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Evaluation of Peripheral Blood Smearand Bone Marrow Findings in Cases of Pancytopenia

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Abstract: ***Background*: Pancytopenia is the reduction in all three major formed blood elements; erythrocytes, leucocytes, and platelets. The severity of pancytopenia and the underlying pathology determines the management and prognosis. The present study was done to evaluate the peripheral blood film and bone marrow findings in cases of pancytopenia. *Materials and methods*: Out of 245 bone marrow studies done during the study period of 2 years (August 2020 to July 2022), 55 patients who presented with pancytopenia were included in the study. The clinical findings were taken from the hospital's clinical records. Complete blood picture bone marrow aspiration and biopsy findings were retrieved from the data available and recorded. The available smears and histopathology sections were examined as and when required. *Results*: Among 55 patients studied, 32% of cases were seen in the age group of 41–60 years with male predominance (M/F 1.6: 1). The most common cause of pancytopenia was megaloblastic anemia (23.7%) followed by aplastic anemia (14.5%). Hematological malignancies though accounted for (21.8%) which included already diagnosed and treated cases and only 5 cases (9.1%) were diagnosed for the first time. *Conclusion*: The complete blood picture and bone marrow findings provide valuable information for diagnosing and managing pancytopenia patients.***

Keywords: Pancytopenia; Megaloblastic Anemia; Bone marrow examination

1. Introduction

Pancytopenia is an important clinico-hematological entity withthe simultaneous presence of anemia, leucopenia, and thrombocytopenia.1Pancytopenia in adults is defined as hemoglobin level<13.5 g/ in males and <11.5 g/dl in females, leucocyte count < 4 x 10^9 /land platelet count <1.5 lakh/dl.2The etiology of pancytopenia varies with geographical distribution, mutations, and genetic predisposition. It can range from non - neoplastic conditions like megaloblastic anemia to neoplastic conditions like myelodysplastic syndromes. A reduction in cell number occurs due to increased destruction, reduced production, or increased pooling in the spleen or other organs.2

Pancytopenia develops due to a decrease in hematopoietic cell production as a result of the destruction of marrow by toxins or suppressed normal marrow growth and differentiation.3Others include ineffective hematopoiesis resulting in cell death in the marrow, sequestration of cells by the action of antibodies, and trapping of normal cells in an overactive reticuloendothelial system.3The diseases leading to pancytopenia vary according to age pattern, nutritional status, and prevalence of infective disorders. Common clinical presentation includes fatigue, pallor, organomegaly, bleeding manifestations, and weight loss. Anemia and thrombocytopenia are the presenting symptoms in most cases whereas leucopenia is uncommon at the initial stages of presentation, but can become a life threat during the course of the illness.4A spectrum of primary or secondary disorders that affect bone marrow may manifest with pancytopenia.5

A complete hematological workup along with clinical correlation is important to evaluate a case of pancytopenia. Integration of peripheral blood findings and bone marrow examination along with supplementary tests like immunophenotyping and cytogenetic analysis is necessary for making an appropriate diagnosis and for planning further treatment.6 Bone marrow examination is extremely useful in the evaluation of pancytopenia. It is indicated in all cases of pancytopenia especially needed in cases of hypoplasia, to exclude leukemias or other malignant infiltration.8It can be easily performed during severe thrombocytopenia without any risk of bleeding. Trephine biopsy is usually done for evaluation of aplasia or hypoplasia on aspiration.9The findings of the study will help in planning the diagnostic and therapeutic approach in cases of pancytopenia.

Aims and objectives

To study the clinical presentation and various causes of pancytopenia and to evaluate the peripheral blood film and bone marrow findings in cases of pancytopenia.

2. Materials and Methods

The present study was aretrospective observational study conducted in the Department of Pathology, GSL Medical College, Rajamahendravaram, Andhra Pradesh over a period of 2 years (August 2020 to July 2022). A total of 245 bone marrow studies were conducted during the given period and patients of all age groups who were found to have pancytopenia on peripheral blood smear were included in the study. A total of 55 cases were included. Patient data were retrieved from the hospital records including age, gender, clinical findings, complete blood picture, and bone marrow findings, and recorded. Bone marrow aspiration was done using the Salah needle. A total of 17 patients underwent a biopsy using a Jamshidi needle. Slides were stained with Leishman and H &E stains. Reticulin stain and Pearl's stain were done when indicated.

