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Adipophilin is a useful marker for identification of Burkitt lymphoma

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Introduction

Burkitt lymphoma (BL) is an aggressive B-cell lymphoma that often presents in extranodal sites or as an acute leukemia and accounts for 30% to 50% of all childhood lymphomas.[1] Morphologically, BL is characterized by a diffuse monotonous growth of medium-sized blastic neoplastic lymphoid cells, with round nuclei, finely clumped chromatin, multiple nucleoli, basophilic cytoplasm, and by the presence of a 'starry sky' appearance due to the presence of benign macrophages with ingested apoptotic tumor cells. The cytoplasm of tumor cells usually contains lipid vacuoles, which are better perceived in the specimens of imprints and fine needle aspirations. However, on histologic preparations the lipid vacuoles disappear during routine fixation and waxing procedures.

The presence of lipid vacuoles in the cytoplasm of BL tumor cells may indicate that lipid metabolism in tumor cells is dysregulated. Recent studies have also shown dysregulation of fatty acid synthesis and an increase in glycolysis in non-Hodgkin lymphomas (NHLs).[2] Anti-adipophilin is a rabbit polyclonal antibody against a protein on the surface of intracytoplasmic lipid droplets. It has been widely used for detecting the intracytoplasmic lipid droplets in sebaceous neoplasms and very useful in differentiating sebaceous tumors from basal cell carcinoma, squamous cell carcinoma, and Paget disease. We conducted a study of this novel IHC marker for the identification of BL and differentiation from similarly-appearing NHLs.

Design

Surgical specimens of 11 cases of BL, 25 cases of diffuse large B-cell lymphoma (DLBCL), 9 cases of lymphoblastic lymphoma (LBL), and 2 cases of B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and BL (BLU) were included in the study. One whole-slide section from each case was stained with the antibody. Staining intensity was scored as 0 (negative), 1-2 (weak), 3 (moderate), 4 (strong); the labeling extent was tabulated as 0 (less than 5% positive cells), 1-2 (5-25% positive cells), 3 (26-75% positive cells), and 4 (greater than 75% positive cells). Cytoplasmic vacuolar and/or dot-like staining patterns are considered as positive staining. Benign macrophages were used as an internal positive control and benign plasma cells were used as an internal negative control together serving as a means to quality-control the staining results.

Results

As shown in table 1, of eleven cases of BL, adipophilin was expressed in nine cases (82%) with a cytoplasmic vacuolar or dot-like staining pattern (Fig. 1, Fig. 2). Of the nine positive cases, two presented strong staining with greater than 75% positive cells being stained; five cases expressed adipophilin moderately in more than 25% but less than 75% of tumor cells; the remaining two cases showed weak staining with 5-25% tumor cells being

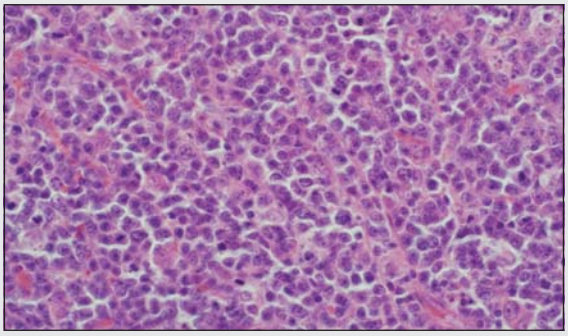

Fig. 1. *H&E of Burkitt lymphoma (400X)*

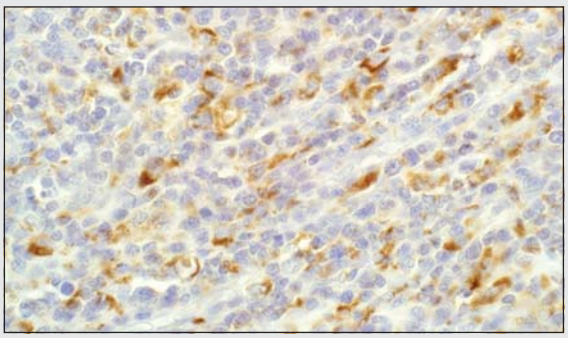

Fig. 2. *The lipid droplets in the cytoplasm of Burkitt lymphoma cells are positive for anti-adipophilin. (400X)*

