

Study of Changes in Peripheral Blood Film and Bone Marrow in Patients of Leukemia's and Lymphomas

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Abstract : Leukemias are abnormal proliferation of immature bone marrow-derived cells (blasts) that may also involve peripheral blood or solid organs while Lymphomas are malignant neoplasms characterized by the proliferation of cells native to the lymphoid tissue. Haematological malignancies have diverse modes of presentation that often diagnosed on peripheral blood examination but then ultimately requires bone marrow examination for both diagnosis and management. This simple and relatively safe procedure is important particularly in resource poor centres since access to adjuvant diagnostic techniques are often lacking or absent Present study was aimed to study changes in cells in PBF (Peripheral Blood Film) and Bone Marrow Aspiration and Bone Marrow Biopsy of patients presenting with new diagnosis of Leukemia and Lymph Node biopsy proven cases of Lymphoma and to correlate them.

Keywords – Leukemia, Lymphoma, Peripheral blood examination, Bone marrow aspiration and Biopsy

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I. Introduction

A hematological malignancy arises when something goes wrong in the regulation of the division or the life span of a blood cell or its precursor [1]. It is characterized by widespread, rapid and disorderly proliferation of leukocytes and their precursor and by the presence of immature leukocytes in blood often in very large numbers. [2]

Leukemias are neoplastic proliferation of hematopoietic cells. Specific genetic events contribute to malignant transformation of the cells and their progeny forming a clone of leukemic cells. They are divided into Acute and Chronic.[3]

The Acute leukemias (ALs) are a heterogeneous group of neoplasms arising from transformation of hematopoietic stem cells¹¹, with a retained partial capacity of differentiation and are divided into acute myeloid (also called non lymphocytic) leukemia (AML) and acute lymphoid leukemia (ALL) (lymphoblastic leukemia/lymphoma).[4]

The overall annual incidence of these disorders in the general population is about 4 per 100,000, with approximately 70% of them being acute myeloid leukemia (AML) [5]

Chronic Myeloid Leukemia (CML) is a clonal disease characterized by the presence of the Philadelphia (Ph1) chromosome. The diagnostic presumptive of CML usually arises with the results obtained in blood cell counts. Definitive diagnosis is obtained by evaluation of bone marrow biopsy (BMB), myelogram and cytogenetic examination.[6,7]

Chronic lymphocytic leukemia is a clinically heterogeneous disease consisting of monoclonal small B-cell lymphocytes expressing CD19, CD5, and CD23. The excessive number of cells occurs because of both increased proliferation and accumulation of cells with an increased lifespan.[8]

Lymphomas are malignant neoplasms characterized by the proliferation of cells native to the lymphoid tissue. They are divided into two broad groups, Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). These are the most common haematological malignancies, accounting for the 5% of all cancers in both genders. Incidence of Hodgkin lymphoma is about 2.8 new cases per 100,000 people per year; overall incidence of non-Hodgkin lymphomas is about 19.7 new cases per 100,000 people per year.[9,10]

Hodgkin's lymphoma (HL) is characterized by the presence of Reed-Sternberg cells and their variants in an appropriate background of inflammatory cells.[11] The non-Hodgkin lymphomas (NHLs) are a diverse collection of lymphoid malignancies with varied pathology, cell of origin, natural history, and response to treatment.[12]

Peripheral Blood film and Bone marrow examination is an important diagnostic tool to evaluate various disorders including both neoplastic and non-neoplastic hematological diseases. The bone marrow evaluation may either confirm clinically suspected disease or may provide the previously unsuspected diagnosis and aid in staging of lymphomas[13,14]

II. Aims and Objectives

- 1) To study changes in cells in PBF (Peripheral Blood Film) and Bone Marrow Aspiration and Bone Marrow Biopsy of patients presenting with new diagnosis of Leukemia and Lymph Node biopsy proven cases of Lymphoma.
- 2) To correlate the PBF and BM Examination findings.

