Impact of EBV Status on Outcomes in Hodgkin Lymphoma

Elif Yilmaz MD[1,2], Heather Reves[1] BA, Aimaz Afrough MD[1,2], Julio Alvarenga MD[1,2], Larry Anderson Jr. MD PhD[1,2], Robert Collins MD[1,2], Stephen Chung MD[1,2], Gurbakhash Kaur MD[1,2], Adeel Khan MD, MPH, MS[1,2], Yazan Madanat MD[1,2], Alka Mallik MD[1,2], Heather Wolfe MD[1,2], Praveen Ramakrishnan Geethakumari MD, MS[1,2], Farrukh T. Awan MD, MS[1,2]

[1]UT Southwestern Medical Center, Dallas, Texas, USA. [2]Harold C. Simmons Comprehensive Cancer Center, Dallas, TX, USA

UT Southwestern Medical Center

Context

About 30-40% of all new cases of classical Hodgkin lymphoma (HL) in developed countries are associated with Epstein-Barr Virus (EBV) infection. Retrospective studies have shown conflicting data regarding the impact of EBV association on outcomes in HL. In this study, we aimed to compare baseline disease characteristics, socioeconomic status, and clinical outcomes between EBV-positive (EBV+) and EBV-negative (EBV-) HL patients.

Design

We conducted an IRB-approved retrospective review of HL patients treated within a tertiary care center from 2009 to 2022. Patients with HIV infection were excluded. We defined EBV association as EBER and/or LMP-1 positivity on diagnostic biopsy samples. Progression-free survival (PFS) and overall survival (OS) from initiation of first treatment were calculated using the Kaplan-Meier method and compared using log-rank test. Multivariate hazard regression analysis was applied to determine the variables associated with outcomes.

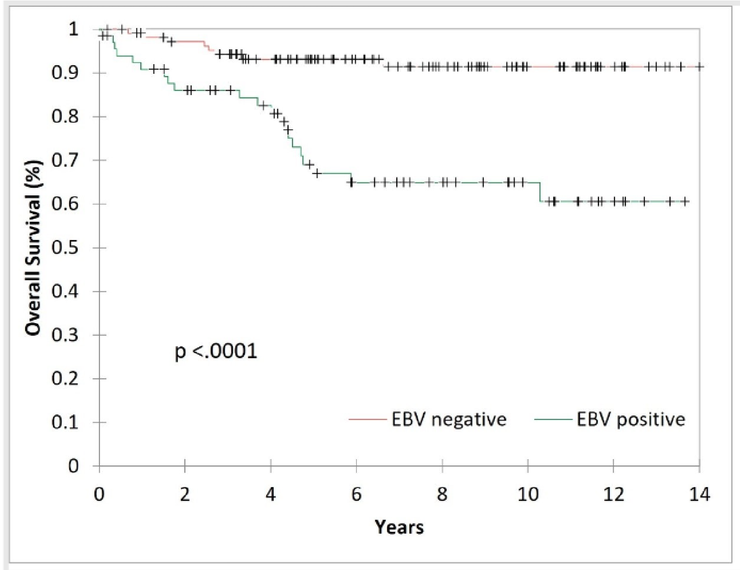


Figure 1. Kaplan-Meier analysis of overall survival (OS)

Table 1. Baseline characteristics

	EBV negative (N = 108)	EBV positive (N = 67)	p
Age at diagnosis (mean (SD))	34.67 (11.95)	46.52 (18.12)	<0.0001
Gender			.16
Male	57 (53)	43 (64)	
Female	51 (47)	24 (36)	
Race			.70
White	76 (70)	50 (75)	
Black	23 (21)	15 (22)	
Asian	5 (5)	1 (1)	
Other	3 (3)	1 (1)	
Unknown	1 (1)	0 (0)	
Ethnicity			.49
Hispanic or Latino	32 (30)	24 (36)	
Non-Hispanic or Latino	76 (70)	43 (64)	
Insurance status			.003
Private	62 (57)	17 (25)	
Medicare	5 (5)	13 (19)	
Medicaid	15 (14)	12 (18)	
None/self-pay	27 (25)	25 (37)	
EBV viremia at diagnosis	0/13 (0)	6/11 (55)	.002
IPS score			.005
0-1	37 (34)	12 (18)	
2-3	44 (41)	23 (34)	
4-7	21 (19)	29 (43)	
Unknown	6 (6)	3 (4)	
ECOG score ≥2	6/88 (7)	13/62 (21)	.01
Marrow involvement	5/82 (6)	18/53 (34)	<0.0001
OI during treatment	41/107 (38)	31/46	.30
Delay during treatment	67 (63)	40 (60)	.70
Delay due to insurance	5/67 (7)	5/40 (13)	.39

Results

A total of 175 patients were included (108 EBV+ HL, 67 EBV- HL). Patients with EBV+ HL presented with higher median age (47 vs 35; P<0.0001); higher ratio of IPS of 4–7 (43% vs 19%; P=0.005), bone marrow involvement (34% vs 6%; P<0.001), and ECOG performance status ≥ 2 (21% vs 6%; P=0.01) compared to EBV- HL patients. Patient demographics (including gender, ethnicity, distance to hospital and median household income), rate of treatment delays and opportunistic infections during therapy were similar between the 2 groups. Both 2-year and 5-year OS rates of EBV+ HL were worse compared to EBV- HL (86% vs 97.1% and 69% vs 93.1%, respectively; P<0.0001). On multivariate regression analysis, factors associated with OS included age (HR 1.04; 95% CI: 1.006–1.08), IPS of 4–7 (HR 2.3; 95% CI: 1.4–3.8) and delays during treatment (HR 6.6; 95% CI: 1.4–31.1). EBV positivity was not significantly associated with OS after other prognostic factors were controlled (HR 1.6; 95% CI: 0.5–5.4).

Conclusion

EBV+ HL patients have an inferior OS compared to patients with EBV- HL. Our study shows that the inferior survival rate is driven by presence of higher-risk disease characteristics at diagnosis in EBV+ HL and not by increased rate of therapy-related complications or socioeconomic disparities. Future research could elucidate the role for biology-driven incorporation of treatment strategies to improve outcomes in EBV+ HL.

UT Southwestern Medical Center