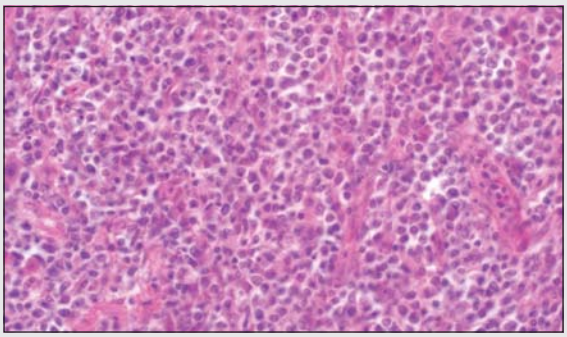

Fig. 3. *H&E of diffuse large B-cell lymphoma (400X)*

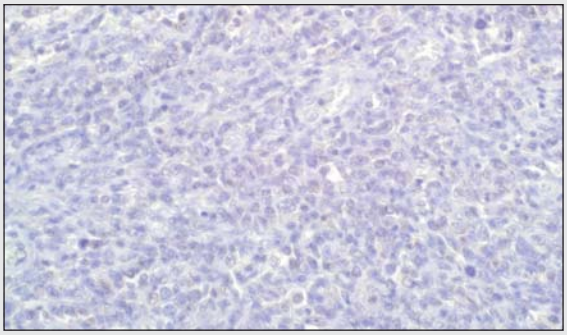

Fig. 4. *Tumor cells of diffuse large B-cell lymphoma are negative for anti-adipophilin. (400X)*

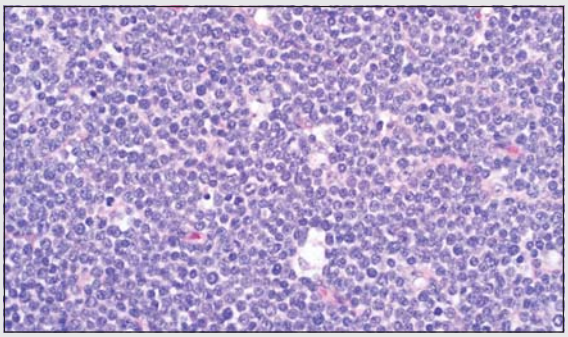

Fig. 5. *H&E of lymphoblastic lymphoma (400X)*

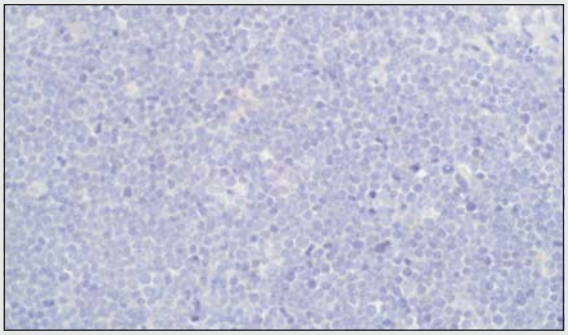

Fig. 6. *Lymphoblastic lymphoma does not express adipophilin. (400X)*

positive for adipophilin. In total, of the twenty five cases of DLBCL, only three cases (12%) were positive with weak staining with the labeling extent being 5-25% positive cells (Fig. 3, Fig. 4). All nine cases of LBL were completely negative (Fig. 5, Fig. 6). One of two cases (50%) of BLU expressed adipophilin in tumor cells at a weak level with a labeling extent of approximately 35% of positive tumor cells.

Table 1
Immunohistochemical Expression of Adipophilin in B-Cell Lymphomas

		Staining Pattern			
	Positive/ Total cases (%)	Strong (%)	Moderate (%)	Weak (%)	Negative (0%)
Burkitt Lymphoma	9/11 (82%)	2 (18%)	5 (46%)	2 (18%)	2 (18%)
Diffuse Large B-Cell Lymphoma	3/25 (12%)	0 (0%)	0 (0%)	3 (12%)	22 (88%)
Lymphoblastic Lymphoma	0/9 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (100%)
B-Cell Lymphoma, unclassifiable, with features between DLBCL and BL	1/2 (50%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)

Conclusion

Anti-adipophilin can be used to label intracytoplasmic lipid droplets in normal and neoplastic tissues. Burkitt lymphoma is known to have intracytoplasmic lipid droplets that are usually lost during fixation and paraffin embedding procedures. Immunohistochemical detection by anti-adipophilin presents a very useful IHC method to identify BL and to differentiate it from its mimics, especially DLBCL.

Reference

1. Leoncini, L., et al. Burkitt lymphoma. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. In Swerdlow, SH et al edited, 2008, Lyon, pp262.

2. Bhatt, AP, et al. PNAS USA 2012;109:11818.

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