Identification of Aggressive Variants of Mantle Cell Lymphoma Based on Flow Cytometry

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BACKGROUND

Mantle cell lymphoma (MCL) is a rare subtype of B-cell non-Hodgkin lymphoma characterized by a (1,14) translocation resulting in overexpression of cyclin D1.[1] MCL variants and a heterogenous disease presentation make this a challenging diagnosis with a highly variable outcome. Pleomorphic and blastic variants have an aggressive clinical course and shorter survival than the classical type.[2] The pleomorphic variant shows a marked variation in nuclear size, shape, and mitotic index.[3] The blastic variant appears small and immature with fine chromatin mimicking acute leukemia.[3] The aim of our study is to explore if flow cytometry analysis can help with the identification of aggressive MCL variants.

DESIGN

67 cases of Mantle Cell Lymphoma diagnosed at William Beaumont Hospital from 2010-2021 were identified and the flow cytometry data were reanalyzed. The forward scatter intensity (FSC INT) of all neoplastic B-cells and reactive T-cells were collected which included: median (Med), arithmetic mean (Amean), geometric mean (Gmean), standard deviation (StDev). Numerical data and graphical histograms for flow cytometry data were correlated with clinical and pathological features on patient derived H&E slides.

RESULTS

Neoplastic B-cells are more variable in size than reactive T-cells

Table 1. Forward scatter between neoplastic B-cells and reactive T-cells of all 67 cases

FSC	Med	AMean	Gmean	StDev
Neoplastic B-cells	486	483	29	139
Reactive T-cells	419	415	27	110
Student's T-test (p-value)	0.001	0.006	0.002	0.02

Three Major FSC Patterns were Identified

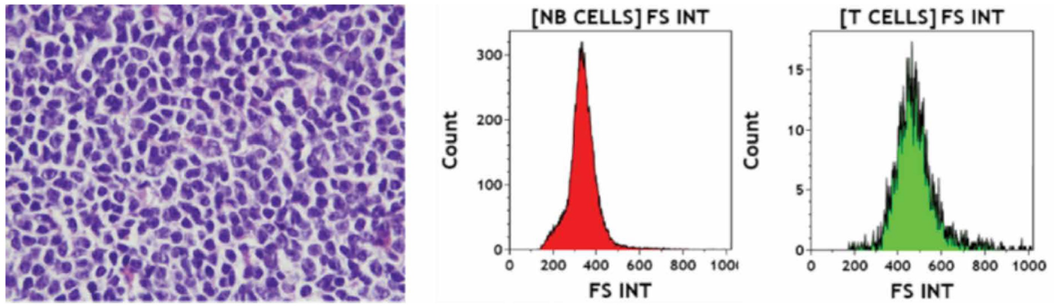

Figure 1. A representative case of classic MCL. The tissue section shows monotonous small to medium sized lymphoid cells (1000X HE-stain, Left). Flow cytometry shows forward scatter intensity that is similar for both neoplastic B-cells (Red) and reactive T-cells (Green).

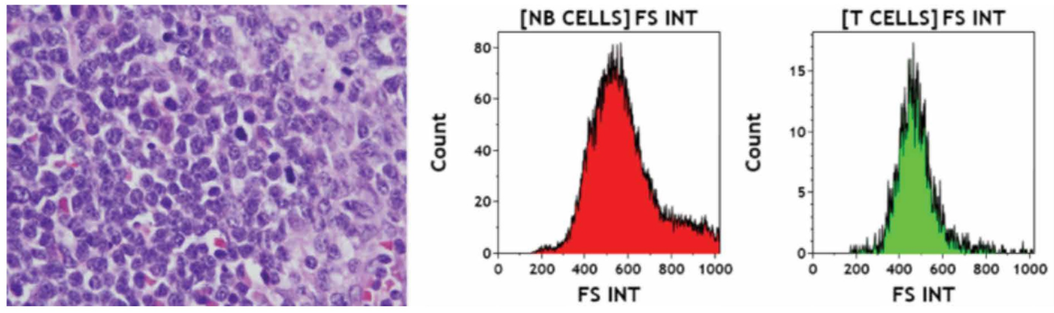

Figure 2. A representative case of blastic MCL. The tissue section shows increased large lymphoma cells and mitotic figures (1000X HE-stain, Left). Flow cytometry shows that the forward scatter intensity in neoplastic B-cells (Red) is significantly larger than that of reactive T-cells (Green).

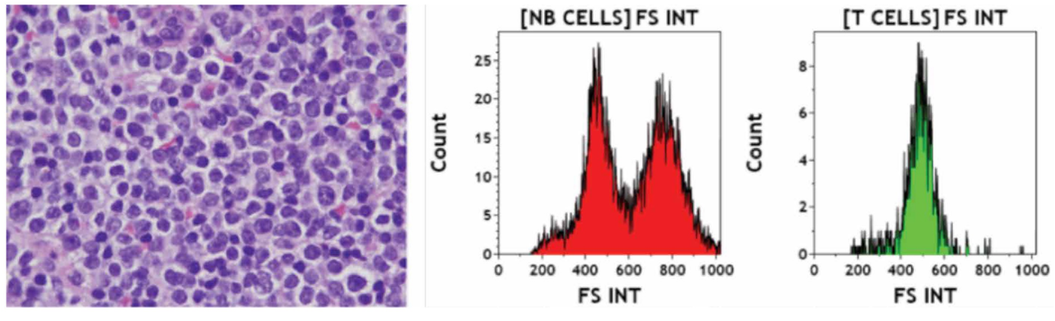

Figure 3. A representative case of pleomorphic MCL. The tissue section shows increased large and pleomorphic lymphoma cells and mitotic figures (1000X HE-stain, Left). Flow cytometry shows that the forward scatter intensity in neoplastic B-cells (Red) is bimodal and significantly larger than that of reactive T-cells (Green).

Atypical FSC patterns more likely seen in aggressive variants

Table 2. Comparison of FSC patterns between aggressive and classical MCL

	Aggressive Histology	Classic Histology
Atypical FSC Pattern	19 (28%)	7 (11%)
Typical FSC Pattern	9 (13%)	32 (48%)

Cases with atypical FSC patterns had significantly higher FSC Median and StDev

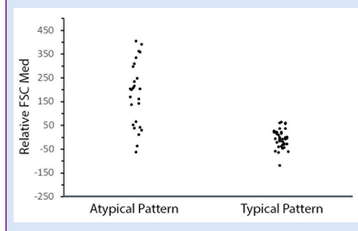

Figure 4. Difference in relative FSC Median (Med) between atypical and typical FSC patterns

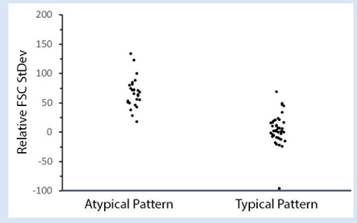

Figure 5 Difference in relative FSC Standard Deviation (StDev) between atypical and typical FSC patterns

CONCLUSION

- Histogram patterns and descriptive statistic of neoplastic B-cell FSC can be assessed and standardized by comparing with that of reactive T-cells
- MCL with increased FSC intensity and atypical histogram patterns are likely to be blastic of pleomorphic variants, requiring careful histopathological evaluation for accurate sub-classification
- Studies with a larger case number, with a controlled prospective evaluation is necessary to see if FSC pattern can be an independent prognostic marker

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