



Original Research Article

Role of bone marrow aspiration and biopsy in evaluation of leucoerythroblastic blood picture

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ABSTRACT

Background: Leucoerythroblastosis was considered as a circulating expression of haematological and non-haematological malignancies. However many benign conditions are also associated with leucoerythroblastosis such as hemolytic anaemia, marked infections and congestive cardiac failure, etc. So the study was performed to determine the various causes of leucoerythroblastic blood picture on bone marrow examination.

Materials and Methods: The current retrospective diagnostic analytical study was performed in the hematology section of post graduate department of pathology over a period of one year. 80 patients with leucoerythroblastic picture on peripheral blood film (PBF), who were subjected to bone marrow aspiration and/or biopsy were included in the study. The findings were documented on a predefined performa and results tabulated.

Results: Majority of cases were seen in 21-30 years age group (25%) with male to female ratio of 1.1:1. Non-neoplastic disorders accounted for majority of cases (65%) while neoplastic lesions were seen in 35% cases. Megaloblastic anaemia was the commonest neo-neoplastic etiology while acute leukemia was the commonest neoplastic disorder in the present study.

Conclusions: Leucoerythroblastosis represents disordered marrow function and is reflected in PBF. Bone marrow aspiration and biopsy help in establishing early diagnosis and management of the underlying condition.

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1. Introduction

Leucoerythroblastosis refers to the presence of immature red cells and few immature cells of the myeloid series in the peripheral blood film (PBF).¹ The incidence of Leucoerythroblastosis is estimated to be around 0.33 to 0.45%.² Leucoerythroblastosis was classically known to be associated with bone marrow infiltrations and disseminated malignancy, however studies in literature have revealed various other causes associated with it.^{3,4} Leucoerythroblastic reactions are frequently caused by non malignant disorders such as hemolysis, infection,

haemorrhage, megaloblastic anemias, & combinations of infections, bleeding and hypoxia.⁵ Myelophthisis represents a form of bone marrow failure caused by replacement of haematopoietic tissue by abnormal tissue.⁶ Myelophthisic anemia may range from an overt leucoerythroblastic picture to the presence of a few tear drop-shaped cells on a PBF.⁷

Leucoerythroblastosis is a non-specific bone marrow response to a variety of disease processes. Presence of leucoerythroblastosis on PBF serves a valuable indicator of underlying disease stressing haematopoiesis or investigate further for the presence of malignancy.⁸ Currently very scare literature is available regarding etiology and pathogenesis of leucoerythroblastosis and mainly

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corresponds to case reports.⁹ Also the reports regarding the prognosis and outcome of leucoerythroblastosis in malignancies are better established, but in numerous other non-malignant diseases, the frequency and significance is still relatively unknown.⁹ So the present study was conducted to study the spectrum of various conditions presenting with leucoerythroblastosis on bone marrow.

2. Materials and Methods

This retrospective diagnostic analytical study was conducted in Department of pathology in a tertiary care institute for a period of one year. Prior approval was taken from Institutional Ethics Committee for the study. Eighty patients with leucoerythroblastic picture on PBF were included in the study. Patients with haemophilia, non-cooperative patients and already diagnosed cases were excluded from the study. The socio-demographic and clinical data pertaining to patient's age and sex were recorded from the requisition forms. The values of Hemoglobin, RBC indices, total leucocyte count and platelet count were noted and morphology of RBCs, WBCs and platelets on PBF recorded. Leucoerythroblastic reaction was diagnosed on the basis of Vaughan's original definition¹ i.e. coexistence of myeloid precursors (metamyelocytes, myelocytes, promyelocytes and myeloblasts) and erythroid precursors in the PBF. Hemoglobin electrophoresis was also performed in suspected patients of thalassemia.

