INTRODUCTION

Effusion is a common complication of lymphomas and may develop at any time during the course of the disease. If present at the time of diagnosis, it adversely affects the overall survival and is associated with a higher rate of disease relapse following treatment [1,2].

Cytology is a method commonly employed in the evaluation of effusions. However, sometimes, it may be extremely difficult to differentiate a reactive process from lymphomatous effusions. Immunocytochemistry, flow cytometry, and cytogenetics help in such situations. However, in the absence of clinical details and ancillary studies, the detection rate of lymphoma in cytologic specimens is low, i.e., approximately 10% [1-3].

The present study was carried out to identify the light microscopic features that are useful in identifying lymphomas on effusion cytology.

METHODS

A retrospective study was conducted on all patients with fluid cytology or tissue biopsy reported as suspicious or positive for non-Hodgkin lymphoma (NHL) in a tertiary care was done. The cytology, histopathology, and immunohistochemistry slides were reviewed.

RESULTS

A total of 27 cases were included in the study. Correlation with the histopathological sections of all the positive cases revealed that the cytomorphology of the abnormal lymphoid cells was monomorphic and similar to those seen in the tissue biopsy. Mercury drop karyorrhexis when present was characteristic of lymphomatous effusions. The detection rates of large cell lymphomas are higher than low-grade counterparts.

Non-lymphomatous effusions showed heterogeneous lymphoid cell population and lacked karyorrhexis.

Conclusion: Lymphomas can give rise to effusions. In the absence of resources in developing countries, it is important to distinguish lymphomatous effusion from a reactive process based on morphology. Monomorphic population of the lymphoid cells and presence of mercury drop karyorrhexis are useful morphological clues in identifying a lymphomatous effusion. Further, tuberculosis is a common non-neoplastic process that can be mistaken for a low-grade NHL.

Keywords: Effusion, Non-Hodgkin’s lymphoma, Cytology, Karyorrhexis.
Of the five cases reported as suspicious, four had monomorphous population of small-sized lymphoid cells while one had polymorphous population of small-to medium-sized cells. The latter smear on review revealed KP and MKD along with binucleate forms and was subsequently reported positive. Two cases were also reported positive as they showed nuclear irregularities. However, there was the absence of KP and MKD. The remaining two cases were negative.

All these cases were finally classified as positive (17) including nine true positives, five false negatives, and three that were initially diagnosed suspicious. The negative (10) group included the eight true negative cases and two which were suspicious for NHL.

The cytomorphological features of these cases (n=27) are shown in Table 1.

Correlation with the histopathological sections of all the positive cases (17/27) revealed that the cytomorphology of the abnormal lymphoid cells was similar to those seen in the tissue biopsy.

The cytology of positive cases showed cells with round-to-oval nuclei with irregular nuclear membranes and one to multiple nucleoli. Five cases showed binucleation. Karyopyknosis (35%) and MKD (59%) when present were characteristic of lymphomatous effusions and were seen more often in high-grade lymphomas. These two features were absent in negative cases. The detection rates of large cell lymphomas were higher than their low-grade counterparts.

Non-lymphomatous effusions showed polymorphous lymphoid cell population, lacked karyorrhexis, and demonstrated mesothelial cells (Fig. 3).

**DISCUSSION**

Effusions in lymphoma may be malignant, as a part of the disease process, or reactive, secondary to infections due to reduced immunity or therapy. The former can be explained by direct infiltration, lymphatic obstruction, hematogenous dissemination, or widespread disease [4]. Cytological examination of the effusion fluid in lymphoma provides a rapid and accurate diagnosis, with diagnostic accuracy of tissue biopsy and has therapeutic and prognostic implications [1,2,5]. In diffuse large B-cell lymphoma, the presence of malignant cells in effusions has been found to be a stronger poor prognostic and predictor factor than high stage [6].

While evaluating fluid cytology, the presence of dyscohesive, single isolated cells favors a neoplastic process. The presence of monomorphic population of large lymphoid cells was a characteristic finding useful in the cytological diagnosis of lymphomatous effusions. Other cytologic clues useful in NHL associated effusions include karyopyknosis and MDKs. The presence of tingible body macrophages though uncommon also served as another useful feature. Hence, the higher grade NHLs were detected more often. The absence of monomorphism may contribute to the low detection of low-grade NHLs [2,5,7]. In the present study, all the

![Fig. 1: Monomorphous population of lymphoid cells in lymphomatous effusion (PAP, ×20)](image1)

