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HEMATOLYMPHOID NEOPLASM IN PLEURAL EFFUSION: CYTOMORPHOLOGY AND IMMUNOCYTOCHEMISTRY-BASED CASE SERIES

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ABSTRACT
Pleural effusion is a frequent finding in various malignancies, including hematolymphoid neoplasms. This case series highlights four cases where pleural fluid cytology played a crucial role in identifying underlying hematologic malignancies such as Acute Myeloid(AML), Non-Hodgkin Lymphoma (NHL) and Leukemic Infiltration. The application of immunocytochemistry alongside cytomorphology was pivotal in reaching a definitive diagnosis. This series emphasizes the utility of cytological analysis and the importance of considering hematolymphoid malignancies in the differential diagnosis of pleural effusion.

Keywords: Pleural fluid, Cytology, Chronic Myeloid Leukemia, Non-Hodgkin Lymphoma, Immunocytochemistry, Hematolymphoid malignancy

INTRODUCTION
Pleural effusion is a common clinical presentation in both malignant and non-malignant conditions. In India, tuberculosis and metastatic carcinomas are among the most frequent causes of exudative pleural effusion. However, hematolymphoid malignancies like leukemias and lymphomas can also involve the pleural cavity either as a primary manifestation or due to disease progression. Cytological examination of pleural fluid offers a rapid, non-invasive, and cost-effective method to detect malignant involvement. Accurate diagnosis in these cases requires a thorough understanding of cytomorphological features, often supplemented by immunocytochemistry for confirmation and subclassification of Case Series.

Case 1: Known Case of AML
A 7 yrs old male child presented to the hospital with fever 3 months, weakness and cough with whitish expectoration, known case of Acute Myeloid Leukemia (AML) presented with pleural effusion. The specimen received was 40 mL of pale yellow, turbid pleural fluid. Cytocentrifuged smears were richly

cellular and predominantly showed mature lymphoid cells, few neutrophils, reactive mesothelial cells, and some atypical cells. Atypical cells have high nuclear-to-cytoplasmic ratio, fine chromatin, prominent nucleoli and scant to moderate basophilic cytoplasm(Figure 1). Flow cytometry reveal CD45 vs SS scatter shows CD45 dim ~90% Blasts population which express heterogenous CD4, bright CD7, moderate CD5, dim CD10, dim CD34, dim CD38 and positive for cytoplasmic CD3.

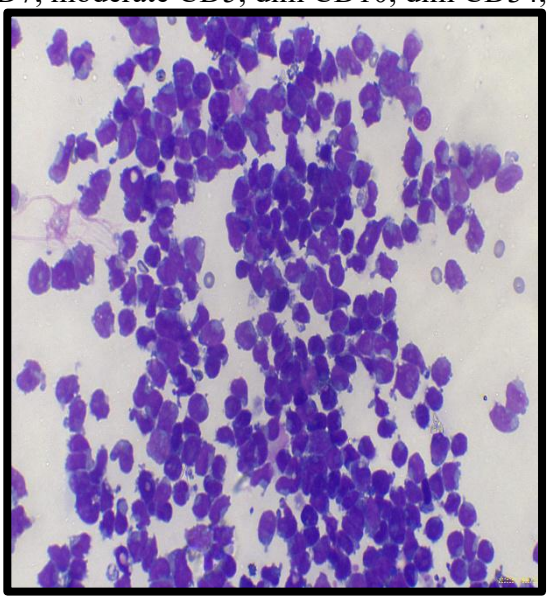

Figure 1. Cytocentrifuge smear showing atypical blasts with high N:C ratio, fine chromatin, prominent nucleoli, and basophilic cytoplasm in pleural fluid.