Routine protocol followed in our Department for the bone marrow examination was also adopted for the present study. Skin overlying the posterior superior iliac spine was cleaned by betadine and alcohol swab and infiltrated with local anaesthetic. Bone marrow aspiration was done using a Salah's needle attached to a 10 ml syringe with holder. The aspirated material was collected on to clean glass slides. Air-dried aspiration smears were stained with MGG stain and perl's stain for iron. Trepchine Biopsy was performed using a Jamshidi's needle and imprint smears were prepared before putting sample in 10% formalin. Descriptive data was presented in the form of percentages and proportions and tabulated.

3. Results

Eighty patients who presented with leucoerythroblastic picture in the peripheral blood smear and underwent bone marrow examination were evaluated. Age range of the patients varied from 1-85 years. Maximum cases were seen in 21-30 years age group followed by 41-50 years (Table 1). Amongst them, 42 patients were males & 38 patients were females with Male to female ratio of 1.1:1.

Majority of the cases with leucoerythroblastosis had erythroid hyperplasia on bone marrow examination (67.5%). Depressed erythropoiesis was seen in 32.5% cases. Non-neoplastic conditions were seen in 65% cases

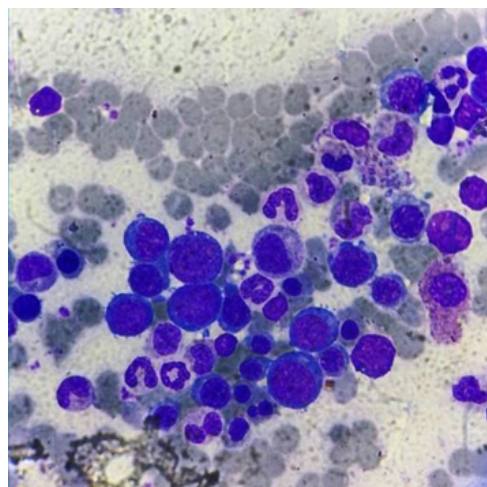


Fig. 1: Megaloblastic anemia: Bone marrow aspiration smear showing early and intermediate megaloblasts with sieve like chromatin (Giemsa stain; x100).

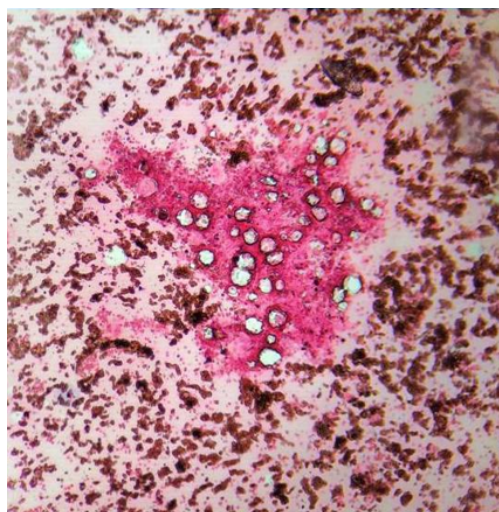


Fig. 2: Dual deficiency anemia: Iron grade 0 in a case of dual deficiency anemia (Perl's stain; x20).

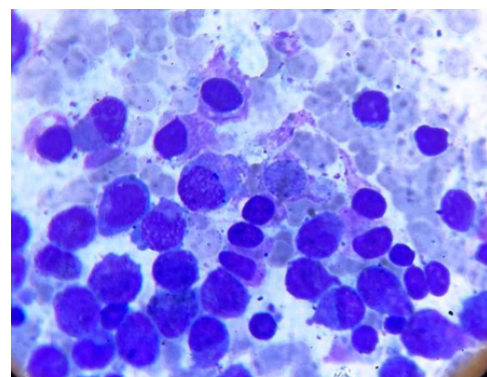


Fig. 3: Acute leukemia: Bone marrow aspiration smear showing numerous myeloblasts (Giemsa stain; x100).

