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TCR- δ Expression and $\gamma\delta$ + T-cell Infiltrates in Primary Cutaneous Gamma-delta T-cell Lymphoma and other Cutaneous T-cell Lymphoproliferative Disorders

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Abstract

Aims—The diagnosis of cutaneous gamma delta T-cell lymphoma (GDTCL) requires the identification of $\gamma\delta$ chains of the T-cell receptor (TCR). Using a new mAb to TCR δ , we evaluated TCR δ expression in formalin fixed paraffin embedded (FFPE) skin tissue from TCR γ -positive cutaneous T-cell lymphoma (CTCL) and assessed TCR δ expression within a spectrum of other cutaneous lymphoproliferative disorders (CLPD).

Methods and results—12 cases (10 patients) with TCR γ -positive CTCL and 132 additional CLPD cases (127 patients) were examined including mycosis fungoides (MF, n=60), cutaneous GDTCL (n=15), subcutaneous panniculitis-like T-cell lymphomas (SPTCL, n=11), and CD30+ lymphoproliferative disorders (CD30+LPDs, n=24). Clone H-41 to TCR δ (Santa Cruz; Houston, TX) was used on a Leica Bond-3 automated stainer to label FFPE slides. H-41 immunostaining was graded as percent infiltrate; high (50–100%), moderate (10–49%), low (0–9%). In TCR γ + tumors, 12/12 (100%) patients showed TCR δ expression comparable to TCR γ . No (0%) TCR γ + cases were negative for TCR δ . In all CLPD TCR δ expression follows: GDTCL (16/20 cases (14/15 patient) high, 2x moderate, 2x low); MF (0/60 cases high, 9x moderate, 51x low); CD30+ LPD (1/24 cases high, 2x moderate, 21x low); and SPTCL, (0/11 cases (0/9 patients) high, 2x moderate, 9x low). Three MF-like and one SPTCL-like cases showed high expression; the remainder were low.

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Conclusions—MAb H-41 to TCR δ matches TCR γ in immunostaining FFPE tissues from GDTCL, supporting H-41 as a replacement for mAb γ 3.20. TCR δ expression in our study suggests that the true occurrence of $\gamma\delta$ + non-GDTCL CTCL/CLPD may be lower than suggested by recent literature.

Keywords

T-cell lymphoma; Lymphoproliferative disorders; immunohistochemistry; immunologic techniques; classification

Introduction

Based on the differential expression of protein chains comprising the heterodimer of the T-cell receptor (TCR), T-cells can be divided into $\alpha\beta$ and $\gamma\delta$ T-lymphocytes. While the vast majority of circulating and peripheral T-cells are $\alpha\beta$ lymphocytes and are part of the adaptive immune response, $\gamma\delta$ T-cells are predominantly confined to a few specific anatomic compartments such as skin, mucosa and submucosa of the gastro-intestinal tract, where they are believed to defend against pathogens at the epidermal or mucosal surfaces with a rapid proinflammatory response as part of the innate immune system.¹

Gamma-Delta T-cell lymphomas (GDTCL) are aggressive hematologic malignancies² that predominantly evolve in spleen and liver (hepatosplenic type) or in skin with rapid progression and involvement of extracutaneous tissues (primary cutaneous GDTCL).^{3–5} Primary cutaneous GDTCL is a cytotoxic cutaneous T-cell lymphoma (CTCL) defined by the expression of TCR $\gamma\delta$, in the absence of expression of TCR $\alpha\beta$, and often in the absence of T-cell maturation markers.^{6, 7}

Historically, GDTCLs were immunohistochemically characterized by the identification of the δ -1 TCR chain on frozen tissue⁸, or later, in formalin fixed paraffin embedded (FFPE) tissues, by verification of the absence of the TCR β chain using a monoclonal antibody to TCR β and cytotoxic marker expression.⁶ More recently, the presence of TCR γ could also be immunohistochemically detected in FFPE tissues employing monoclonal antibody (mAb) clone g3.20.^{9, 10} However, the use of an anti-TCR γ reagent for the detection of GDTCLs has not been without challenges. Atypical simultaneous expression of mutually exclusive TCR chains has been observed in lymphoma. TCR γ positivity, for example, has been described in cases with TCR $\alpha\beta$ expression^{11–13} and monoclonal TCR β gene rearrangements.¹⁴

In our study, we have validated the use of a monoclonal antibody to the TCR δ chain in FFPE tissue of CTCL. Additional objectives were to assess the utility of TCR δ labeling in FFPE for diagnostic and prognostic purposes in GDTCL, and within a spectrum of CTCL/CLPDs to see if the pattern of expression might be distinct from recently reported promiscuous patterns of TCR γ . Finally, we aimed to qualitatively characterize the presence of $\gamma\delta$ T-cells in CTCL/CLPD in order to improve diagnostic/prognostic algorithms.

