CSF Flow Cytometry in Patients with Leukemia and Lymphoma

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Introduction

It has been observed that in patients with a previous history of lymphoma or a hematopoietic malignancy, a majority of the patients with an "atypical" or "suspicious" diagnosis on cerebrospinal fluid (CSF) will ultimately have malignant cells identified in the CSF by cytology and/or flow cytometry. Central nervous system (CNS) involvement in patient with leukemia and lymphoma can be identified more efficiently with the utilization of flow cytometry[1]. Flow cytometric immunophenotyping of CSF also has been demonstrated to have high sensitivity and specificity for the detection of lymphoma and leukemia. They are able to determine a definitive diagnostic information from even very low cellularity samples[2]. Flow cytometric analysis markedly improves sensitivity when used in combination with cytology in the evaluation of lymphoid cells in CSF[3]. In this study, we reviewed the experience of our clinical flow cytometry laboratory in evaluating CSF specimens in order to find the disease distribution of positive CSF samples.

Aims and Objectives

By comparing CSF flow cytometry previously collected and studied at Beaumont Hospital, we hope to find a difference in the CSF analysis between the positive and negative samples. Additionally, we want to find the correlation of high positivity of flow cytometry with a specific diagnosis. The result of this study will help to establish a practice guideline to improving utilization of flow cytometry in evaluation of CSF specimens for possible hematolymphoid malignancy.

Methods

We retrospectively analyzed 382 cases with CSF sample that previously been studied with flow cytometry for B-cell lymphoproliferative disorders in the Beaumont Hospital. Their ages ranged from 9-90 (median: 58). The process of case identification requires us to reanalyze archived flow cytometry data using Kaluza software, a software package that is routinely used in the Beaumont Flow cytometry lab. Specifically, CSF samples are reanalyzed to see if they contain any abnormal cells. We then separated the cases based on the flow cytometry results and these cases will be further examined by their diagnosis, CSF WBC, CSF lymphocyte, CSF monocytes, CSF neutrophils and CSF proteins.

Results

1. Acute Myeloid Leukemia is the disease that is most associated with positive CSF flow cytometry.

Disease Distribution	Total case numbers	Positive flow cytometry N (%)
AML	13	7(54%)
ALL	56	6(11%)
LPL	3	3(0%)
DLBCL	98	2(2%)
BL	101	2(2%)
PTCL	9	2(22%)
MCL	12	1(8%)
MZL	10	1(10%)
CLL/SLL	4	0(0%)
FL	3	0(0%)
BNKL	1	0(0%)
ALCL	1	0(0%)
No history of lymphoma or leukemia	71	0%

ALL: Acute Lymphocytic Leukemia, AML: Acute Myeloid Leukemia, ALCL: Anaplastic Large-Cell Lymphoma, APL: Acute Promyelocytic Leukemia, BL: Burkitt Lymphoma, CLL: Chronic Lymphocytic Leukemia, SLL: Small Lymphocytic Lymphoma, DLBCL: Diffuse Large B-Cell Lymphoma, FL: Follicular Lymphoma, BNKL: Blastic Natural Killer Cell Leukemia/Lymphoma, LPL: Lymphoplasmacytic Lymphoma, MCL: Mantle Cell Lymphoma, MZL: Marginal Zone Lymphoma, PTCL: Peripheral T-Cell Lymphoma.

2. White blood cells and age are significantly elevated in positive CSF flow cytometry.

	White Blood Cells	Lymphocytes	Monocytes	Neutrophils	Protein
Student T-test (p-value)	.02	0.16	0.41	0.06	0.00

3. Distribution of CSF white blood cells, CSF lymphocytes, CSF monocytes, CSF neutrophils, CSF protein and age.

a. CSF WBC

Flow Cytometry	Mean	Median	Minimum	Maximum
Negative	7	0	0	576
Positive	143	41	1	1140

b. CSF Lymphocytes

Flow Cytometry	Mean	Median	Minimum	Maximum
Negative	55	59	0	100
Positive	40	34	2	98

c. CSF Monocytes

Flow Cytometry	Mean	Median	Minimum	Maximum
Negative	24	8	0	100
Positive	17	6	0	97

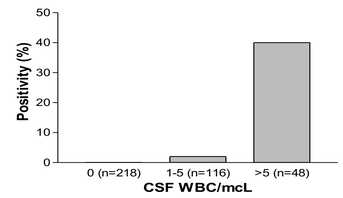
d. CSF Neutrophil

Flow Cytometry	Mean	Median	Minimum	Maximum
Negative	20	2	0	93
Positive	7	3	0	37

e. CSF Protein

Flow Cytometry	Mean	Median	Minimum	Maximum
Negative	38	29	3	349
Positive	184	145	10	542

4. No WBC in CSF differential predict negative flow cytometry results



Conclusions

- Patient has abnormal white blood cells counts in the CSF or atypical cells identified on cytological preparation should have further flow cytometry study to confirm or to rule out CNS involvement by hematological malignancy.
- Flow cytometry study is should not be performed on specimen with zero WBC in CSF differential count. Following this rule, 57% of unnecessary flow cytometry workup on CSF could be potentially eliminated, which may save a significant amount health care resource.

References

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