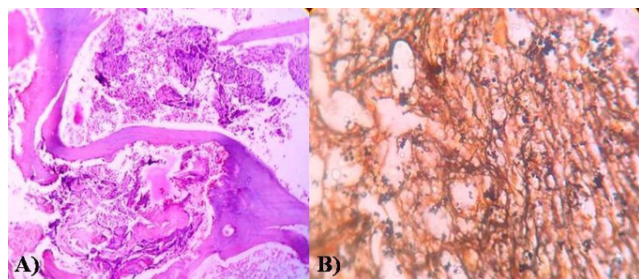


Fig. 4: Myelofibrosis; **A):** Trephine biopsy showing evidence of marrow fibrosis (H&E stain; x40). **B):** Reticulin Grade 2 in the same case (Reticulin; x40).

Table 1: Age distribution of 80 patients with leucoerythroblastosis on PBF

Age in Years	No of Patients	Percentage
0-10	14	17.5
11-20	12	15
21-30	20	25
31-40	8	10
41-50	13	16.25
51-60	4	5
61-70	5	6.25
71-80	3	3.75
>80	1	1.25

Table 2: Bone marrow diagnosis of the haematological disorders presenting with leucoerythroblastosis (n=80)

Diagnosis	Number	Percentage	
Megaloblastic Anaemia	21	26.25	
Non-neoplastic (52)	Dual Deficiency	11	13.75
	Infections	11	13.75
	Bleeding	6	7.5
	Thalassemia	2	2.5
	Gaucher’s Disease	1	1.25
Neoplastic (28)	Leukemia A) Acute	10	12.5
	Leukemia B) Chronic	2	2.5
	Myeloid Leukemia		
	Multiple Myeloma	6	7.5
	Metastasis	5	6.25
	Myelofibrosis	3	3.75
	Myelodysplastic Syndrome	2	2.5
Total	80	100	

Table 3: Comparative spectrum of non-infiltrating and infiltrating conditions presenting with leucoerythroblastosis

Diagnosis	Our study	Shubha HV et al ⁹	Burkett LL et al ⁵
Non-Infiltrative			
Megaloblastic Anaemia	21	21	8
Dual Deficiency	11	0	10
Infections	11	2	8
Bleeding	6	1	5
Thalassemia/Hemolytic Anaemia	2	2	11
Infiltrative			
Leukemia	12	4	18
Multiple Myeloma	6	3	4
Metastasis	5	1	8
Myelofibrosis	3	4	6
Gaucher’s Disease	1	-	-
Lymphoma	-	2	6

while neoplastic lesions were seen in 35% cases on bone marrow examination (Table 2). Dry tap on bone marrow aspiration was seen in 6 cases, including 3 cases of myelofibrosis, 2 cases of Acute Myeloid Leukemia and 1 case of multiple myeloma. In these cases, cellularity was assessed on trephine biopsy and final diagnosis made. Trephine biopsy was also performed in 10 other cases of neoplastic disorders, including leukemias.

Megaloblastic anaemia (Figure 1) was the commonest cause of leucoerythroblastosis and was observed in 26.25% cases (Table 2). Leukemias (Figure 2) were the second commonest cause of leucoerythroblastosis (15%) followed by Dual deficiency (Figure 3) and infections (13.75% each). Other disorders observed in our study are summarised in Table 2. Comparative Spectrum of non-infiltrating and infiltrating conditions presenting with leucoerythroblastosis is described in Table 3.

4. Discussion

Leucoerythroblastosis is a manifestation of extramedullary hematopoiesis.⁹ Leucoerythroblastosis was originally defined by Vaughn as anemia characterized by the presence of immature red cells and few immature myeloid cells in the peripheral blood.¹ However Wintrobe, after 37 years, suggested that anemia can be replaced from the definition as it is not always present.¹⁰ Leucoerythroblastosis is associated with malignancies and metastatic disease and is frequently seen in non malignant disorders such as hemolysis, infection, haemorrhage, megaloblastic anemias, & combinations of infections, bleeding and hypoxia.⁵ Leucoerythroblastosis is occasionally also seen in congestive heart failure.⁹ Recently, Leucoerythroblastosis has also been associated with SARS-CoV-2 infection.^{11,12}

