

Cutaneous extranodal natural killer/T-cell lymphoma: Clinical implications of whole blood Epstein-Barr virus DNA



To the Editor: Extranodal natural killer/T-cell lymphoma (ENKTCL) is a rare and aggressive disease that is closely associated with Epstein-Barr virus

(EBV) infection.¹ Several clinical features can predict the prognosis of patients with ENKTCL, but these are insufficient.^{2,3} Previous studies have demonstrated that plasma EBV DNA was associated with clinical stages and poor outcomes in patients with ENKTCL.^{4,5} However, little is known about the clinical features and prognosis of cutaneous

Table I. Correlation of clinical characteristics and initial whole blood EBV DNA levels

Characteristics (N = 37)	Whole blood EBV DNA, copies/ μ L		P value
	≤ 125.9 , n (%)	> 125.9 , n (%)	
Patients	23 (62.2)	14 (37.8)	
Age, years, median (range)	57 (26-80)	46 (14-68)	.0314*
Sex			.6995
Male	13 (56.52)	7 (50)	
Female	10 (43.48)	7 (50)	
Primary site			.2777
Skin	20 (54.05)	9 (64.29)	
Nasal cavity	11 (29.73)	2 (14.29)	
Others	6 (16.22)	3 (21.43)	
Number of skin lesions			.0566
Single	14 (60.87)	4 (28.57)	
Multiple	9 (39.13)	10 (71.43)	
Location of skin lesions			.3653
Extremities	14 (60.87)	6 (42.86)	
Trunk	3 (13.04)	2 (14.29)	
Head and neck	2 (8.7)	0 (0)	
Generalized	4 (17.39)	6 (42.86)	
Presenting skin lesions			.0149*
Cellulitis-like	8 (34.78)	3 (21.43)	
Nodule	10 (43.48)	1 (7.14)	
Ulcer	1 (4.35)	4 (28.57)	
Patch	4 (17.39)	6 (42.86)	
B symptoms			.0807
No	15 (65.22)	5 (35.71)	
Yes	8 (34.78)	9 (64.29)	
Cytopenia			.0058*
No	19 (82.61)	5 (35.71)	
Yes	4 (17.39)	9 (64.29)	
International Prognostic Index score			.0112*
0-2	13 (56.52)	2 (14.29)	
3-5	10 (43.48)	12 (85.71)	
Extranodal sites			.0647
< 2	12 (52.17)	3 (21.43)	
≥ 2	11 (47.83)	11 (78.57)	
Ann Arbor stage			.0027*
I and II	13 (56.52)	1 (7.14)	
III and IV	10 (43.48)	13 (92.86)	
Lactate dehydrogenase level			.7099
Elevated	7 (30.43)	3 (21.43)	
Normal	16 (69.57)	11 (78.57)	
ECOG score			.1459
0-1	18 (78.26)	7 (50)	
2-5	5 (21.74)	7 (50)	

EBV, Epstein-Barr virus; ECOG, Eastern Cooperative Oncology Group.
*Statistically significant.

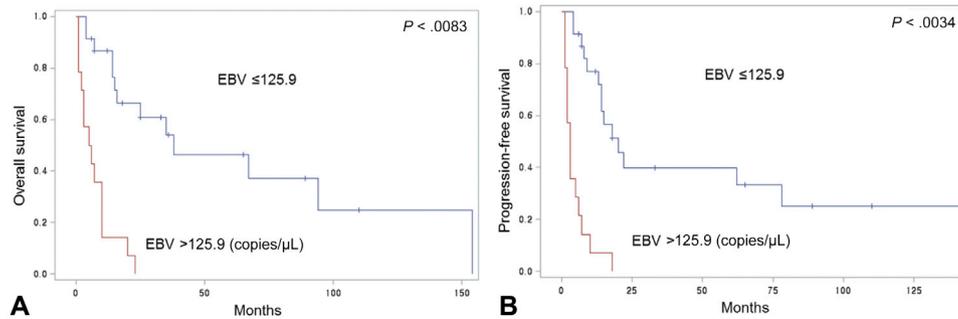


Fig 1. Survival analysis of overall survival (**A**) and progression-free survival (**B**) of patients with cutaneous extranodal natural killer/T-cell lymphoma according to whole blood EBV DNA. EBV, Epstein-Barr virus.

ENKTCL according to different whole blood EBV DNA levels.

The institutional review board (2018-02-120-001) approved our study. We identified 53 biopsy-proven cases of cutaneous ENKTCL diagnosed at Samsung Medical Center during 1996-2015 and analyzed clinical records, clinical photographs, and biopsy specimens.

In all, 53 patient charts were reviewed. Median age at diagnosis was 55 years. Primary tumors were in the skin ($n = 28$), nasal cavity ($n = 15$), or other locations ($n = 10$). The clinical presentation consisted of cellulitis-like lesions (26.4%), nodules (28.3%), ulceration (17%), and patches (28.3%); 54.7% were localized cutaneous lesions and 45.3% multiple cutaneous lesions. Whole blood EBV DNA was detected in 37 of 53 (69.8%) patients with cutaneous ENKTCL at the time of initial diagnosis. The median concentration of whole blood EBV DNA for all patients was 78 (range 0-6757.9) copies/ μL .

