Expression of Galectin-1 by EBV-Positive Lymphoproliferative Disorders

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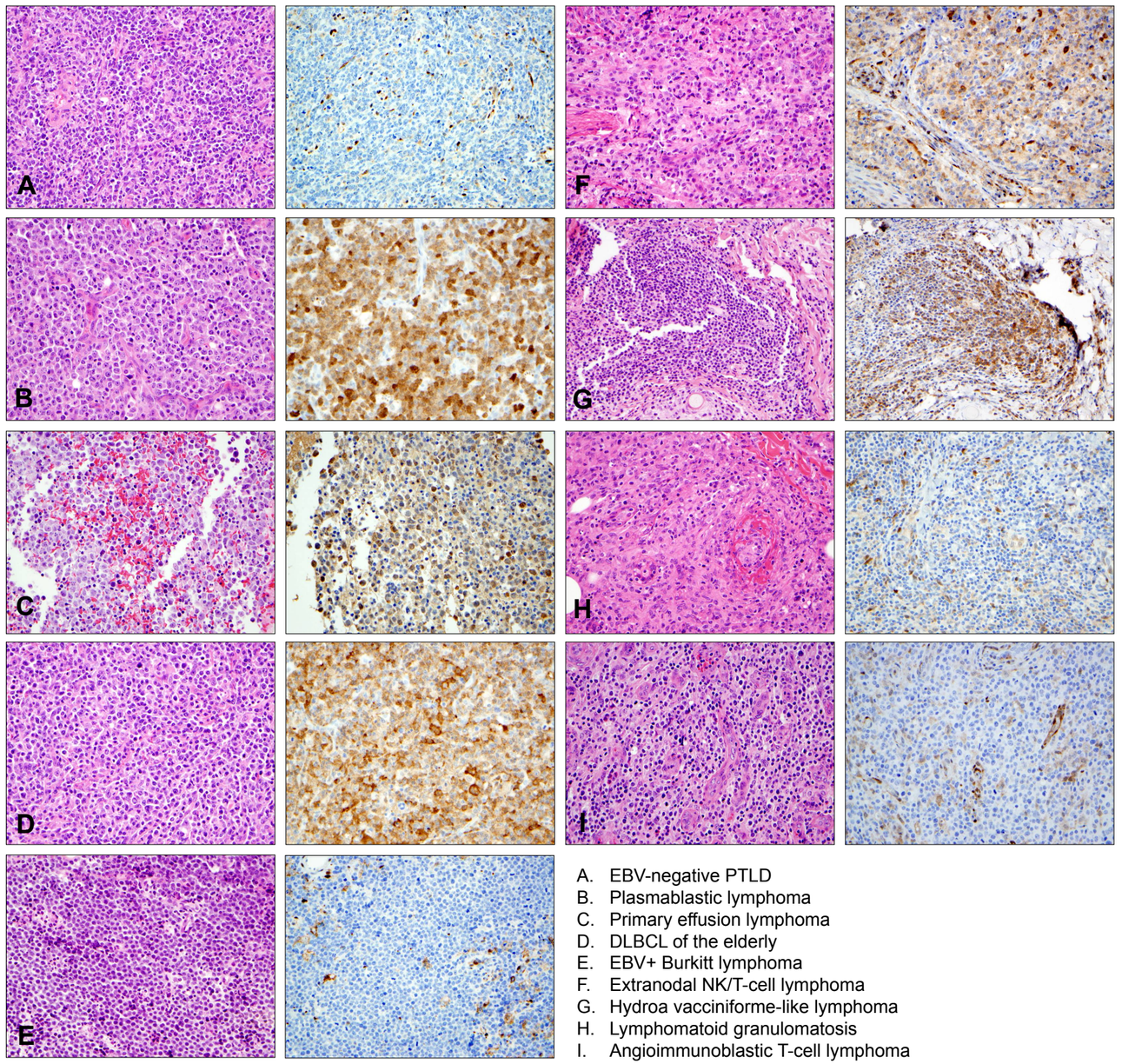
BACKGROUND

Galectin-1 (Gal1) is an immunomodulatory carbohydrate-binding protein upregulated in EBV+ B cells and promotes immune evasion by inducing the apoptosis of EBV-specific CD8+ T cells. We recently showed that Gal1 is expressed by the majority of EBV+ posttransplant lymphoproliferative (PTLDs) and described a novel, neutralizing Gal1 monoclonal antibody that inhibits Gal1-mediated T cell apoptosis, thereby providing a novel therapeutic strategy for the treatment of PTLD (*Blood*, 2011. 117:4315-22). In this study, we sought to expand the categories of lesions that may benefit from such targeted immunotherapy by examining additional EBV and immunodeficiency-related lymphoproliferative disorders (LPDs) for the expression of Gal1.

DESIGN

Whole tissue sections from 46 tumors were evaluated: 7 EBV+ diffuse large B-cell lymphomas (DLBCL) of the elderly/immunodeficiency-related, 8 plasmablastic lymphomas (PBL), 8 extranodal NK/T-cell lymphomas (ENKTCL), 3 primary (PEL), 4 lymphomatoid granulamotosis (LYG), 7 angioimmunoblastic T-cell lymphomas (AITL), 1 hydroa vacciniforme-like lymphoma, 1 EBV+ Burkitt lymphoma (BL), and 7 EBV-negative PTLDs. Immunohistochemistry was performed using a mouse anti-Gal1 monoclonal antibody. Staining intensity (0-3+) and the percentage of positive tumor cells (0-100%) was scored. Staining of 2-3+ in greater than 20% of tumor cells was considered positive.



A. EBV-negative PTLD
B. Plasmablastic lymphoma
C. Primary effusion lymphoma
D. DLBCL of the elderly
E. EBV+ Burkitt lymphoma
F. Extranodal NK/T-cell lymphoma
G. Hydroa vacciniforme-like lymphoma
H. Lymphomatoid granulomatosis
I. Angioimmunoblastic T-cell lymphoma

RESULTS

The majority of EBV+ DLBCLs (5/7), PBLs (6/8), ENKTCLs (6/8), and PELs (3/3) were positive for Gal1 expression. The case of hydroa vacciniforme-like lymphoma was also positive. In contrast, EBV+ BL, EBV+ B cells within LYG and AITL, and all EBV-negative PTLDs were negative for the protein.

Diagnosis	n	Neg 0-1+ <20%	Pos 2-3+ >20%
EBV-negative PTLD	7	7	0
Plasmablastic lymphoma	8	2	6
Primary effusion lymphoma	3	0	3
EBV-positive DLBCL of the elderly or immunodeficient	7	2	5
EBV-positive Burkitt lymphoma	1	1	0
Extranodal NK/T-cell lymphoma	8	2	6
Hydroa vacciniforme-like lymphoma	1	0	1
Lymphomatoid granulomatosis	4	4	0
Angioimmunoblastic T-cell lymphoma	7	7	0

CONCLUSIONS

We find that a variety of EBV+ tumors, including EBV+ DLBCLs, PBLs, ENKTCLs, and PELs express levels of Gal1 comparable to that observed for EBV+ PTLDs. These results suggest that EBV-mediated Gal1 expression is a general mechanism of immune evasion among LPDs and expands the spectrum of tumors that may benefit from Gal1-directed targeted therapy.