Materials and Methods

Tissue samples

The study was conducted with approval of the institutional review board of Memorial Sloan Kettering Cancer Center. All included patients were evaluated and treated at our institution. Cases were identified by a pathology database and tissue archive search for cutaneous GDTCL and other CTCL/CLPD. A total of 144 skin biopsies from 137 patients were identified with sufficient available archival material. Clinical charts, anatomic, hematologic and molecular pathology reports and histologic and immunohistochemical material were reviewed.

The complete cohort of cases evaluated included 60 MF (44%), 15 primary cutaneous GDTCLs (11%), 11 subcutaneous panniculitis-like T-cell lymphomas (SPTCL) (8%), 5 LyP (4%), 5 primary cutaneous CD30+ anaplastic large cell lymphoma (ALCL) (4%), 14 unspecified CD30+LPD (10%), 5 CD8+ aggressive epidermotropic T-cell lymphoma (AETCL) (4%), 3 primary cutaneous peripheral T-cell lymphoma, NOS (2%), 4 NK/T-cell lymphoma (3%), 3 CD4+ small/medium pleomorphic T-cell lymphoproliferative disorders (SMPTCL)(2%), and 1 adult T-cell leukemia/lymphoma (<1%). Cases lacking unequivocal clinical certainty included 5 cases in which ALCL vs transformed CD30+MF were difficult to discern (4%), 3 TCR γ + epitheliotropic lymphomas which have yet to declare themselves as MF with gamma+ phenotype or GDTCL (2%), and 3 panniculitic partial TCR γ + lymphoma intermediate between GDTCL vs SPTCL (<1%). Clinical histories and presentation were elucidated for GDTCL cases and other cases with increased staining by TCR δ immunohistochemistry.

Histopathology and Immunohistochemistry

H&E stained sections were reviewed in order to confirm diagnosis as per the 2016 revision to the World Health Organization classification of lymphoid neoplasms.⁷ Previously performed and archived immunohistochemical stains were reviewed for T-cell marker expression including CD3, CD4, CD7, CD8, CD30, TCR β , EBER-ISH and TCR γ . For straightforward MF or older cases of other CTCLs, available immunohistochemical stains often included only CD3, CD4, CD7, and CD8. Particularly, TCR β and TCR γ were not available for these cases, being either not necessary for diagnosis, or not available at the time of diagnosis.

TCR δ Immunohistochemistry

Immunohistochemical analysis of the TCR δ chain was performed with mAb H-41 (SC-100289, Santa Cruz Biotechnology, Santa Cruz, CA). H-41 (1:150; 0.7ug/ml) was used on an automated stainer platform (Leica Bond-3, Leica, Buffalo Grove, IL) using a heat-based antigen retrieval technique and hipH buffer solution (ER2, Leica) as previously described.¹⁵ TCR δ immunohistochemistry was performed for all 144 lesions. Based on our prior experience, in which lower percentages of TCR γ + cells which couldn't be unequivocally correlated with morphologically/immunophenotypically malignant cells due to low density and high mixed cell background, were disregarded in patients with subsequent more diagnostic biopsies of GDTCL, we opted to assess immunostaining for

TCR δ as a percentage of total T-cell infiltrate. For the same reasons (suspected intratumoral variability), we accepted any intensity of cytoplasmic and/or membranous staining as positive. Each case received an individual numerical assignment, and was subsequently stratified into one of three categories based on the extent of TCR δ + cells: low: 0–9% (baseline-negative comprised by scattered TCR δ positive cells), moderate: 10–49%, high: 50–100%. All non-GDTCL CTCL with >10% labeling, all GDTCL with any labeling, and all cases of unclear disease type were further analyzed for pathologic distinctions and detailed clinical information.

Results

Clinical Data

Breakdown of the clinicopathologic diagnoses of the 137 patients is listed in Table 1. Further clinical data on the 40 cases with high and moderate TCR δ expression levels are presented below and in Table 2.

