Cutaneous post-transplantation lymphoma: Clinical features and survival outcomes

To the Editor: Post-transplant lymphoproliferative disorders (PTLDs) are lymphoid proliferations that can develop after organ transplantation.[1] Although case series of cutaneous PTLD have been reported, the epidemiology and characteristics of cutaneous post-transplantation lymphoma (PTL, ie, monomorphic PTLD and classical Hodgkin lymphoma) have not been extensively characterized. Herein, we report clinical features and survival outcomes of cutaneous PTL compared with extracutaneous PTL.

After receiving approval from the institutional review board, we searched the Asan Medical Center database of 14,490 transplantation recipients. We identified 115 cases of PTL and 11 cases of cutaneous PTL (Table I). The overall prevalence rate of cutaneous PTL was 0.07%.

In comparison between cutaneous and extracutaneous PTL, there were no significant differences in mean age and sex ratio (Table II). The interval from transplant to PTL was significantly longer for cutaneous PTL (mean 66.8 months) than extracutaneous PTL (mean 56.3 months; $P = .044$). Six of 11 patients (55%) with cutaneous PTL were positive for Epstein-Barr virus (EBV), and EBV positivity was nonsignificantly lower in extracutaneous PTL (70%, $P = .287$). T-cell lineage was significantly more common in cutaneous PTL (73%) than in extracutaneous PTL (16%, $P < .001$). There were no significant differences in the frequency of an advanced Ann Arbor stage or an elevated serum lactate dehydrogenase between cutaneous PTL and extracutaneous PTL. The 5-year overall survival rates of cutaneous PTL and extracutaneous PTL were 64% and 58%, respectively ($P = .586$).

In contrast with PTLDs presenting in extracutaneous sites, PTLDs with isolated cutaneous presentation were rare; only 56 cases of cutaneous PTL have been reported thus far.[2,3] In the present study, cutaneous PTL represented 9.57% of all PTLs, and the overall prevalence rate was 0.07%. Further studies are needed to verify our epidemiologic data.

In our analysis, cutaneous PTL was found to develop significantly later after organ transplantation than extracutaneous PTL was found to develop. The risk for systemic PTLD is greatest in the first year post-transplant,[4] but our study reveals cutaneous PTL and extracutaneous PTL at means of 66.8 months and 56.3 months post-transplant, respectively. As the present study included only patients with monomorphic PTLD and classical Hodgkin lymphoma, the onset of cutaneous PTL or extracutaneous PTL could be different from that of systemic PTLD. A previous study reported the proportion of cutaneous PTLDs of T-cell origin to be 68.6%.[2] Therefore, our finding of T-cell lymphoma predominance could be a characteristic of cutaneous PTL. EBV infection is regarded as a pathogenic mechanism of the development of PTLD.[5] However, the association between EBV positivity and cutaneous PTL was unclear. In our present analysis, we observed that EBV was positive in 55% of cutaneous PTL, and the EBV positivity rate in cutaneous PTL was lower than that in extracutaneous PTL (70%). This might be because T-cell lineage—PTLD in general has a lower rate of EBV infection and cutaneous PTL has a high rate of T-cell lineage lymphoma.

In conclusion, cutaneous PTLs have distinct clinical features from extracutaneous PTLs. This study improves our understanding of the cutaneous presentation of PTL. Further studies are needed to elucidate the differences in pathogenesis between cutaneous PTL and extracutaneous PTL.

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Table I. Clinical features of cutaneous PTL cases in this study

Patient no./sex/age, year	Transplanted organ	Interval to onset of PTL, months	Subtype of PTL	Primary or secondary cutaneous*	Skin lesion	EBV status	Ann Arbor stage	LDH value	Length of follow-up from onset of PTL, months	Current status	Cause of death
1/F/37	Kidney	31	MZBL	Primary	Solitary erythematous nodule on right eyelid	Negative	1	NA	42	Alive	
2/M/44	Kidney	108	PTCL NOS	Primary	Solitary erythematous nodule on chest	Negative	1	Normal	152	Alive	
3/M/49	Heart	41	LyP	Primary	Multiple crusted papules on legs	Positive	1	NA	65	Died	Progression of PTL
4/F/65	Bone marrow	3	ALCL	Primary	2 subcutaneous nodules on scalp	Negative	2	NA	71	Died	Progression of PTL
5/M/54	Bone marrow	26	DLBCL	Secondary	Multiple erythematous papules and nodules on face, trunk, and arms	Positive	3	Elevated	42	Died	Progression of PTL
6/M/60	Kidney	204	DLBCL	Primary	Multiple erythematous to flesh-colored nodules on scalp, face, legs, and trunk	Positive	2	Normal	19	Alive	
7/M/72	Kidney	156	LyP	Primary	Multiple flesh-colored papules and nodules on trunk and limbs	Negative	1	NA	82	Alive	
8/F/5	Bone marrow	21	ALCL	Secondary	Multiple erythematous nodules and papules on trunk and neck	Negative	3	Normal	84	Died	Progression of PTL
9/M/53	Bone marrow	42	PTCL NOS	Secondary	Multiple erythematous-to-brownish patches on trunk	Positive	2	Normal	17	Alive	
10/M/65	Liver	26	NKTL	Secondary	Multiple erythematous-to-purpuric patches on trunk	Positive	3	Elevated	4	Alive	
11/F/55	Liver	31	PTCL NOS	Secondary	Multiple subcutaneous nodules on both legs	Positive	4	Elevated	36	Died	Progression of PTL