Case 2: Consistent with Non-Hodgkin Lymphoma

A 60 year old male presented to the hospital with fever, night sweats on examination bilateral cervical lymphadenopathy was seen. 3 mL sample of pale yellow, slightly turbid pleural fluid was examined. Cytocentrifuged smears revealed a diffusely scattered population of medium to large atypical mononuclear cells with high nuclear-to-cytoplasmic (N:C) ratio, irregular nuclear contours, prominent nucleoli, and basophilic cytoplasm. Immunocytochemistry revealed LCA positivity and Pan-CK negativity, indicating lymphoid origin(Figure2). Impression: Pleural fluid cytology positive for malignant cells, consistent with Non-Hodgkin lymphoma (NHL).

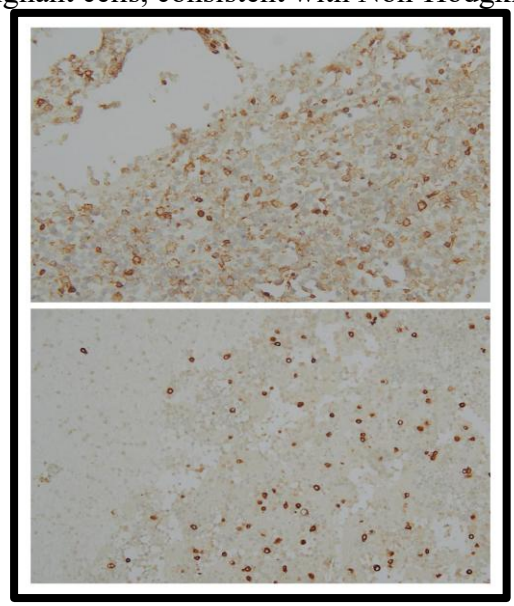

Figure 2. Immunocytochemistry showing strong LCA positivity and Pan-CK negativity in pleural fluid cells, confirming lymphoid origin.

Case 3: Consistent with Non-Hodgkin Lymphoma

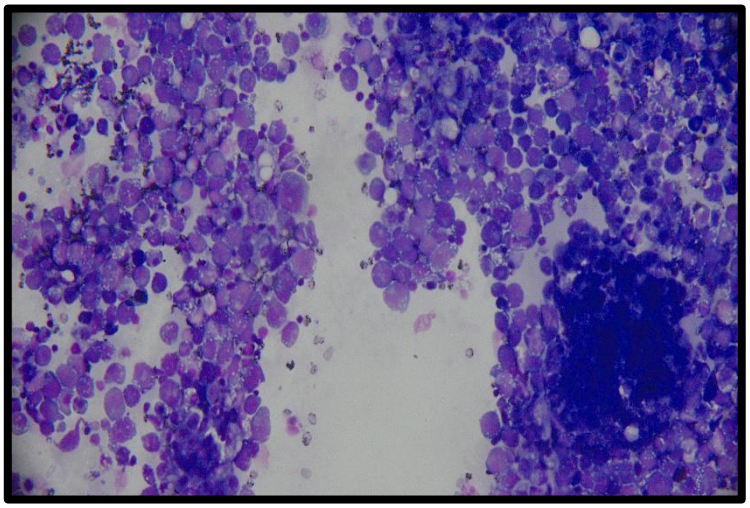

Figure 3. Discohesive large atypical lymphoid cells with high N:C ratio and basophilic

A 66 year old male patient presented with a mediastinal mass and pleural effusion. About 10 mL of pale yellow, turbid pleural fluid was received. Richly cellular cytocentrifuged smears showed discohesive large mononuclear atypical cells with high N:C ratio, hyperchromatic nuclei, and moderate basophilic cytoplasm(Figure 3). Immunohistochemistry showed positivity for CD45 and negativity for Desmin. Impression: Malignant cells consistent with Non-Hodgkin lymphoma.

Case 4: Leukemic Infiltration

A 28 year old male patient presented with fever, fatigue , loss of appetite and chest pain. Pleural fluid (35 mL, pale yellow, slightly turbid) was examined. Cytology revealed blast cells scattered singly, showing variable size, high N:C ratio, pleomorphism, hyperchromatic nuclei with irregular membranes, and coarse chromatin(Figure 4). Background showed hemorrhage with lymphocytes, plasma cells, benign mesothelial cells and macrophages.
Impression: Malignant pleural effusion due to leukemic infiltration.