3. Results

Out of 245 bone marrow examinations performed for various indications, 55 cases presented with pancytopenia were studied. They constituted 34 males and 21 females with a male preponderance having an M: F ratio of 1.6: 1. The youngest patient was 4 years old and the oldest was 75 years old with a mean age of 40 years. The maximum number of cases was seen in the age group of 41-60 years (32%) followed by 21-40 years (30%). Sex-wise distribution and Age-wise distribution were shown in Figure 1 and Figure 2 respectively.

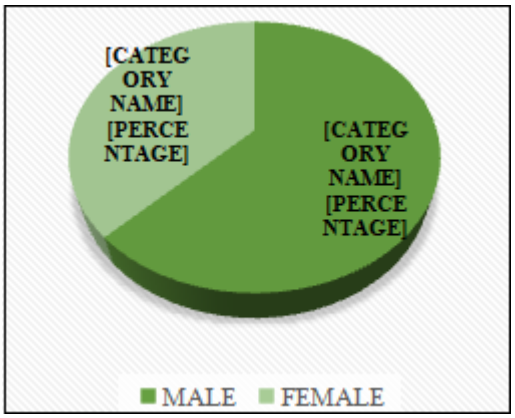

Figure 1: Sex-wise Distribution

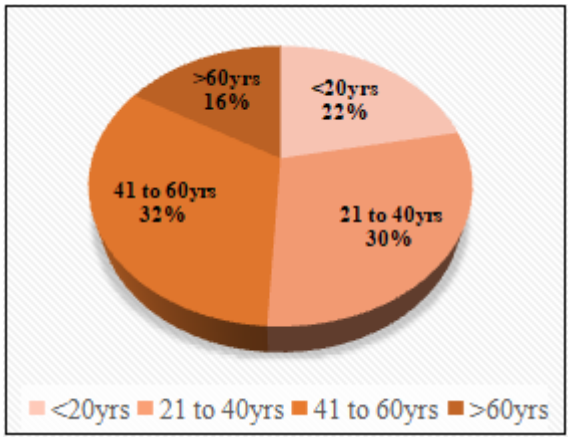

Figure 2: Age-wise Distribution

The clinical features of the patients presenting with pancytopenia were shown in Table 1. The most common clinical presentation was generalized weakness (62.2%), followed by fever (44.4%) and shortness of breath (33.3%). In this study, on examination splenomegaly (26.7%) was the most common finding followed by pallor with (15.5%). Others symptoms were hepatomegaly and bleeding tendencies.

Table 1: Clinical features at presentation

S. No	Clinical findings	No. of cases	Percentage
1	Weakness	28	62.2%
2	Fever	20	44.4%
3	Shortness of breath	15	33.3%
4	Splenomegaly	12	26.7%
5	Pallor	7	15.5%
6	Bleeding tendencies	5	11.1%
7	Hepatomegaly	5	11.1%

The peripheral smear findings were shown in Table 2. The predominant blood picture findingswere normocytic picture (52.8%) followed by a microcytic picture (23.6%) and a macrocytic picture (16.3%).7.3% of cases had a dimorphic picture and (17.1%) of cases had hyper - segmented neutrophils. Hypersegmented neutrophils were seen in 69.2% (9 out of 13 cases) of megaloblastic anemia cases. Circulating blasts are seen in 9% (5) cases, which were diagnosed as acute leukemia.

Table 2: Peripheral smear findings

S. No	Findings	No. of cases	Percentage
1	Normocytic	29	52.8%
2	Microcytic	13	23.6%
3	Macrocytic	09	16.3%
4	Dimorphic Picture	04	7.3%

Table 3: Haematological disorders behind pancytopenia blood picture

S. No	Disorders	No. of cases	Percentage
1	Megaloblastic Anemia	13	23.7%
2	Aplastic Anemia	8	14.5%
3	Acute Leukemia	5	10.9%
4	Erythroid Hyperplasia with Megaloblastoid change	8	14.5%
5	Drug - induced pancytopenia	7	12.7%
6	Hypersplenism	3	5.5%
7	Others	11	20%
	Total	55	100%

Bone marrow was hypercellular in 38.2% of cases, hypocellular in 34.5% and 27.3% had normocellular marrow. The most common marrow finding was megaloblastoid erythroid hyperplasia seen in 16 out of 55 cases (29%). Out of 55 cases, the commonest cause of pancytopenia was megaloblastic anemia accounting for 13 cases (23.7 %) followed by aplastic anemiawith 8 cases (14.5%) and acute leukemia with 5 cases (9.1%) Haematological malignancies account for 12 cases (21.8%). These include chemotherapy - induced pancytopenia 7 cases (12.7%) and 5 (9.1%) newly diagnosed cases of acute leukemia, confirmed by immunophenotyping. Three cases of hypersplenism constitute 5.5% of cases. Bone marrow biopsy was done in 17 cases.7 cases of megaloblastic anemia, 2 cases of erythroid hyperplasia, and 8 cases of aplastic anemia where the biopsy was performed, the diagnosis was found to be consistent with aspiration. In two cases where aspiration was dry tap, the biopsy was performed and diagnosed as acute leukemia.