Common mechanism exists in all the conditions leading to Leucoerythroblastosis: presence of stress or damage to the marrow and the evolution of areas of extramedullary hematopoiesis, where a well organised sinusoidal structure may not exist and the physiologic and physical barriers restraining immature cells may not be effective as in the marrow.⁸ Though little is known about the premature release of immature cells in pathologic states, it has been reported that leucoerythroblastosis is more common when fibrosis accompanies tumour in the bone marrow.¹¹ Bone marrow examination is the most important diagnostic test to establish the correct diagnosis in presence of leucoerythroblastic blood picture on PBF.² The indications for bone marrow examination include determining marrow involvement and infiltration associated with hematologic and solid malignancies.⁹ In one series with 90 patients undergoing bone marrow procedures, 16 patients presented with metastatic non-hematologic malignancies and leucoerythroblastosis was seen in 43.75% of the latter.¹²

In this study, maximum number of cases was seen in 21-30 years age group with male to female ratio of 1.1:1. Shubha HV et al¹³ and Waghmare T et al¹⁴ also observed maximum cases in 3rd decade in their study with no significant sex distribution. On Bone marrow examination, non-neoplastic conditions were seen in 65% cases while neoplastic lesions were seen in 35% cases (Table 2). Megaloblastic anaemia was the commonest disorder seen in our study (26.25%) followed by leukemias. The results were similar to that observed by Shubha HV et al.¹³

Wide spectrum of non-infiltrative and infiltrative marrow disorders were observed in our study (Table 3). Non infiltrative conditions were seen in 63.75% cases while infiltrative diseases were seen in 36.265% cases (Table 1). Shubha HV et al¹¹ observed non infiltrative and infiltrative conditions in 52% and 48% patients in their study. In study by Burkitt LL et al,⁵ non infiltrative conditions were seen in 40% cases, infiltrative conditions in 44.8% cases and bone marrow infiltrative disorders complicated by another condition which might have produced the leucoerythroblastosis in 15.2% cases. In a study by Makoni SN et al,⁶ 1/3rd patients with leucoerythroblastosis on PBF had underlying malignancy.

Dry tap was observed in 6 cases in our study which were subjected to biopsy for further evaluation. These included 3 cases of myelofibrosis (Figure 4), 2 cases of Acute Myeloid Leukemia and 1 case of multiple myeloma. Humphries JE et al¹⁵ in their study observed 87 cases of dry tap on marrow aspiration that showed significant pathology on trephine biopsies. Sitalakshmi S et al¹⁶ in their study observed dry tap on aspiration in 33 out of 176 patients of myelofibrosis. Bone marrow biopsy in myelofibrosis revealed mixed granulocytic and megakaryocytic proliferation, a reduction of erythroid precursors & significant megakaryocytic abnormalities.^{17,18}

Our study had few limitations. First it was a retrospective study. Secondly immunophenotyping and molecular analysis was not available in cases of leukemias. So more such studies should be carried out in future to further substantiate the results obtained in our study.

5. Conclusions

Available literature on leucoerythroblastosis is scarce and not widely available. Wide spectrum of haematological disorders present with leucoerythroblastic blood picture on PBF. Evidence of leucoerythroblastosis in peripheral smear provides an invaluable clue to the presence of an underlying serious condition. Presence of leucoerythroblastosis in malignancies is an indicator of disease progression and associated with adverse prognosis and poor survival. Bone marrow examination is paramount to determine the cause & analyze the frequency of various conditions presenting with leucoerythroblastosis. Patient's clinical and haematological profile along with bone marrow examination helps in establishing an early definitive diagnosis and better management.

6. Conflict of Interest

The authors declare that they have no conflict of interest.

7. Source of Funding

None.

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