![Fig. 2: Polymorphous population of lymphoid cells in lymphomatous effusion (PAP, ×20) Inset: Arrowed structure: Mercury drop karyorrhexis resembling neutrophil (×40)](image2)

| Table 1: Cytomorphological features of effusions (n=27) |
|----------------------------------|----------------------------------|----------------------------------|
| Morphologic characteristics | Positive cytology (n=17), n (%) | Negative cytology (n=10), n (%) |
|----------------------------------|----------------------------------|----------------------------------|
| **Cell population** | High grade (n=15) | Low grade (n=2) |  |
| Monomorphous | 7 (41) | 1 (6) |  |
| Polymorphous | 8 (47) | 1 (6) | 0 (100) |
| Dyscohesive cells | 15 (88) | 2 (12) | 10 (100) |
| **Cell size** | | | |
| Small | 0 (0) | 2 (12) | 10 (100) |
| Small to medium | 6 (35) | 0 (0) |  |
| Medium | 1 (6) | 0 (0) |  |
| Medium to large | 5 (29) | 0 (0) |  |
| Large | 3 (18) | 0 (0) |  |
| Karyopyknosis | 6 (35) | 0 (0) | 2 (20) |
| MDK | 10 (59) | 0 (0) |  |
| Mesothelial cells | 2 (12) | 0 (0) | 7 (70) |
| Tingible body macrophages | 3 (19) | 0 (0) |  |
| Lymphoplasmacytoid cells | 3 (18) | 0 (0) | 1 (10) |
Differentiating between tuberculosis-related and mesothelial cells helped to identify the neoplastic effusions. Further, the presence of karyopyknosis, nuclear irregularities, and paucity of background MDK and fewer viable tumor cells in between them. The presence of polymorphous population of lymphoid cells, is tuberculosis. Biochemical and cytological overlaps contribute to the diagnostic difficulty in distinguishing between the two.

In the present study, all the false negative cases were of effusions from high-grade lymphoma. On review, these effusions appeared to be polymorphous on low power examination due to numerous MKD and fewer viable tumor cells in between them. The presence of karyopyknosis, nuclear irregularities, and paucity of background mesothelial cells helped to identify the neoplastic effusions. Further, the negative cases had polymorphous population of lymphoid cells with the absence of karyopyknosis and MDKs.

Cell necrosis in the form of fragmented nuclei with small round cytoplasmic particles called mercury drop karyorrhexis (MKD) may be mistaken for neutrophils, giving a false heterogeneous appearance to the cell population in a lymphomatous effusion, especially in low power examination [8]. MKD was present in 59% of positive cases and was absent in negative cases. Hence, this is a useful feature to differentiate neoplastic from inflammatory effusions. There is usually a paucity of stimulated or reactive lymphoid cells including LP cells in reactive effusions. The presence of >10% stimulated lymphoid cells in an effusion should raise a suspicion for malignancy. Three of 17 positive cases (18%) showed LP cells in the present study [9].

Cytological characteristic of the lymphoid cells is an important indicator of lymphomatous effusions. Effusions in high-grade lymphomas were more readily detected due to the presence of medium to large cells with irregular nuclei, coarse chromatin, prominent nucleoli, karyopyknosis, and frequent mitosis. However, it was difficult to distinguish neoplastic cells in low-grade lymphoma from benign lymphocytes in reactive effusions which are also small sized with regular nuclear contour and inconspicuous nucleoli. The presence of polymorphous population of small-sized cells in the latter was the clue for excluding lymphomatous effusions in these cases.

In our country, a common non-neoplastic cause of effusion, which shows predominance of lymphoid cells, is tuberculosis. Biochemical clues such as elevated fluid protein and adenosine deaminase levels can be seen in both tuberculous and lymphomatous effusions. Effusions due to tuberculosis also show sparse mesothelial cells (<5%) which is a common feature of lymphomatous effusions [10-12]. Hence, these biochemical and cytological overlaps contribute to the diagnostic difficulty in distinguishing between the two.

In the present study, all the false negative cases were of effusions from high-grade lymphoma. On review, these effusions appeared to be polymorphous on low power examination due to numerous MKD and fewer viable tumor cells in between them. The presence of karyopyknosis, nuclear irregularities, and paucity of background mesothelial cells helped to identify the neoplastic effusions. Further, the monomorphous small-sized cells in the effusions reported as suspicious were identified as positive due to the nuclear characteristics [13]. The major limiting factor in the present study is the small sample size of the study group due to which adequate statistical analysis cannot be done.

CONCLUSION

Early and rapid identification of the involvement of body cavities is essential for prompt and appropriate treatment. It is challenging but very important to distinguish lymphomatous effusion from a reactive process based on cytomorphology in the absence of modern ancillary tests in resource poor. Cytomorphological features favoring lymphomatous over reactive effusions include monomorphous singly placed lymphoid cells with nuclear indentations/protrusions, prominent nucleoli, and mitosis. A background containing nuclear fragmentation, karyorrhexis, and absence or sparse mesothelial cells can also serve as cytologic clues to initiate ancillary testing. However, similar studies with larger cohort are warranted to ascertain a statistical significance.

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AUTHORS’ CONTRIBUTIONS

Dr. Bhavna Nayal - Collection of data and manuscript writing.
Dr. Geetha V - Data analysis and manuscript editing.

CONFLICTS OF INTEREST

Nil.

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