

TITLE OF THE ABSTRACT : EPSTEIN BARR VIRUS RELATED DIFFUSE LARGE B CELL LYMPHOMA OF THE ELDERLY- ASSESSMENT OF FREQUENCY IN AN INDIAN TERTIARY CARE CENTRE AND COMPARISON OF THE MORPHOLOGICAL FEATURES OF THE EBER-ISH POSITIVE AND EBER-ISH NEGATIVE CASES

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OBJECTIVES:

To identify cases of lymph nodal EBV Positive Diffuse Large B Cell Lymphoma (EBV+DLBCL) and assess the disease frequency in patients older than 45 years of age in a tertiary care centre in India, and to do a detailed histologic study of all cases to identify morphologic features that may help suspect EBV positivity.

METHODS:

We included cases of lymph nodal DLBCL occurring in patients older than 45 years of age, and excluded cases with a prior history of therapy for lymphoma, with a documented seropositive status, with features of a double hit or grey zone lymphoma on initial biopsy and cases with an initial presentation at an extranodal site with subsequent involvement of lymph nodes. Slides and blocks from 129 cases of lymph nodal DLBCL occurring in patients older than 45 years of age were retrieved from the department archives based on a keyword search. Clinical data including the age, gender, state of residence, clinical stage and international prognostication index score at presentation, presence/absence of B symptoms and details of marrow involvement at presentation were noted from the patient files. The histological parameters evaluated on the H&E stained slides were the pattern, morphologic subtype, reactive background, necrosis, multinucleate giant cells, tingible body macrophages, vascular proliferation, angioinvasion, intra-nodal fibrosis and perinodal extension. The available CD3, MIB-1 and EBV-LMP1 immunohistochemistry slides were assessed for percentage of positive cells. EBER-ISH stained slides were examined for proportion and pattern of staining, and a threshold of >10% positively staining cells was considered as a positive test. The statistical methods used included frequency table, Chi square test and Fisher's exact test, with a p value of <0.05 considered as significant.

RESULTS:

EBER-ISH was not assessable in 5 of the 114 cases owing to an overwhelming background staining, and was positive in 7 of the remaining 109 cases with a calculated frequency of 6.42%. This frequency is lesser than that reported from Japan and Korea, and more than that reported from the USA and Europe. The mean age at presentation of patients with EBV+DLBCL in our study was 66 years, which is younger than the reported global average of 71-75 years. Among the histologic features, increased number of tingible body

macrophages and prominent vascular proliferation were significantly different between the EBV positive and EBV negative groups of DLBCL (p value <0.05), while increased multinucleate giant cells showed a borderline significance (p value 0.06). There was a slight discordance between EBV-LMP1 and EBER-ISH, with 1 EBER-ISH positive case showing a negative staining for EBV-LMP1, which is known to occur. Edge artifacts and non-specific background staining for EBER-ISH were also seen more often in core biopsies, and could possibly have been related to formalin fixation.

Key words: EBER-ISH, EBV positive DLBCL, elderly, Epstein Barr Virus.