Using the minimum P value approach of the log-rank test, the cut-off value was calculated to be 125.9 copies/ μL ; 62.2% patients had a high level of EBV DNA (>125.9 copies/ μL) and 37.8% had a low level of EBV DNA (≤ 125.9 copies/ μL). Whole blood EBV DNA levels were compared according to clinical features (Table I). Patients with whole blood EBV DNA levels >125.9 copies/ μL were more likely to have a younger median age ($P = .0314$) and were more often associated with ulceration than the subcutaneous nodules ($P = .0285$). Other skin lesion types were not statistically significant when compared in pairs. Moreover, patients with whole blood EBV DNA levels >125.9 copies/ μL were significantly correlated with cytopenia ($P = .0058$), International Prognostic Index score ≥ 3 ($P = .0112$), and advanced stage disease ($P = .0027$). The median follow-up period was 14 (range 1-154) months. In total, 37 patients had disease progression or relapse at a median of 7 (range 1-142) months, of whom 27 patients died of tumor progression at a median of

10 (range 1-154) months. Patients with whole blood EBV DNA levels >125.89 copies/ μL had an inferior overall survival (median 38 months [≤ 125.9 copies/ μL] vs 5.5 months [>125.9 copies/ μL], $P < .0001$) and progression-free survival (median 20 months [≤ 125.9 copies/ μL] vs 3 months [>125.9 copies/ μL]; $P < .0001$) (Fig 1).

Limitations include the study's small sample size, retrospective nature, and the patient population being from 1 academic medical center. In conclusion, our study suggests that the level of EBV DNA in whole blood could serve as a valuable biomarker to predict the prognosis for a patient with cutaneous ENKTCL.

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Masculine norms and sunscreen use among adult men in the United States: A cross-sectional study



To the Editor: Traditional gender roles have been shown to influence health-related behaviors. Masculinity is often linked with health-harming behaviors, whereas femininity is often linked with health-promoting behaviors.^{1,2} Focus groups suggest that men avoid sunscreen because of its association with beauty products and have difficulty asking male peers to help apply sunscreen because it violates male-to-male body contact norms.³ Despite these findings and men's higher incidence of melanoma,⁴ sun protection interventions rarely focus on men. We hypothesized that men strongly adhering to masculine norms have poor sun safety compared with men moderately adhering to masculine norms.

We used cross-sectional questionnaire data from 961 adult men recruited through ResearchMatch, a national recruitment tool. The study sample consisted primarily of older (range, 18-92 years; mean, 51.8), heterosexual, white, and educated men (Table D). The questions captured information regarding demographics, masculine ideologies, and sun safety. The Male Role Norms Inventory—Short Form's Avoidance of Femininity subscale was used to classify men as displaying less adherence (Less-M), medium adherence (Med-M), or more adherence (More-M) to masculine norms. Previous studies have provided evidence for this scale's construct validity.⁵ Stratification was determined before data collection. For each variable, a multivariate logistic regression generalized logit model was constructed. The dependent variable was the degree of adherence to masculine norms, and the independent variables were related to sun safety. Med-M was selected as the reference category so that More-M and Less-M could be compared with Med-M. Because our hypothesis compares men moderately and strongly adhering to masculine norms, the More-M-to-Med-M odds ratios are reported. The multivariate models included age, race, education, and sexual orientation. The study was approved by Northwestern Institutional Review Board. Statistical analysis was performed with SAS software (SAS OnlineDoc 9.4, SAS Institute Inc, Cary, NC).

Table I. Participant characteristics

Variable	Value
Age, y	
Mean	51.8
Median	55
Range (SD)	18-92 (17.00)
Masculinity, (%)	
Less-M	277 (28.8)
Med-M	514 (53.5)
More-M	170 (17.7)
Race, (%)	
White	860 (89.5)
Nonwhite	101 (10.5)
Education, (%)	
High school or less	42 (4.4)
Some college or more	919 (95.6)
Sexual orientation, (%)	
Bisexual	66 (6.9)
Heterosexual/straight	792 (82.4)
Homosexual/gay	103 (10.7)
Geographic region, (%)	
Northeast	142 (14.8)
West	193 (20.1)
Midwest	318 (33.1)
South	308 (32.0)
Skin type, (%)	
I or II	255 (26.5)
III or IV	654 (68.1)
V or VI	52 (5.4)

Less-M, Less adherence to masculine norms; *Med-M*, medium adherence to masculine norms; *More-M*, more adherence to masculine norms; *SD*, standard deviation.

Logistic regression models revealed that men who did not use sunscreen regularly (adjusted odds ratio [aOR], 1.44; 95% confidence interval [CI], 1.00-2.07) or believed that tanning protects them from skin damage (aOR, 1.74; 95% CI, 1.10-2.76) had increased odds of strongly adhering to traditional masculine norms. Men who viewed young-looking skin as not at all important (aOR, 0.39; 95% CI, 0.22-0.70), slightly important (aOR, 0.40; 95% CI, 0.24-0.67), or important (aOR, 0.47; 95% CI, 0.28-0.81) compared with very important had decreased odds of strongly adhering to traditional masculine norms (Table II).

These findings suggest that men strictly adhering to masculine norms are less likely to use sunscreen regularly or demonstrate tanning knowledge, despite valuing young-looking skin. One proposed explanation is that sun safety is a feminine concern that is at odds with traditional male roles. This study's large sample size lent power to statistical models and controlled for potentially confounding variables. Limitations include self-reported data, inclusion of men with a history of skin cancer, and