Epstein-Barr-Virus infection patterns in nodular lymphocyte predominant Hodgkin-lymphoma

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We investigated 19 cases of Epstein-Barr virus (EBV)-positive nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) as information regarding latency types is currently incomplete.
Immunohistochemistry for CD20, CD79a, PAX5, OCT2 CD30, CD15, CD3, and PD1 was performed. For EBV-detection, in-situ hybridization for EBV-encoded RNAs (EBER) was employed combined with IHC for EBV-encoded latent membrane protein-1, -nuclear antigen (EBNA)-2 and -BZLF1. In 95% of the cases, neoplastic cells with features of Hodgkin- and Reed-Sternberg cells (HRS cells) were present, mostly showing expression of CD30. In all cases, the B-cell phenotype was largely intact, and delineation from classic HL (CHL) was further supported by MEF2A detection. All tumor cells were EBER-positive except two cases. EBV-latency type II was most frequent (89%) and type I rare. Cases with latency type I were CD30-negative. Five cases contained some BZLF1 and/or EBNA2-positive bystander lymphocytes.
As HRS-morphology of neoplastic cells combined with CD30 expression are frequent features of EBV-positive NLPHL, preservation of B-cell-transcription program, MEF2B expression combined with NLPHL-typical architecture and background composition facilitate distinction from CHL. EBER-ISH is the method of choice to identify these cases. The majority present with an EBV latency type II and only rarely with latency type I, which can be associated with missing CD30 expression. The presence of occasional bystander lymphocytes expressing BZLF1 and/or EBNA2 and the partial EBV-infection of neoplastic cells in some cases could indicate that EBV is either not primarily involved or only a transient driver in the pathogenesis of EBV-positive NLPHL.