

Editorial-2

Incidence and clinical implications of Epstein-Barr Virus-associated Hodgkin's Lymphoma

We read with interest the report of the fourth Indian study from Bangalore on Hodgkin's lymphoma and Epstein-Barr virus (EBV), by Rajalakshmi et al.¹ Immunohistochemical detection of EBV was positive in 55% of the cases and was associated with a lower Hasenclever prognostic score than EBV negative cases.

This new study comes to strengthen earlier Indian studies on Hodgkin's lymphoma from Madras,² Bombay³ and Vellore,⁴ as well as our own report from Delhi.⁵ In the latter, EBV immunohistochemical detection was positive in 91.1% of 146 children with Hodgkin's lymphoma. Multiple studies have shown that EBV association in Hodgkin's lymphoma is more frequent in children below 10 years of age, in males, in less-developed regions and in mixed cellularity subtype.^{6,7} Similar to earlier reports there was a stronger association in children than in adults (98% vs. 78% in Bombay;³ 96% vs. 82% in Vellore Study⁴) and in males than in females. However, there was no consistency in the histological subtype more often associated with EBV. This might be related to the small number of cases available as compared with most international studies.

The impact of EBV detection in Hodgkin's and Reed-Sternberg cells on treatment outcome remains controversial. Various studies have shown an improved prognosis of EBV-associated Hodgkin's lymphoma,^{3, 8, 9} while others have shown a poorer prognosis, particularly in patients older than 50 years.^{10, 11} This conflicting

data might be due to the heterogeneous nature of the disease, variations in the treatment protocols and the age distribution of the patients. Naresh et al reported a better 10-year relapse-free survival and overall survival in EBV-associated cases.³ We also reported a better 5-year event-free survival in EBV positive cases (82.5% vs. 78.7%), though the difference was not statistically significant⁵. In the report presented in this issue,¹ as information about treatment response and long-term survival of study patients was not available, the authors have correlated their pathological findings with a prognostic scoring system based on clinical and laboratory features at the time of diagnosis. Though the small number of patients did not allow statistical analysis, the finding of higher Hasenclever prognostic score,¹² indicator of a poor prognosis in EBV latent membrane protein-1 negative cases is of interest. The prognostic value of this scoring system has not yet been validated in large series of Indian patients, and additional large scale studies are required to identify poor prognostic factors for treatment response and survival in Indian patients, amongst which EBV status might play a particular role, in order to guide optimal treatment strategy.

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REFERENCES :

1. Rajalakshmi T, Payal K, Purnima Makhija, Karuna V. Epstein-Barr virus in Hodgkin's lymphoma – Incidence and prognostic implications. *Ind J Med Paed Oncol* 2006;27:23-26.
2. Radha K, Shanthi P, Madhavan M, Senthamarai A. Study of association of Epstein-Barr virus with Hodgkin's disease. *Ind J Pathol Microbiol* 1997;40(3):351-354.
3. Naresh KN, Johnson J, Srinivas V, et al. Epstein-Barr virus association in classical Hodgkin's disease provides survival advantage to patients and correlates with higher expression of proliferation markers in Reed-Sternberg cells. *Ann Oncol* 2000;11:91-96.
4. Karnik S, Srinivasan B, Nair S. Hodgkin's lymphoma: immunohistochemical features and its association with EBV LMP-1. Experience from a South Indian hospital. *Pathology*. 2003;35(3):207-211.
5. Dinand V, Arya LS, Dawar R. Prevalence and significance of Epstein-Barr virus latent membrane protein-1 detection in Hodgkin's and Reed-Sternberg cells. *Ind J Med Res* 2005;121(Suppl):157 (abstract).
6. Glaser SL, Lin RJ, Stewart SL, et al. Epstein-Barr virus-associated Hodgkin's disease: epidemiologic characteristics in international data. *Int J Cancer* 1997;70:375-382.
7. Dinand V, Arya LS. Epidemiology of childhood Hodgkin's disease: is it different in developing countries? *Indian Pediatr* 2006;43(2):141-147.
8. Murray PG, Billingham LJ, Hassan HT, et al. Effects of Epstein-Barr virus infection on response to chemotherapy and survival in Hodgkin's disease. *Blood* 1999;94(2):442-447.
9. Montalban C, Abaira V, Morente M, et al. Epstein-barr virus-latent membrane protein 1 expression has a favorable influence in the outcome of patients with Hodgkin's disease treated with chemotherapy. *Leuk Lymphoma* 2000;39(5-6):563-572.
10. Stark GL, Wood KM, Jack F, Angus B, Proctor SJ, Taylor PR; Northern Region Lymphoma Group. Hodgkin's disease in the elderly: a population-based study. *Br J Haematol*. 2002;119(2):432-440.
11. Jarrett RF, Stark GL, White J, et al. Impact of tumor Epstein-Barr virus status on presenting features and outcome in age-defined subgroups of patients with classic Hodgkin lymphoma: a population-based study. *Blood* 2005;106(7):2444-2451.
12. Hasenclever D, Diehl V: A Prognostic score for Advanced Hodgkin's Disease. *N Engl J Med* 1998;339:1506-1514.

