

Epstein-Barr virus and non-Hodgkin lymphoma: A study in Kermanshah, Iran

Ali Shahriari-Ahmadi¹, Babak Izadi², Masoud Sadeghi^{3,4,*}, Mehrdad Payandeh², Edris Sadeghi^{3,4}

¹Rasool-Akram Hospital, Oncology and Hematology ward, Iran University of Medical Sciences, Tehran, Iran

²Department of Medical Oncology, Kermanshah University of Medical Sciences, Kermanshah, Iran

³Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

⁴Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

*Corresponding author: Sadeghi_mbrc@yahoo.com

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Abstract Background: Epstein-Barr virus (EBV) infection is highly associated with specific subtypes of malignant lymphoma such as types of aggressive non-Hodgkin lymphoma (NHL). We aimed to evaluate the prevalence of EBV in NHL and its association with clinical parameters. **Patients and Methods:** twenty cases entered to our study. After re-blocking of previous paraffin embedded specimens, new slides were prepared and DNA was extracted. DNA contents were confirmed by spectrophotometry. Then PCR assay was used for total DNA and its product evaluate for presence of EBV by electrophoresis. **Results:** The mean age at diagnosis for all patients was 45±13 years (range, 28-73) years that 12 patients (60%) were male. Based on histopathology reports, 13 patients (65%) had immunoblastic Lymphoma, 5 (25%) had burkitt Lymphoma and 2 (10%) had LL (lymphoblastic Lymphoma). **Conclusion:** There is no EBV infection in NHL patients with LLs and percent of EBV infection in our study is lower than other studies.

Keywords: EBV infection, NHL, Burkitt lymphoma

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1. Introduction

Epstein-Barr virus (EBV) is an ancient virus, and has probably coevolved with its different hosts over the last 90–100 million years [1]. During the recent decade, methods for detecting and quantifying cellular and extracellular EBV in peripheral blood have improved significantly. Initially applicable only to small series of patients, modern techniques such as real-time PCR have now made large studies feasible. However, the majority of these have been performed to investigate EBV viral loads in specific diseases, and knowledge on EBV viral load in healthy individuals has mainly been generated from the control groups, rarely selected randomly from the population [2]. EBV infection is highly associated with specific subtypes of malignant lymphoma [3] such as types of aggressive non-Hodgkin lymphoma (NHL) [4,5]. Individuals with primary or secondary immunodeficiency are susceptible to developing B cell lymphoproliferation due to outgrowth of EBV-infected B cells that express type III latency characterized by expression of all nine latent-cycle EBV antigens. These cells would normally be susceptible to control by EBV-specific T cells, and strategies to restore EBV-specific immune responses may be effective therapeutically [4]. The prevalence of EBV was very high among B cell lymphomas particularly

Burkitt lymphoma. This is not surprising as it has been previously reported by Olweny and others [6,7]. However, the diffuse large B cell lymphomas (DLBCL) showed weaker EBV association of 44.4%. This is similar to what Cool found in neighbouring Kenya: 43% prevalence [8].

We aimed to evaluate the prevalence of EBV in NHL and its association with clinical parameters.

2. Patients and Methods

By evaluation of patients in cancer network, 20 cases entered to our study. After re-blocking of previous paraffin embedded specimens, new slides were prepared and DNA was extracted. DNA contents were confirmed by spectrophotometry. Then PCR assay was used for total DNA and its product evaluate for presence of EBV by electrophoresis.

3. Results

The mean age at diagnosis for all patients was 45±13 years (range, 28-73 years). Twelve patients (60%) were male and 8 patients (40%) were female (Table 1). Involvement anatomic sites were GI, cervical, inguinal, femoral, Para aortic, soft tissue, tonsillar, omentum and mediastinal for 8 patients (40%), 2 (10%), 2 (10%),

2(10%), 2 (10%), 1 (5%), 1 (5%), 1 (5%) and 1(5%), respectively. Based on histopathology reports, 13 patients (65%) had IL (Immunoblastic Lymphoma), 5 (25%) had BL(Burkitt Lymphoma) and 2 (10%) had LL(Lymphoblastic Lymphoma) (Figure 1- Figure 3).