Pathologic data

Of CTCL cases with strong and T-cell specific TCR γ expression, 12/12 (100%) showed high expression (50–100%) labeling with TCR δ (range 60–95%, mean 85%, median 82%) (Fig 1A–D).

The percent of immunohistochemical staining in all CTCL biopsies is depicted in Table 1. Twenty-one of 144 (15%) of all cases showed high TCR δ labeling as follows: 16/20 (80%) GDTCL (14/15 (93%) patients), 1/24 CD30+LPD, 1/1 GDTCL vs SPTCL, and 3/3 unusual/CD4–/CD8– MF-like histologies. Nineteen of 144 cases (13%) showed moderate TCR δ + infiltrates comprised by 2/20 (10%) GDTCL, 9/60 (15%) MF, 2/11 (18%) SPTCL, 2/24 (8%) CD30+LPD, and 4/4 (100%) unclear SPTCL versus GDTCL cases. The remainder of cases (106 cases; the majority of all lymphoma subtypes excluding GDTCL) were low. Twenty-one cases from 19 patients showed high numbers of TCR δ + cells. Indeed 16/21 (76%) high expression cases (14/19 patients, 74%), were bona fide GDTCL cases. The remainder were not. One case was a TCR β negative borderline CD30+LPD with 90% TCR δ labeling in the epidermal lymphocytes, and 80% TCR δ labeling in the dermal lymphocytes; this patient is alive 94 months after diagnosis with occasional solitary lesions easily treated with surgery or XRT to individual lesions (Fig 2A–D). One patient was considered clinicopathologically to have SPTCL (occasional subcutaneous nodules that localized to the adipose tissue with a CD8+ infiltrate), and is alive 84 months after diagnosis with responses to different therapies, despite 70% TCR δ + T-cells in this study (Fig 3L–M). In this patient, immunohistochemistry was performed as a negative control for TCR γ validation, and for the purpose of this study on TCR δ , and the strong positive result was a surprise. Three patients were diagnosed as having epidermotropic T-cell lymphomas with CD4–/CD8– diffuse TCR δ intraepidermal positivity (80%, 100% and 100%), but so far with an indolent clinical course and an MF-like clinical appearance of patches and plaques (84, 24 and 1 month survival at the time of this study) (Fig 3A–G).

Of nineteen cases with moderate TCR δ + infiltrates, nine (50%) were MF patients, and two each were GDTCL, SPTCL or CD30+LPD patients (11% each) (Fig 3H–K). MF patients' infiltrates harbored up to 10–25% $\gamma\delta$ T-cells, and were not diagnostically confusing, whereas the other cases in the moderate category were more difficult.

Four cases from 3 patients with known GDTCL showed low (2) or moderate (2) labeling. To better understand this unexpected finding, we re-examined the cases. The first case showed only limited patch-disease with no TCR γ reactivity in the original biopsy, despite later biopsies that progressed to pathologic TCR γ + tumors and consecutive death. One patient's biopsy showed only 30% positivity, which on retrospective review was the best characterization of a limited low tumor-burden lymphoid infiltrate in almost-exhausted tissue. Two biopsies from a third patient showed 1% and 30% TCR δ labeling respectively, but the TCR β immunostain on each was difficult to interpret, suggesting that the sample was not adequate for meaningful pathologic assessment despite molecular monoclonality. A later biopsy in this patient showed clear-cut GDTCL with 70% TCR δ staining and was positive for TCR γ at an outside institution.

TCR δ delineated lymphoma and clear-cut GDTCL; survival

10/19 patients (53%) with TCR δ positive cells comprising 50–100% of their infiltrates, died in follow-up, all of whom were GDTCL patients. Two of them had been thought to have MF with large cell transformation, but were reclassified upon review of charts and evaluation of immunohistochemical staining patterns as GDTCL (Fig 4A–H). No clinicopathologically equivocal patient with TCR δ positive cells comprising 50–100% of their infiltrates died in follow up.

In total 10/15 clear-cut GDTCL patients (67%, 10/14 GDTCL patients with high TCR δ) died. One patient was lost to follow up. Seven of the GDTCL patients who died (7/10, 70%) showed both intraepidermal and dermal and/or subcutaneous TCR δ expressing lymphocytes. One patient had dermal-only localization of TCR δ + lymphocytes. One patient had an initial intraepidermal TCR δ , TCR γ , CD4 and CD8 negative presentation but developed systemic disease with florid visceral TCR δ + tumors. Three GDTCL patients who are currently alive showed mixed intraepidermal and dermal/subcutaneous TCR δ + T-cells, one had dermis-limited tumor, and the patient lost to follow up had a biopsy of fat only (no epidermis present to assess).

