

METASTATIC HEMATOLOGICAL MALIGNANCIES TO THE CEREBROSPINAL FLUID CYTOLOGY (CSF): A SINGLE INSTITUTIONAL EXPERIENCE

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Abstract

A Cerebrospinal Fluid (CSF) that is known to harbor malignant metastatic tumor cells often heralds a poor prognosis. It poses challenges in clinical management of these patients, demanding an urgency in diagnosis. Thus, a cytological analysis of CSF helps in early diagnosis. The objective of the current study is to evaluate the utility of CSF cytology in the preliminary diagnosis of Metastatic Hematological malignancies to the CSF. The present study included 30 cases, collected from 2018 to 2020. All cases with metastatic hematological malignancies to the CSF were included in the study. The relevant data was obtained from patient records. The stained slides were studied under the microscope. In each case, a total cell count, 200 cell differential count and other relevant data was recorded. The percentage and morphology of blasts / abnormal lymphoid cells was also noted. The data thus obtained was analyzed. A total of 30 cases were included in the present study. Hepatosplenomegaly was the most common examination finding and microbiological cultures did not yield any growth in all the cases and total protein value was found to be raised in 8 cases with normal glucose value in 8 cases and lymphocyte predominance was seen in most of the cases. The most common hematological malignancy that involved CSF was acute leukemia followed by Non-Hodgkin lymphoma. We concluded that CSF cytology is an indispensable first line diagnostic modality for early diagnosis and prognostication of Metastasis of Hematological malignancies to the CNS, particularly when used in adjunct with clinical findings and radiological investigations.

Keywords: Cerebrospinal Fluid; Cytology; Metastasis; Malignancy; Acute Leukemia.

INTRODUCTION

A Cerebrospinal Fluid (CSF) that is known to harbor malignant metastatic tumor cells often heralds a poor prognosis and is often associated with concurrent neurological damage.¹ Furthermore, it also poses challenges in clinical management of these cancer patients, and thus demands urgency in diagnosis and treatment.^{1,4} Although promising advances in diagnostic biomarkers using investigative modalities such as Polymerase Chain reaction, Fluorescence in situ hybridization, capillary electrophoresis etc., enable early detection of circulating tumor cells in CSF, they are often limited by cost and equipment, particularly in the low income countries.¹ Often, in suspect clinical scenarios, a cytological analysis of CSF helps in confirming clinical suspicion.⁶ Previous studies have emphasized the role of CSF cytology as the gold standard in the detection of Metastasis.^{7,8,9,10}

In the present study, we attempt to study the utility of CSF cytology as a first line investigative modality in the diagnosis of Metastatic hematological malignancies to the CSF.

Aim and Objectives:

1. To evaluate the utility of CSF cytology in the preliminary diagnosis of Metastatic Hematological malignancies to the CSF.
2. To study the morphology and characteristics of malignant cells in Metastatic Hematological Malignancies to the CSF.

MATERIALS AND METHODS

The present study was a retrospective study that included 30 cases of CSF cytology samples collected between November, 2018 to June, 2020. All cases with Metastatic Hematological malignancies to the CSF were included in the study. The demographic data, clinical history and examination findings, relevant laboratory and radiological investigations were obtained from patient records. The stained slides (Papanicolaou and May-Grundwald Giemsa) were retrieved from the Archives and studied under the microscope. In each case, relevant data such as Total Cell count using an Improved Neubauer's chamber, a 200 cell Differential count on stained slides, gross appearance of CSF, Biochemical and Microbiological studies was noted. The percentage and morphology of Blasts/ Abnormal Lymphoid cells was also recorded. Cell block study, Histopathological correlation and Bone marrow study findings were obtained wherever available. The data thus obtained were tabulated and analysed.

Inclusion Criteria:

All the cases with hematological metastasis to the CSF were included in the study.

Exclusion Criteria:

The cases of Metastatic CNS tumors and Metastatic Epithelial tumors to the CSF were excluded from the study.

RESULTS

A total of 30 cases were included in the present study. The study included 18 males (60%) and 12 females (40%). The age of patients varied from 4 to 56 years (mean- 32 years). The most common presenting complaints in the present study was headache, followed by vomiting. Of the clinical examination findings, hepatosplenomegaly was the most common finding noted in 8 cases (26%), followed by lymphadenopathy in 4 cases (13%), two cases had Optic Neuropathy (6%). Radiological findings (MRI) were available in 10 cases in which features were suggestive of Metastasis to the CNS. In all the cases, Microbiological culture studies did not yield any microorganisms. The biochemical parameter that was found to be consistently raised was protein (8 cases, 26%). Glucose levels were normal in majority of the cases (8 cases, 26%). The gross appearance of CSF was hazy in 21 cases, turbid in 5 cases and clear in 4 cases. The most common Hematological malignancy that metastasized to the CSF was Acute Leukemia (20 cases, 66%), followed by Non Hodgkin Lymphoma (NHL) (10 cases, 33%). The Total Cell Count ranged from 1-2500 cells/cumm (mean- 1250 cells/ cumm).

Lymphocyte predominance was seen in all the cases (100%). Acute Lymphoblastic Leukemias (ALL) constituted 90% of the cases of Acute Leukemia (90%). The percentage of Blasts ranged from 60 to 95%.