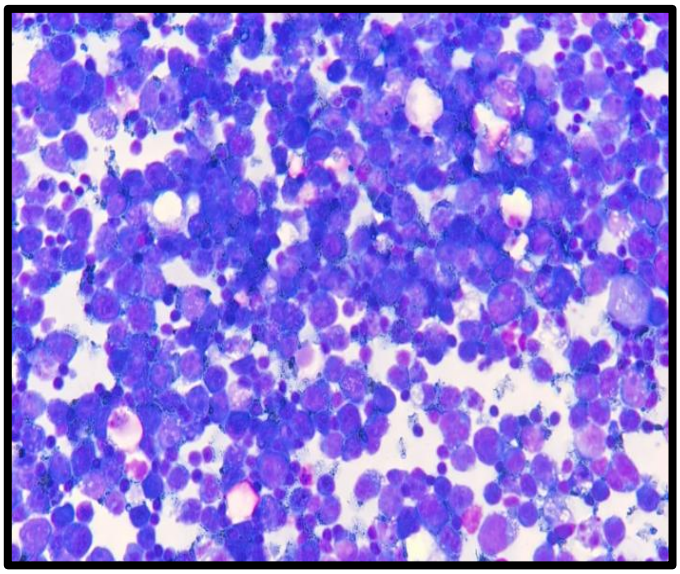

Figure 4. Pleural fluid cytology shows scattered blast cells with high N:C ratio, pleomorphism, coarse chromatin, and hemorrhagic background.

Discussion

In our case series, we presented four cases of pleural fluid involvement by hematologic malignancies. Two cases were positive for Non-Hodgkin Lymphoma (NHL), one was a known case Acute Myeloid Leukemia (AML), and one showed leukemic infiltration. Pleural fluid cytology in these cases revealed atypical lymphoid or blastoid cells with high nuclear-to-cytoplasmic (N:C) ratios, irregular nuclear membranes, and coarse chromatin. The presence of lymphoglandular bodies, single-cell distribution, and absence of cell clustering or cohesion supported the diagnosis of hematolymphoid malignancy over metastatic carcinoma or mesothelial proliferation.
Immunocytochemistry (ICC) markers such as leukocyte common antigen (LCA or CD45), Pan-Cytokeratin (PanCK), and Desmin were applied in selected cases. These markers were instrumental in establishing the lymphoid nature of the atypical cells and ruling out carcinoma or mesothelial cell origin. For instance, CD45 positivity with PanCK negativity strongly favoured lymphoma, while

Desmin negativity helped exclude reactive mesothelial hyperplasia. The combined use of cytomorphology and IHC significantly enhanced diagnostic accuracy, as supported by earlier studies[1,3,6].

Pleural involvement in CML is rare and may indicate blast crisis or extramedullary hematopoiesis. Similarly, NHL presenting with effusion may be primary or secondary, and in some cases, may be the first manifestation of disease. Distinguishing between reactive lymphocytosis and neoplastic lymphoid infiltrates is a frequent challenge in effusion cytology. Key morphological clues, including nuclear atypia, high mitotic activity, and prominent nucleoli, assist in this distinction. However, cytomorphology alone may be insufficient in equivocal cases, necessitating ICC [2,4,5,7].

CONCLUSION

Cytological evaluation of pleural fluid is an essential, frontline diagnostic modality for detecting hematologic malignancies. The combination of morphologic assessment and targeted immunocytochemistry significantly improves diagnostic accuracy, allowing differentiation between reactive processes and malignant infiltrates. Early recognition of malignant cells in pleural fluid provides critical diagnostic and prognostic information and guides timely management. Pathologists must keep hematolymphoid neoplasms in mind when evaluating unexplained pleural effusions.

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