III. Material and Method

3.1 Source of data:

The study was carried out in the department of Pathology, Sardar Patel Medical College and associated group of hospitals, Bikaner. This study was a hospital based prospective and retrospective study, including the newly diagnosed patients of Leukemia or Lymph node Biopsy proven cases of Lymphoma.

3.2 Method of collection of data (including sampling procedures):

Patients diagnosed with Leukemia or Lymphoma were studied for changes in hematological parameters. Relevant clinical data including patient history, physical examination, complete hematological study along with other relevant investigations were collected from the patient as well as hospital records and proforma was filled.

After obtaining the informed written consent, blood was collected under aseptic precautions for performing investigations for assessment of hematological changes.

3.3 Inclusion criteria:

- 1) Patients with newly diagnosed Leukemia
- 2) Patients with newly diagnosed Lymph Node Biopsy proven case of Lymphoma under evaluation for hematologic involvement.

(Leukemia: Acute: AML; ALL
Chronic: CML; CLL

Lymphoma: Hodgkin Lymphoma
Non Hodgkin Lymphoma)

3.4 Exclusion criteria:

- 1) Patients already on treatment for Leukemia or Lymphoma
- 2) Pregnancy
- 3) Patient suffering from Myelodysplastic Syndrome(MDS) and Myeloproliferative neoplasms other than CML.
- 4) Aplastic anemia
- 5) Known case of Infection or Inflammatory disorder of Bone marrow.

Eligible patients were selected and the evaluation of their hematological parameters was done by collecting 2 ml of sample on EDTA prefilled vial and transported to the laboratory immediately. The analysis was done by the automated Analyzer. Peripheral blood smears were studied after staining with the Leishman's stain. Then for the selected suspected cases Bone Marrow Examination was performed.

Both BMA (by Klima needle) and BMB (using Jamshidi needle) were taken separately or together (using Jamshidi needle) from posterior superior iliac spine. 0.2 to 0.5 ml of fluid was aspirated, smears prepared, dried and stained with Leishman and Hematoxylin & Eosin stain.

IV. Results and Conclusion

In the index study, a total of 100 cases of newly diagnosed cases of Leukemias and newly diagnosed Lymph node biopsy proven cases of Lymphomas were selected and Peripheral blood examination, Bone marrow aspiration and trephine biopsy examination were performed.

The study highlighted the following findings:

- ❖ The maximum number of cases observed were of Non Hodgkin lymphomas (29%) for whom peripheral blood and bone marrow examination was performed mainly for staging (TABLE 4.1)

- ❖ Among leukemias, Acute myeloid leukemias (AMLs) showed the highest incidence with mean age incidence of 36 years. Male to female ratio was 2.7:1
- ❖ The overall incidence of leukemias and lymphomas was more among males (70%) probably because of higher exposure rate to occupational carcinogens; and the most common diagnosis was NHL (29%) followed by HL (18%) (TABLE 4.2)
- ❖ Most common age group affected in our study was 41-50 years.
- ❖ Peripheral blood examination was complementary to bone marrow aspiration and diagnostic in almost all cases except the one with NHL infiltration, for which BMA and BMB was useful.
- ❖ Bone marrow biopsy inspite of providing an additional information relative to surrounding environment was observed to be more sensitive than BMA for diagnosing Infiltration of marrow by lymphoma cells in NHL
- ❖ Incidence of Dry tap was 4%, which was either due to infiltration of marrow by NHL or due to compactness of marrow due to high cellularity. In all these cases bone marrow biopsy provided correct diagnosis.
- ❖ Peripheral blood examination in CML is enough for diagnosis, still Bone marrow aspiration and biopsy are being performed so as to look for evidence of early fibrosis. Even a small quantity of fibrosis (i.e. grade I) in CML holds a very poor prognosis.