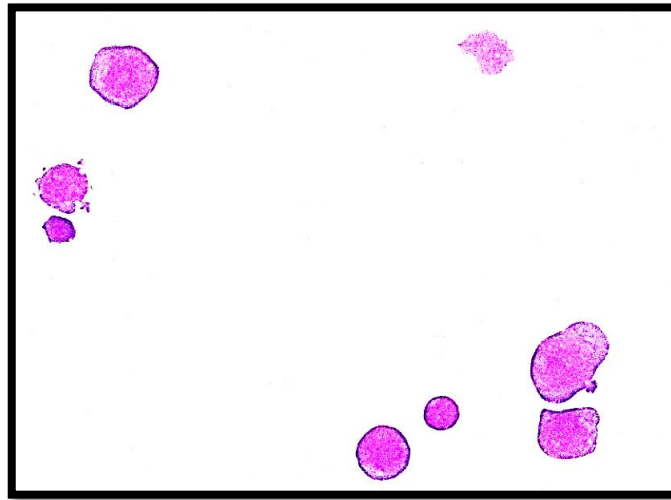


Figure 1: Photomicrograph Depicting Lymphoblasts. The Cells are Medium to Large with High N: C Ratio, Scant Cytoplasm, Round Irregular Hyperchromatic Nuclei with Prominent Nucleoli. MGG

Table 1: Flow Cytometry Findings were Available for 14 Cases and the Results are Summarized

Diagnosis	Flow cytometry findings
CALLA positive B cell ALL(11 out of 30)	HLA-DR, CD 10, CD79a, CD34, CD5, CD7, cCD3
T cell ALL(2 out of 30)	CD34, HLA DR, Ccd3, CD2, CD4, CD8, CD3
AML-M4/M5(1 out of 30)	CD34, CD117, CD19, CD10, CD22, CD2, CD20, cCD79a, CD3, Td

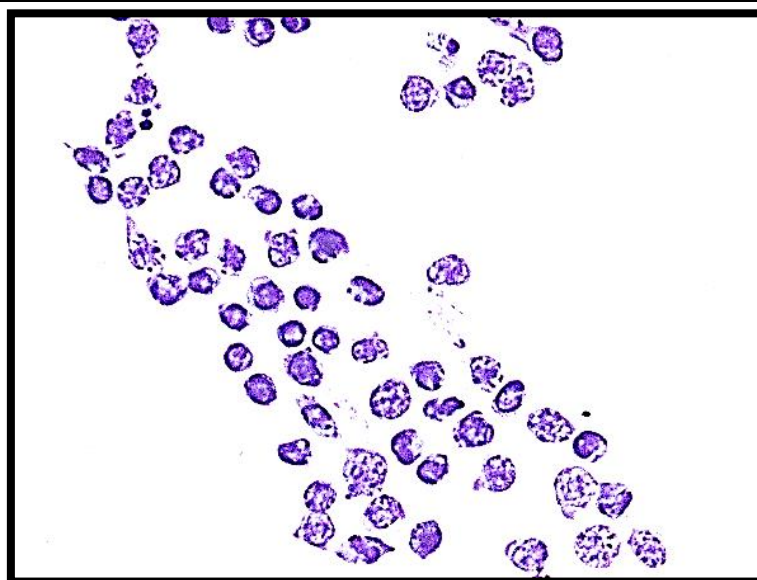


Figure 2: Photomicrograph Depicting Abnormal Lymphoid Cells. The Cells have a High N: C Ratio, Irregular Nuclear Contours, Condensed Chromatin and Scant Cytoplasm, PAP

In 2 cases, atypical cells were observed, which was difficult to characterize as either ALL or as NHL. Histopathological correlation was available in one case, which confirmed NHL. The Bone marrow study was available in 12 cases, in which marrow infiltration by Lymphoblasts was noted in 11 cases and by myeloblasts in 1 case. On Follow up, two patients succumbed to their illness.

DISCUSSION

Cytology remains the gold standard for the diagnosis of CSF metastasis. Although it has high specificity, it is often limited by low sensitivity.¹ Studies by Patel AS et al.⁴ have noted the need for additional literature on the pathobiology of metastatic lesions to CSF. The authors also emphasized that prompt diagnosis was crucial for patient management and better outcome.⁴

Furthermore, sequential CSF cytology is an excellent tool to monitor CNS involvement particularly in children who otherwise appear to be asymptomatic.⁹ Some authors are of the opinion that metastasis to the CSF could be diagnosed by clinical examination findings; albeit quite challenging, in view of concomitant confounding factors.¹ In the present study, the most common presenting complaint was headache. Abnormality of CSF indices is often noted in cases with CSF metastasis.² In the present study, Total counts and CSF protein was consistently found to be elevated. During cytological examination of the CSF, authors have recommended shortened delay in transport time to combat degenerative artifactual changes which may pose diagnostic difficulties.⁶ Leal T et al.² were of the opinion that high index of suspicion along with repeat samples may be necessary to confirm diagnosis, in the event that the initial sample is negative for malignancy. Useful tools such as Flow cytometry analysis and Immunocytochemistry (ICC) are valuable adjuncts to cytology, particularly in difficult cases.^{7,6} In the present study, the most common hematological metastatic malignancy was Acute Lymphoblastic Leukemia, similar to a study by Patel et al.⁹

CONCLUSION

Metastasis to CSF often confers a poor prognosis in patients with hematological malignancy. Prompt management is often crucial for better patient outcome. Even in patients in remission, who may appear otherwise asymptomatic, CSF cytology plays an important role in the detection of relapse. Thus, CSF cytology is an indispensable first line diagnostic modality for the early diagnosis and prognostication of Metastasis of Hematological malignancies to the CNS, particularly when used in adjunct with clinical findings and radiological investigations.

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