Discussion

Cutaneous GDTCL is a distinct aggressive rare cutaneous lymphoma, comprising <1% of all skin lymphomas. It presents with variable clinical features and histological patterns and therefore its diagnosis is challenging.^{6,3} Due to the lack of a reliable marker of $\gamma\delta$ T-lymphocytes in routine FFPE tissue sections, a presumptive diagnosis used to rely on the absence of $\alpha\beta$ TCR expression using a monoclonal antibody to TCR β .⁶ However, it is known that TCR β expression may be lost by neoplastic $\alpha\beta$ T-cells and therefore the lack of TCR β cannot and should not be used to assure a $\gamma\delta$ origin.^{9, 16} Specific antibodies that label γ or δ chains of the $\gamma\delta$ TCR heterodimer can allow recognition of $\gamma\delta$ T-cells in skin tissue and are more specific for GDTCL diagnosis. Routine immunolabeling with a γ chain marker

in FFPE tissue (clone gamma 3.20)^{3, 12, 14} had been used successfully for this purpose, but recently became unavailable. Additional challenges with the use of TCR γ protein have included the potential for its more promiscuous expression in $\alpha\beta$ lymphomas, as translation and expression of the TCR γ chain may occur in the context of TCR β gene rearrangement whereas the TCR δ gene is deleted in that context, pre-empting TCR δ expression. This suggests that the presence of TCR δ expression could be yet more specific in the diagnosis of GDTCL than TCR γ . In the current study we aimed to evaluate the detection and occurrence of $\gamma\delta$ T-cells in CTCL and CLPDs using the mAb H-41 to TCR δ in FFPE tissue and we have found that TCR δ expression is comparable to TCR γ labeling in TCR γ ⁺ tumors, with 12/12 cases positive for both TCR chains. All cases that were strongly and diffusely TCR γ positive were also TCR δ positive; we did not identify any TCR γ ⁺ cases that were TCR δ ⁻. TCR γ and TCR δ appeared to label the same cell populations in the examined biopsies although some samples were not sequentially assayed (Fig 1). None of the TCR δ ⁺ cases was found to co-express TCR β .

In normal skin, $\gamma\delta$ T-cells are extremely rare, comprising less than 1% of all CD3 positive cells, although up to 30% of intraepidermal T-cells,^{17–19} while GDTCL is characterized by predominantly TCR δ ⁺ T-cell infiltration.⁶ All GDTCL patients in our study were TCR δ ⁺, with 93% of the patients (14/15) and 80% of their studied biopsies (16/20) showing high labeling of 50%–100% of the lymphocytic infiltrate. On retrospective review, outliers were explainable by sampling error. TCR δ expression in 30% of the infiltrate was revealed in one patient who went on to have another biopsy six years later showing 80% labeling. While we considered that this change in expression could represent disease evolution, upon review of the early biopsy, the tissue was found to be nearly exhausted at the time of TCR δ staining, precluding accurate interpretation. Two cases showed 0% and 1% TCR δ expression, however additional biopsies from each of these showed high TCR δ expression; one patient died within a year of florid GDTCL, and the other had a synchronous biopsy showing 70% labeling. This suggested either that we had reviewed early non-diagnostic disease (in the former case), or inadequately sampled or poorly processed tissue (in either case).

As expected, a high mortality rate was found among GDTCL patients in our study (67%, 10/15). Unexpectedly, 70% (7/10) of GDTCL patients who died from disease showed histologic involvement of both intraepidermal and dermal and/or subcutaneous skin compartments, versus 60% (3/5) of GDTCL patients who were alive at last follow up. This pattern of skin involvement in aggressive disease is not in line previous reports on decreased survival in cases with subcutaneous versus epidermotropic or dermal GDTCL⁴. Our findings align more closely with reports of intraepidermal MF-like GDTCL noted to evolve into aggressive cytotoxic lymphomas after many years of follow up.²⁰ We concur that caution is warranted when following such patients. Of note, we did not include CD4⁻/CD8⁻, TCR δ high patch/plaque type T-cell lymphomas within our MF cohort, as we feel that the follow-up on these cases is too limited for meaningful classification. However, inclusion of such cases within our survival analysis of TCR δ high infiltrates, resulted in improved OS when compared to clear cut clinicopathologic GDTCL (67% vs 53%), suggesting that a decision to include such cases as GDTCL needs further study.