ALCL, Anaplastic large cell lymphoma; *DLBCL*, diffuse, large B-cell lymphoma; *EBV*, Epstein-Barr virus; *LDH*, serum lactate dehydrogenase; *Lyp*, lymphomatoid papulosis; *MZBL*, marginal zone B-cell lymphoma; *NA*, not applicable; *NKTL*, natural killer/T-cell lymphoma; *PTCL NOS*, peripheral T-cell lymphoma not otherwise specified; *PTL*, posttransplantation lymphoma.

*Primary cutaneous PTL was defined as lymphoma that was present with no evidence of extracutaneous disease at the time of diagnosis. Secondary cutaneous PTL was defined as lymphoma that presented disseminated cutaneous lesions after primary disease during follow-up.

Table II. Comparison between cutaneous and extracutaneous PTL group

Category	All PTL, n = 115	Cutaneous PTL, n = 11	Extracutaneous PTL,* n = 104	*P* value
Male sex, n (%)	77 (67)	7 (64)	70 (67)	.806
Mean age at diagnosis of PTL, years	45.92	45.45	50.81	.370
Mean interval between first transplant and PTL, months	66.8	66.8	56.3	.044
Early onset (<12 months), n (%)	64 (56)	3 (27)	60 (58)	.054
Late onset (≥12 months), n (%)	51 (44)	8 (73)	44 (42)	
Type of transplantation, n (%)				
Liver	46 (40)	2 (18)	44 (42)	
Kidney	33 (29)	4 (36)	29 (28)	
Bone marrow	25 (22)	4 (36)	21 (20)	
Heart	9 (7.8)	1 (9)	8 (7.7)	
Pancreas	2 (1.7)		2 (1.9)	
Epstein-Barr virus positivity, n (%)	79 (69)	6 (55)	73 (70)	.287
Subtypes of lymphoma, n (%)†				
B-cell lineage lymphoma	90 (78)	3 (27)	87 (84)	<.001
Diffuse, large B-cell lymphoma	70 (61)	2 (18)	68 (65)	
Marginal zone B-cell lymphoma	11 (9.5)	1 (9)	10 (9.6)	
Hodgkin lymphoma	5 (4.3)	0	5 (4.8)	
Burkitt lymphoma	4 (3.5)	0	4 (3.8)	
T-cell lineage lymphoma	25 (22)	8 (73)	17 (16)	<.001
Peripheral T-cell lymphoma, not otherwise specified	16 (14)	3 (27)	13 (12.5)	
Anaplastic large cell lymphoma	4 (3.5)	2 (18)	2 (1.9)	
Natural killer/T-cell lymphoma	3 (2.6)	1 (9)	2 (1.9)	
Lymphomatoid papulosis	2 (1.7)	2 (18)	0	
Advanced (III or IV) Ann Arbor stage, n (%)	37 (32)	4 (36)	33 (32)	.744
Elevated serum lactate dehydrogenase, n (%)	51/89 (57)	3/7 (43)	48/82 (59)	.341
Outcome				
Median follow-up, months	79	81	79	
Alive, n (%)	66 (57)	6 (55)	60 (58)	
5-year survival rate, %	58	64	58	
Median overall survival, months	71	71	65	.586

PTL, Posttransplantation lymphoma.

*These included cases of PTL not involving the skin during follow-up. Secondary cutaneous PTLs that had a disseminated lesion on the skin during follow-up were excluded.

†This series did not contain any cases of mycosis fungoides or folliculotropic mycosis fungoides, which is inconsistent with the existing literature.

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The association among thyroid dysfunction, thyroid autoimmunity, and clinical features of alopecia areata: A retrospective study

To the Editor: Alopecia areata (AA) is a common form of nonscarring hair loss that is classified as an autoimmune disorder due to its association with other autoimmune diseases, such as thyroid autoimmunity.[1] In this study, we investigated the frequency of thyroid dysfunction and thyroid autoimmunity in AA patients and also examined the associations among thyroid dysfunction, thyroid autoimmunity, and 8 prognostic clinical features of AA.

A retrospective chart review led to the identification of 1408 Korean patients with AA diagnoses at KyungHee University Hospital in Gangdong, South Korea, during June 2006-March 2014. The severity of hair loss was assessed at the first visit in accordance with the Severity of Alopecia Tool,[2] and thyroid autoantibodies and thyroid hormones were measured. We defined thyroid dysfunction as any thyroid hormone level >10% or <10% of reference ranges (thyroxine [70-180 nmol/L], triiodothyronine