Table 1. The characteristics for all patients (n=20)

Variables	n(%)	Mean±SD	Range
Age(year)			
Sex			
Male	12(60)		
Female	8(40)		
Anatomic sites			
GI	8(40)		
Cervical	2(10)		
Inguinal	2(10)		
Femoral	2(10)		
Para aortic	2(10)	45±13	28-73
Soft tissue	1(5)		
Tonsilar	1(5)		
Omentum	1(5)		
Mediastenal	1(5)		
Histopathology			
IL	13(65)		
BL	5(25)		
LLs	2(10)		

IL: Immunoblastic Lymphoma, BL: Burkitt Lymphoma, LL: Lymphoblastic Lymphoma, GI: Gastrointestinal

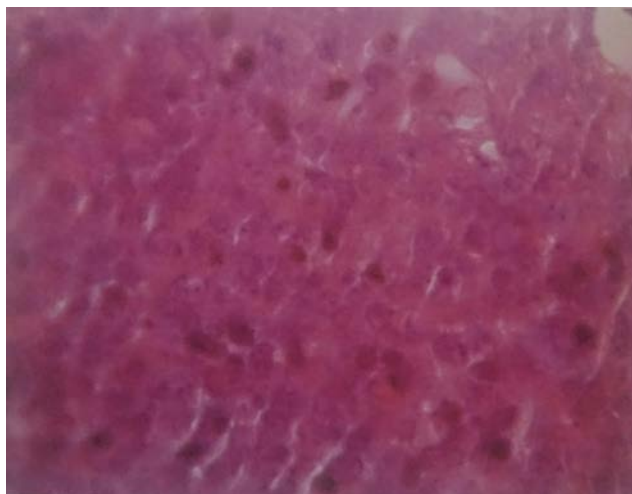


Figure 1. Histopathology image for Lymphoblastic Lymphoma

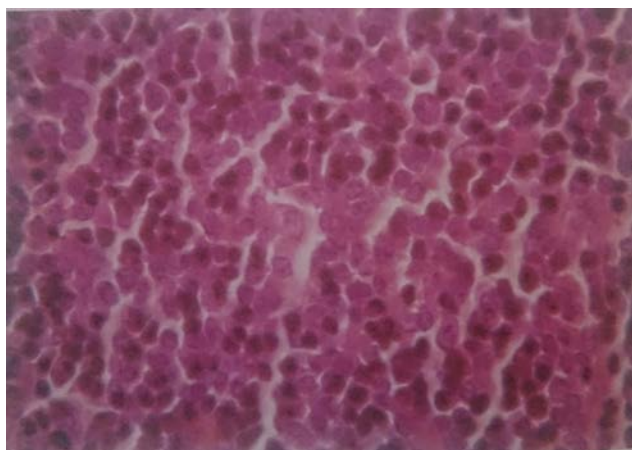


Figure 2. Histopathology image for Burkitt Lymphoma

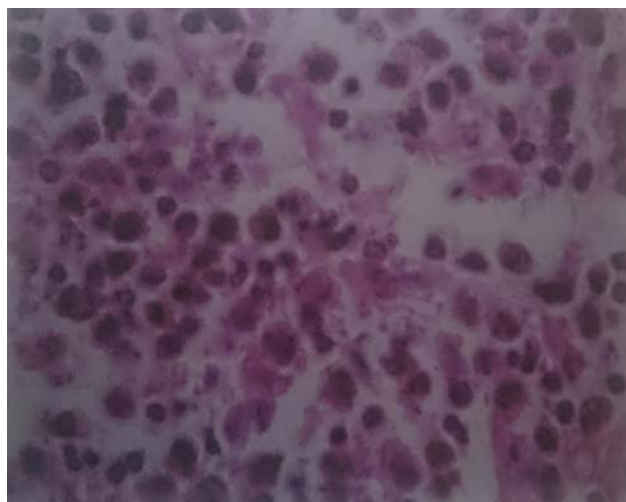


Figure 3. Histopathology image for Immunoblastic Lymphoma

Out of 20 patients, 5 cases were EBV DNA- positive that 2 cases had age ≤ 45 years and 3 cases had age >45 years. Of 5 cases, 3 cases were male and 2 cases were female. Also, 3 cases had IL, 2 cases had BL and there is no LL (Table 2).

Table 2. The results of electrophoresis for EBV in samples (n=20)

	Positive, n(%)	Negative, n(%)
Age(year)		
≤45	2(18.2)	9(81.8)
>45	3(33.3)	6(66.7)
Sex		
Male	3(25)	9(75)
Female	2(25)	6(75)
Histopathology		
IL	3(23.1)	10(76.9)
BL	2(40)	3(60)
LL	0(0)	2(100)

IL: Immunoblastic Lymphoma, BL: Burkitt Lymphoma, LL: Lymphoblastic Lymphoma

4. Discussion

EBV causes rare, malignant lymphomas. The role of EBV in other NHLs remains unclear, but mildly reduced immune function could lead to reactivation of EBV and subsequent NHL [9]. These data support the theory that chronic EBV infection is often found in association with cases of NHL of B-cell origin [10]. EBV has been classically associated with 3 malignancies, Burkitt lymphoma, B-cell lymphoproliferative syndromes, and nasopharyngeal carcinoma, and more recently with Hodgkin disease, T-cell lymphomas, and gastric and breast carcinomas, as well as with leiomyosarcoma and leiomyoma associated with immunosuppression [11]. Eight out of the 32 (25%) non-Hodgkin lymphoma cases showed EBV infection [11]. The high