Numerous $\gamma\delta$ expressing T-cells can be found not only in GDTCL, but also in low-grade CTCL, CLPDs¹⁴, and inflammatory self-limited and indolent skin conditions^{10, 17, 20, 21} In our study, 13 cases with typically indolent CTCL and CLPDs were shown to have lymphocytic infiltrates with 10%–25% TCR δ positivity, including 9 MF cases, 2 SPTCLs and 2 CD30-positive LPDs. One case of CD30-positive LPD showed TCR δ expression in 80–90% of the T-cell infiltrate and negative TCR β labeling. This unusual case presented with indolent, recurrent lesions and was similar to the recently published six $\gamma\delta$ T-cell-rich LyP cases that were identified by TCR γ + and/or β F1-negative immunostaining.²¹ Identification of $\gamma\delta$ T-cells by use of TCR δ stain in our cases supports that bona fide $\gamma\delta$ T-cells comprise components of similar infiltrates. In such indolent CTCL/CLPD, $\gamma\delta$ T-cells have been reported as up to 20% of lymphocytes. It has been suggested that these cells may represent either a subset of the malignant clone or a reactive T-cell population.²⁰ While we did not comparatively assess the intensity of staining within the different compartments of individual patients' infiltrates in this study, we did observe qualitative differences in staining between small peripheral or intraepidermal TCR δ + cells and larger clearly neoplastic cells. Comprehensive characterization of these subsets may help to better understand these diseases in the future. For now, given our experience, with 90% of MF cases showing fewer than 9% $\gamma\delta$ T-cells, and the remainder with 10–25%, we suggest closer clinical surveillance and possibly additional biopsies when infiltrates are comprised of greater than 25% $\gamma\delta$ T-cells.

Finally, TCR- γ expressing T-cells have been described within CD8+ AETCL, and may confound the diagnosis.²² However, in our study all five (5/5) AETCLs were negative for $\gamma\delta$ T-cells by TCR δ IHC, suggesting that TCR δ may have a better negative predictive value for AETCL than TCR γ . Larger numbers of AETCL should be evaluated to better assess this possibility.

Overall, our findings highlight the need for cautious evaluation even when low expression of $\gamma\delta$ (<10%) is identified if the clinical picture is not consonant with the pathologic interpretation, given that two of our GDTCL patients who initially had low-labeling of TCR δ died. Repeated biopsies of multiple sites and lesions in a manner that allows proper evaluation of the relevant tissue depth, (sampling the subcutis in panniculitis-like lesions), and consideration of flow cytometric evaluation, are needed to compensate for any possible sampling errors, fixation problems, and disease evolution. In cases of intermediate to high TCR δ labeling, in which diagnosis remains unclear, close follow-up is vital and re-biopsy of any change is mandated.

In conclusion, mAb H-14 to TCR δ is comparable to TCR γ immunohistochemistry and is reliable for the detection of TCR δ chain in malignant and potentially reactive $\gamma\delta$ T-cells in FFPE skin tissue specimens of CTCL/CLPD. While high numbers of TCR δ expressing T-cells are most often diagnostic for GDTCL, lower numbers of TCR δ + cells can be found in indolent CTCL and CLPDs. As outliers to these conventions may exist, assurance of adequacy of biopsy and cautious follow-up are essential in all cases with positive TCR δ labeling.

