, recurrent, $CD30^+$ lymphoproliferative disorder with various histopathologic subtypes (A-F), described. The diagnosis of LyP can be histologically challenging because of its variability and overlapping features of other cutaneous lymphomas. Clinical correlation is crucial for diagnosis and appropriate management. Type D is a rare subtype of LyP, typically composed of $CD8^+$ T cells, which can histologically mimic aggressive epidermotropic $CD8^+$ cytotoxic T-cell lymphoma.[9,10] Although LyP type D is rare, the expression of TCR-γδ is even more uncommon. This type of LyP was first reported by Morimura et al[3] in 2011, and subsequently TCR-γδ expression has been found in a few additional cases of PL and LyP.[3-5] To date, all reported cases have shown an indolent course (follow-up ranging from 3-64 months).

With advancing immunohistochemistry and gene rearrangement techniques, more cases of γδ LyP type D will likely emerge. Clinical awareness of this indolent entity is prudent given the poor prognosis of primary cutaneous γδ T-cell lymphoma. Unlike patients with primary cutaneous γδ T-cell lymphoma, patients with LyP do well and do not require aggressive intervention. However, as with other cases of LyP, patients require long-term follow-up and should be routinely screened for other systemic lymphomas.

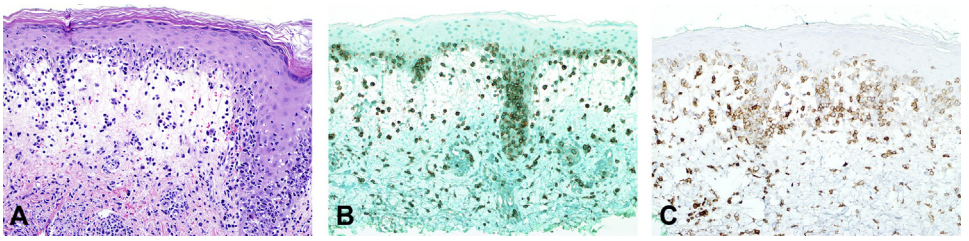

Fig 2. Histopathologic findings in γδ lymphomatoid papulosis, type D. Biopsy reveals epidermotropic enlarged and atypical lymphoid cells (**A**, Hematoxylin-eosin stain; original magnification: ×200). These cells express TCR gamma (**B**, ×200) and TCR delta (**C**, ×200).

Although histologically similar, the clinical behavior of γδ LyP type D differs greatly from that of primary cutaneous γδ T-cell lymphoma. This newly described entity should be kept in mind, as clinicopathologic correlation is necessary for correct diagnosis.

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REFERENCES

1. Girardi M. Immunosurveillance and immunoregulation by gammadelta T cells. *J Invest Dermatol*. 2006;126:25.
2. Swerdlow SH, Campo E, Harris NL, et al., eds. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. Lyon: International Agency for Research on Cancer; 2008.
3. Morimura S, Sugaya M, Tamake Z, Takekoshi T, Sato S. Lymphomatoid papulosis showing γδ T-cell phenotype. *Acta Derm Venereol*. 2011;91:712-736.
4. Martinez-Escala ME, Disiropoulos M, Deonizio J, Gerami P, Kadin ME, Guitart J. γδ T-cell-rich variants of pityriasis lichenoides and lymphomatoid papulosis: benign cutaneous disorder to be distinguished from aggressive cutaneous γδ T-cell lymphomas. *Br J Dermatol*. 2015;172:372-379.
5. King RL, Yan AC, Sekiguchi DR, Choi JK. Atypical cutaneous γδ T cell proliferation with morphologic features of lymphoma but with clinical features and course of PLEVA or lymphomatoid papulosis. *J Cutan Pathol*. 2015;42:1012-1017.
6. Cai Y, Zheng J. γδ T-cell-rich benign cutaneous disorders: good or bad? *Br J Dermatol* 2015;172:313-322.
7. Toro JF, Beaty M, Sorbara L, et al. gamma delta t-cell lymphoma of the skin: a clinical microscopic, and molecular study. *Arch Dermatol*. 2000;136:1024.
8. Willemze R, Jansen PM, Cerroni L, et al. Subcutaneous panniculitis-like T-cell lymphoma: definition, classification, and prognostic factors: an EORTC Cutaneous Lymphoma Group study of 83 cases. *Blood*. 2008;111:838.
9. Bekkenek MW, Geelen FA, van Voorst Vader PC, et al. Primary and secondary cutaneous CD30(+) lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patient and guidelines for diagnosis and treatment. *Blood*. 2000;95:3653-3661.
10. Mani V, George R, Vijayakumar K, Nair S. Type D lymphomatoid papulosis simulating aggressive epidermotropic cytotoxic lymphoma. *Indian J Pahol Microbiol*. 2016;59(1):81-83.