detectability of EBV-positive cases both in the group of B-cell NHLs (77%) [12]. In a study, the mean age of the patients with NHL was 53.6 years that a total of 50 (70.4%) were male and 21 (29.6%) were female. Some 9 (12.7%) out of 71 cases were positive for EBV-LMP-1 immunostaining, 2 (22.2%) follicular lymphoma cases, 1 (11.1%) case of T-cell lymphoblastic lymphoma, 4 (44.4%) cases of diffuse large B cell lymphomas, 1 (11.1%) mantle cell lymphoma and 1 (11.1%) angioimmunoblastic T cell lymphoma case [13]. In our study, out of 20 patients with NHL, 5 patients

(25%) had EBV infection that mean age for the patients was 45 years and 12 patients (60%) were male.

Burkitt lymphoma (BL) can be classified into three forms which differ in geographic distribution and EBV association: endemic (eBL), sporadic (sBL) and HIV - associated BL. There is a low background incidence of BL worldwide (sBL), which is rarely associated with EBV and accounts for 1–2% of adult lymphoma in Western Europe and America, but eBL is associated with (EBV) in over 95% of cases and is predominant in the equatorial belt of Africa and other parts of the world where malaria is hyperendemic [14]. In other study, the majority (92%) of the Burkitt lymphomas and only 34.8% of the diffuse large B cell lymphomas were EBV positive. None of the precursor B lymphoblastic lymphomas or the mantle cell lymphomas showed EBV integration in the lymphoma cells [15]. Also, EBV was associated with 90% of immunoblastic cases [16]. In this study, 40% patients with BL and 23.1% with IL had EBV infection that is lower than other results and also none of LLs had EBV infection.

The association of EBV with Hodgkin's disease seems to depend on factors such as country of residence, histological subtype, sex, ethnicity, and age [17]. In our study, there is no correlation between age and sex with EBV infection.

5. Conclusion

There is no EBV infection in NHL patients with LLs and percent of EBV infection in our study is lower than other studies.

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