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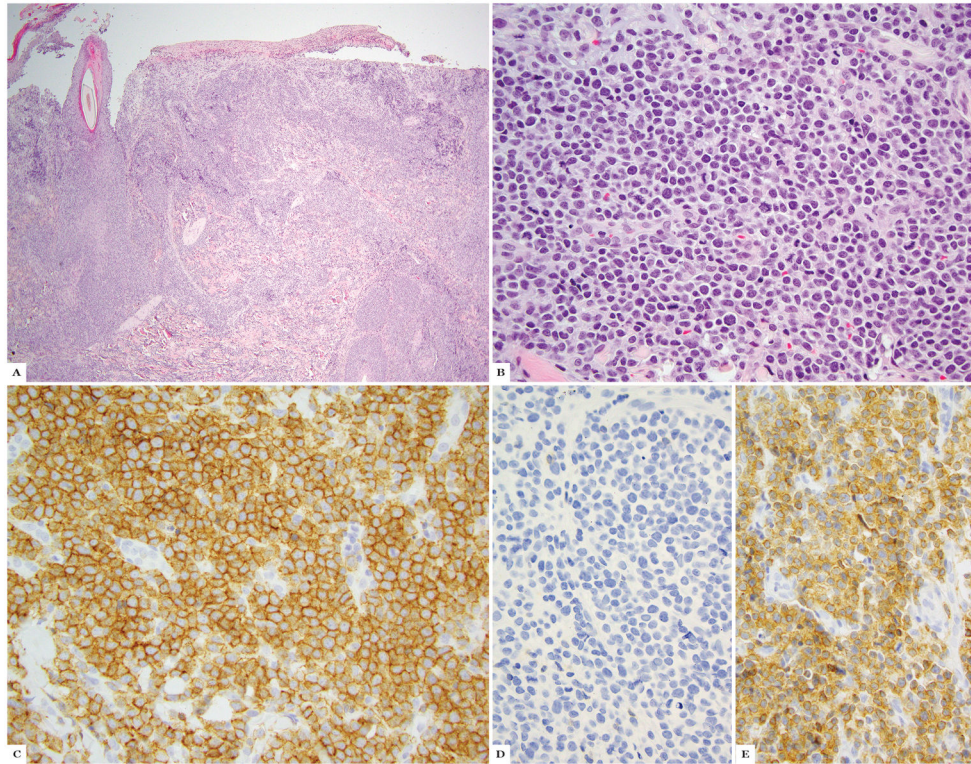


Figure 1. Primary cutaneous gamma-delta T-cell lymphoma; A, B hematoxylin and eosin stain. C shows TCR δ immunohistochemistry, D shows TCR β and TCR γ immunohistochemistry.

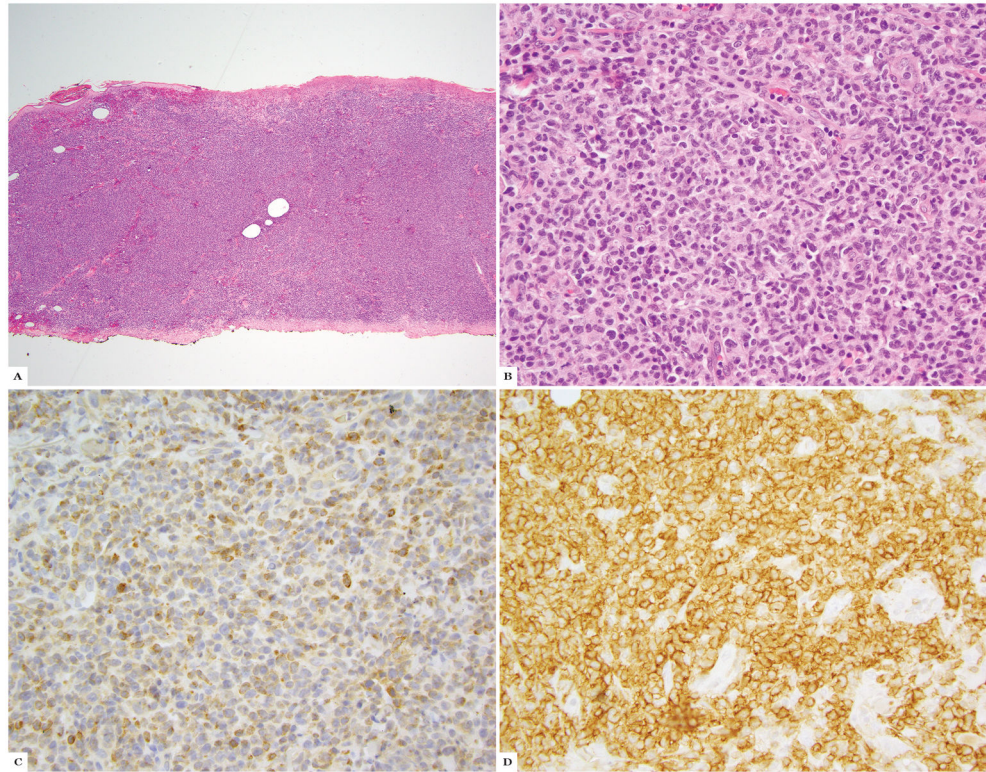


Figure 2. TCR $\gamma\delta$ expression in a borderline primary cutaneous CD30+ lymphoproliferative disorder: A, B, Hematoxylin and eosin; C, 80% TCR δ in dermis; D, Immunohistochemistry for CD30 in dermal population.