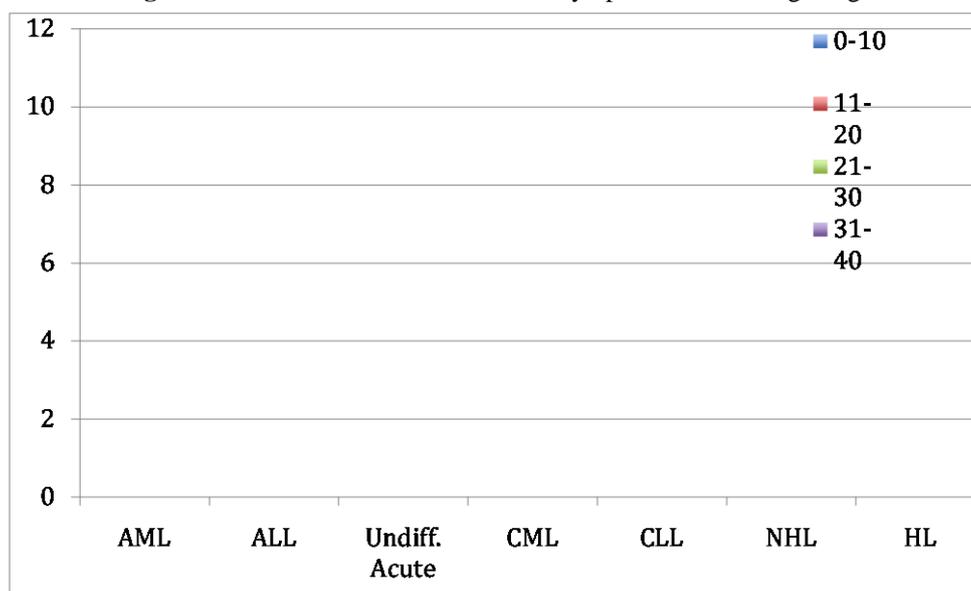
Table 4.1. Distribution of various leukemias and lymphomas observed in our study

DIAGNOSIS	No. Of cases	Percentage(%)
Acute Myeloid Leukemia	11	11
Acute Lymphoblastic Leukemia	8	8
Acute Undifferentiated Leukemia	9	9
Chronic Myeloid Leukemia	13	13
Chronic Lymphocytic Leukemia	12	12
Non Hodgkin Lymphoma	29	29
Hodgkin Lymphoma	18	18
TOTAL	100	100

Table 4.2. Distribution of lymphomas & leukemias according to sex

Diagnosis	Cases in males	Cases in females
AML	8	3
ALL	5	3
Undifferentiated Acute Leukemia	8	1
CML	7	6
CLL	9	3
NHL	20	9
HL	13	5
TOTAL	70	30
Percentage(%)	70%	30%

Figure 4.1. Distribution of leukemias & lymphomas according to age



- ❖ The overall sensitivity of Peripheral blood examination in diagnosis of Acute and Chronic Leukemias was 86.8%; that of BMA was 96.24% and Trephine biopsy had a sensitivity of 88.04%.
- ❖ The overall sensitivity of Bone marrow aspiration in diagnosis of infiltration of marrow by lymphoma was 75% and that of bone marrow biopsy was 100%.
- ❖ The overall positive correlation of Peripheral blood examination and Bone marrow aspiration cytology in Leukemias was 91.5%; and positive correlation between BMA and BMB examination was 92.14%.
- ❖ The overall positive correlation among Bone marrow aspiration and biopsy in diagnosing lymphoma infiltration was 87.5%

In conclusion, this study yielded some important information that Peripheral blood examination and Bone marrow aspiration are important for cytological assessment with analysis directed mainly towards morphology and obtaining a differential count, Bone marrow aspiration although yields better information in cases of pancytopenia of peripheral blood. Bone marrow trephine biopsy is slightly more painful and requires more skill to perform but is more reliable in assessing the marrow cellularity, bone marrow architectural pattern, distribution and fibrosis. Bone marrow biopsy is also diagnostic in investigation of 'Dry tap' on aspiration.

Overall, Peripheral blood examination, Bone marrow aspiration and biopsy are complementary to each other and must be performed together for better evaluation of disease under study.

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