

Expression of Epstein-Barr virus in classical Hodgkin's lymphomas in Brazilian adult patients

We studied the frequency of Epstein-Barr virus (EBV) expression in Hodgkin's lymphoma (HL) among 78 adult Brazilian patients and correlated it with clinical findings and survival. Latent membrane protein-1 (LMP-1) was detected by immunohistochemistry and EBV-encoded RNA (EBER) by in situ hybridization. EBV was expressed in 50 patients (64.1%), more frequently in those with mixed cellularity (MC). There was no relation between EBV expression and sex, age or stage of the disease. Expression of LMP-1 correlated with better overall survival ($p = 0.02$). EBV expression in adult patients with HL in our study was similar to that in other developing countries. Expression of LMP-1 was associated with better prognosis.

In previous studies by our group, it was demonstrated that in Campinas, São Paulo (Brazil) the frequency of histologic subtypes of Hodgkin's lymphomas (HL) is similar to that in developed countries.^{1,2} Except for studies including only pediatric patients, expression of Epstein-Barr virus (EBV) in Brazilian adults with HL has not yet been reported.³ Furthermore, the prognostic significance of EBV expression in HL remains controversial.⁴⁻⁸ Thus, our aim was to determine EBV expression in classical HL (cHL) in Brazilian adult patients and correlate these findings with patients' clinical data and survival.

Adult patients with cHL treated at our institution between 1987 and 1998 were studied. Patients' data were obtained from clinical files. Immunohistochemistry was performed on paraffin sections to detect the LMP-1 protein, using the EnVision peroxidase system (both Dakopatts, USA). In situ hybridization on paraffin sections was carried out using both the EBER probe and the reading system from Novocastra (UK). EBER expression and a rate of more than 10% LMP-1 positive neoplastic cells were considered for the survival analysis. Clinical data from EBV-positive and negative patients were compared using the Mann-Whitney test. Survival was analyzed using the Kaplan-Meier method.

Seventy-eight patients were studied: 36 males and 42 females. Clinical data are summarized in Table 1. The patients' ages ranged between 15 and 75 years (median 31 y). The histologic types of cHL were nodular sclerosis (NS) in 61 patients, mixed cellularity (MC) in 15, lymphocyte depletion in 1 patient and unclassified in 1 other patient. EBV was detected in 50 cases (64.1%): 36/61 NS (59%), and 14/15 MC (93.3%). EBV expression was significantly higher in the MC type ($p = 0.02$). LMP-1 was detected in 36 cases (46.1%): 26 (42.6%) with NS and 10 (66.6%) with MC.

There was no influence of EBER expression on patients' survival. However, patients with more than 10% LMP-1 positive neoplastic cells had better survival ($p = 0.02$; Figure 1).

Although in our cases the frequencies of histologic subtypes of HL were similar to those in developed countries, the frequency of expression of EBV tended to follow that observed in developing regions. Ethnically, our population is very heterogeneous, being a mixture of Europeans, Africans and native Brazilians. Our institution is part of a governmental university and cares for people with lower economic income. The factor in common which links our patients with those from other developing countries does not seem to be ethnicity or climate but, most probably, low socioeconomic status, supporting other studies.^{9,10}

Comparing age, sex, presence of B-symptoms and staging of cHL patients with and without EBV expression no difference was found in our patients.⁹ A prognostic significance of EBV expression in cHL demonstrated by EBER could not be supported by our study. However, patients with more than 10% neoplastic cells

Table 1. Clinical features of patients according to EBV expression.

	EBV positive	EBV negative	p
Age (median)	35	30	NS
Sex (male/female)	25/25	11/17	NS
Stages I + II	14	9	
Stages III + IV	31	18	NS
B symptoms	25	17	NS

NS: not statistically significant.

positive for LMP-1 had better survival. This fact suggests that only the stronger expression of LMP-1, and not the simple presence of the virus, might play a role in patients' outcome. In some reports no relation between EBV expression and prognosis was found.^{4,5} More recently, better survival was reported in HL patients presenting LMP-1 expression.⁶ Others demonstrated that, although there was no difference in overall survival in patients with EBV positive HL, this group of patients showed a better response to chemotherapy.⁷ Survival was also improved in pediatric patients with EBV-related HL.⁸

Our results show that EBV expression in our patients is similar to that in other developing regions, probably related to patients' socioeconomic status. Our data support the prognostic relevance of LMP-1 expression in this disease.

José Vassallo,* Konradin Metzke,* Fabiola Traina,^o Cármino A. de Souza,^o Irene Lorand-Metze^o

*Department of Anatomic Pathology; ^oDepartment of Internal Medicine, Faculty of Medicine State University of Campinas (UNICAMP), São Paulo, Brazil

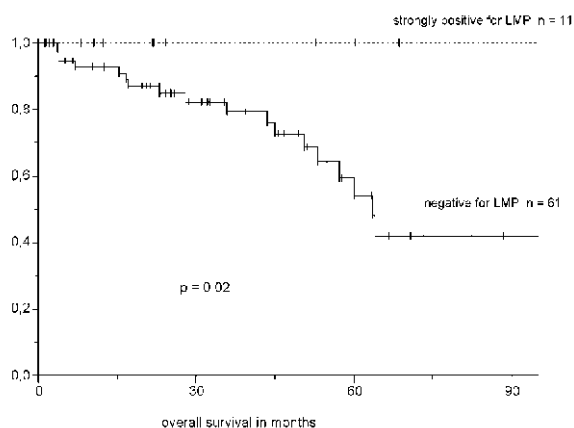


Figure 1. Influence of LMP-1 expression on overall survival (LMP-1 positive $\geq 10\%$ n = 11; LMP-1 negative [0 or < 10%] n = 61; $p = 0.02$).

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Key words: Hodgkin's lymphoma; Epstein-Barr virus; immunohistochemistry; in situ hybridization; prognosis.

Correspondence: José Vassallo, MD, Department of Anatomic Pathology, Faculty of Medicine UNICAMP, PO Box 6111, 13081-970 Campinas, SP/Brazil.

Phone/Fax: international +55.19.3289-3897.

E-mail: glaujv@obelix.unicamp.br

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