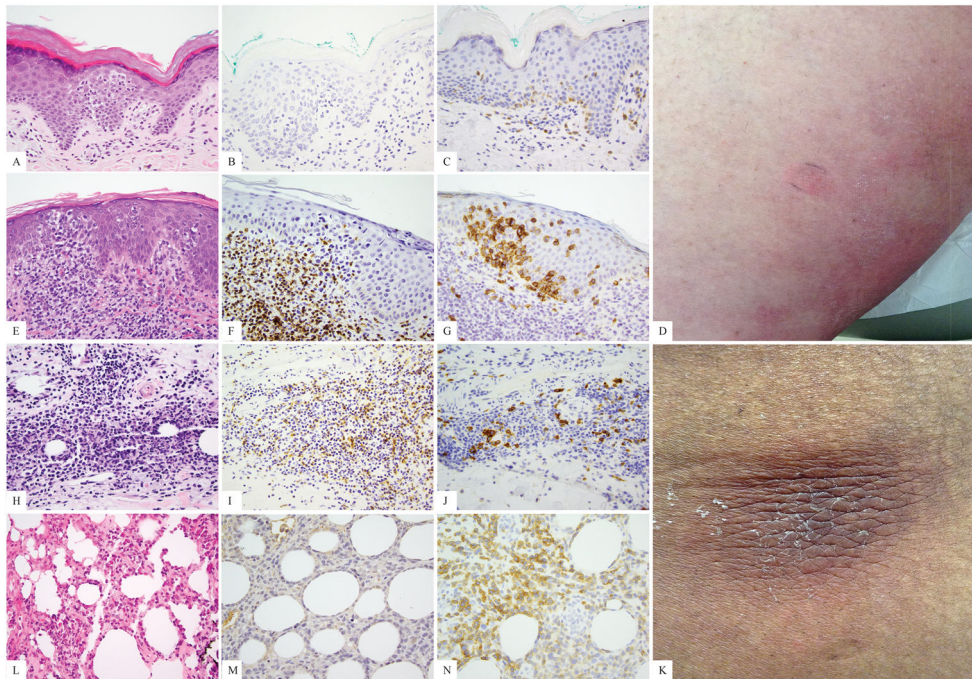


Figure 3. Examples of primary cutaneous T-cell lymphomas with clinical behavior of mycosis fungoides or subcutaneous panniculitis like T-cell lymphoma, and prominent TCR $\gamma\delta$ phenotype as shown by TCR δ immunohistochemistry. A–D, hematoxylin-eosin, TCR β , TCR δ , and clinical patch lesions in a patient with a mycosis fungoides presentation and 84 months of follow-up; E–G, hematoxylin-eosin, TCR β , and TCR δ in a recently diagnosed patient with a mycosis fungoides-like presentation; H–K hematoxylin-eosin, TCR β , TCR δ , and clinical subcutaneous nodule in a panniculitic patient with indolent course through limited (several month) follow up; L–N, hematoxylin-eosin, TCR β , and TCR δ in a panniculitic presentation with indolent course through 84 months.

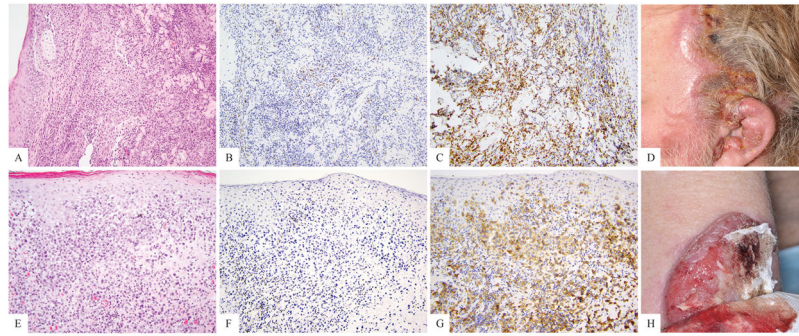


Figure 4.

Two patients with primary cutaneous T-cell lymphoma, retrospectively classified as gamma-delta T-cell lymphoma upon review of their clinical history, after tissue evaluation with TCR δ immunohistochemistry. A–D hematoxylin and eosin, TCR β , TCR δ and clinical images illustrating a large facial tumor in the absence of patches or plaques. E–H, hematoxylin and eosin, TCR β , TCR δ and clinical image showing a large ulceration in the absence of patches or plaques.

Table 1

Percent of labeling of cutaneous LPD type by delta immunohistochemistry

Cutaneous T-cell LPD	Number of cases (patients)	0–9% cells	10–49% cells	50–100% cells
Mycosis fungoides	60 (60)	51	9	0
CD30 LPD	24 (24)	21	2	1
SPTCL	13 (11)	11 (9)	2 (2)	0
GDTCL	20 (15)	2 (2)	2 (2)	16 (14)
CD8+ cytotoxic CTCL	5 (5)	5	0	0
NK/T cell lymphoma	4 (4)	4	0	0
PTCL NOS	3 (3)	3	0	0
CD4+ SMTCL	3 (3)	3	0	0
ATLL	1 (1)	1	0	0
Diagnostic conundrums	GDTCL vs SPTCL 4(3)	0	4 (2)	1
	GDTCL vs MF(3)	0	0	3
	TMF vs CD30LPD (5)	5	0	0

CLPD, cutaneous lymphoproliferative disorder; LPD, lymphoproliferative disorder; SPTCL, subcutaneous panniculitis-like T-cell lymphoma; GDTCL, gamma delta T-cell lymphoma; CTCL, cutaneous T-cell lymphoma; NK, natural killer; PTCL, peripheral T-cell lymphoma; SMTCL, small medium T-cell lymphoma; ATLL, adult T-cell leukemia/lymphoma; MF, mycosis fungoides; TMF, transformed MF

Table 2

High and moderate expressors (cases) of TCR Delta

	Cutaneous T-cell lymphoma	Percent delta expression	Other information including time of follow up from first disease
1	Mycosis fungoides	20	Alive, folliculotropic, granulomatous, 39 months
2	Mycosis fungoides	20	Alive, hypopigmented lesions, 24 months
3	Mycosis fungoides	25	Alive, hypopigmented lesions, 5 months
4	Mycosis fungoides	20	Alive, PPD-like lesions, 24 months
5	Mycosis fungoides	10	Alive, patch lesion, 60 months
6	Mycosis fungoides	25	Alive, patch lesion, 59 months
7	Mycosis fungoides	10	Alive, Sezary syndrome/MF, 41 months
8	Mycosis fungoides	15	Alive, large cell transformation, 72 months
9	Mycosis fungoides	15	Alive, patch/plaque lesion 74 months
10	SPTCL	10	Died 6 months
11	SPTCL	15	Alive 180 months
12	CD30 LPD LYP	10	LFU solitary lesion
13	CD30 LPD LYP	12	Alive 84 months
14	CD30 LPD borderline	90/80 *	Alive 94 months
15	GDTCL vs. SPTCL	10 *	DOD 34 months
16	GDTCL vs. SPTCL	20 *	DOD 34 months
17	GDTCL vs. SPTCL	30 **	Alive 6 months
18	GDTCL vs. SPTCL	40 **	Alive 6 months
19	GDTCL vs. SPTCL	70	Alive 84 months
20	GDTCL vs. MF	80	Alive 84 months
21	GDTCL vs. MF	100	Alive 24 months
22	GDTCL vs. MF	100	Alive 1 month
23	GDTCL	30 ***	DOD 81 months
24	GDTCL	30 ****	DOD 111 months
25	GDTCL	60	Alive 3 months
26	GDTCL	70 ****	DOD 111 months
27	GDTCL	70	DOD 26 months
28	GDTCL	70	Alive 21 months
29	GDTCL	80 ***	DOD 81 months
30	GDTCL	90	LFU after 24 months
31	GDTCL	90	Alive 32 months
32	GDTCL	95 *****	DOD 17 months
33	GDTCL	95 *****	DOD 17 months
34	GDTCL	95	DOD 90 months
35	GDTCL	100	DOD 8 months
36	GDTCL	100	DOD 37 months
37	GDTCL	100	DOD 8 months

	Cutaneous T-cell lymphoma	Percent delta expression	Other information including time of follow up from first disease
38	GDTCL	100	DOD 62 months
39	GDTCL	100	DOD 14 months
40	GDTCL	100	Alive 12 months

GDTCL, gamma-delta T-cell lymphoma; SPTCL, subcutaneous panniculitis like T-cell lymphoma, LFU, lost to follow-up; DOD, Dead of disease; LPD lymphoproliferative disorder; MF, mycosis fungoides; PPD, pigmented purpuric dermatosis; LYP, lymphomatoid papulosis;

* epidermis/dermis;

** , ***, **** *and* ***** occurred in same patient

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