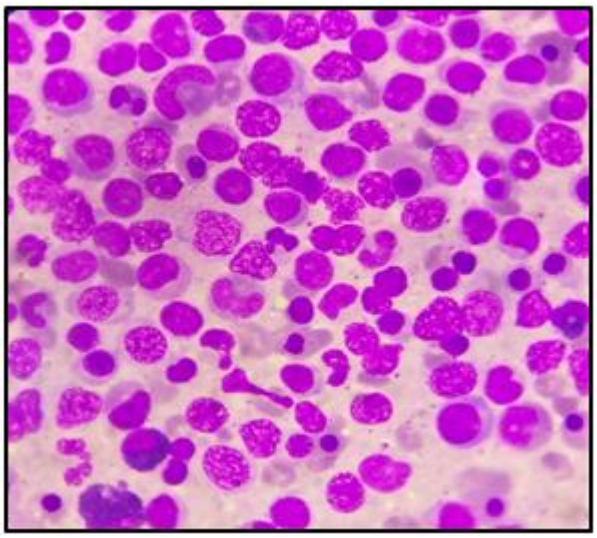

Figure 3: Bone marrow aspiration showing erythroid hyperplasia (1000x, Leishman stain)

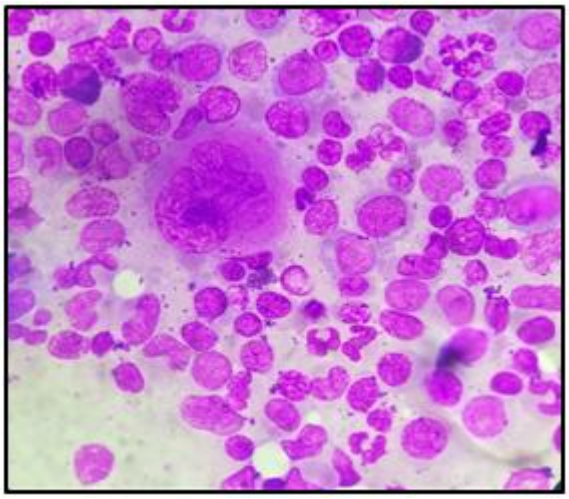

Figure 4: Bone marrow aspiration showing megaloblastic anemia (1000x, Leishman stain)

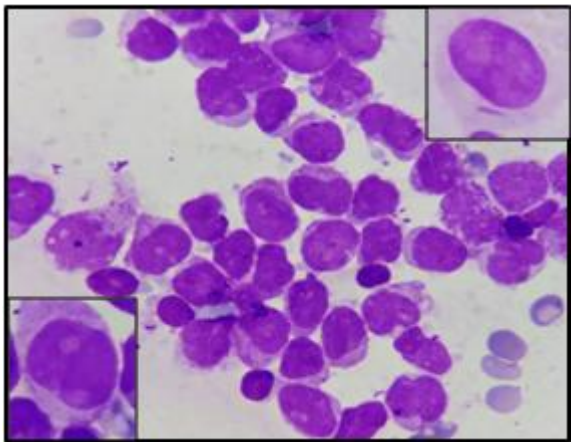

Figure 5: Bone marrow aspiration of AML (M3) Showing Auer Rods (1000x, Leishman stain)

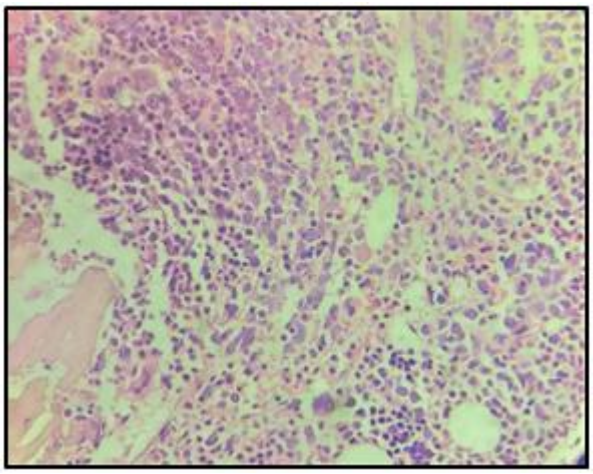

Figure 6: Bone marrow biopsy showing Hypercellular Marrow (400x, H&E stain)

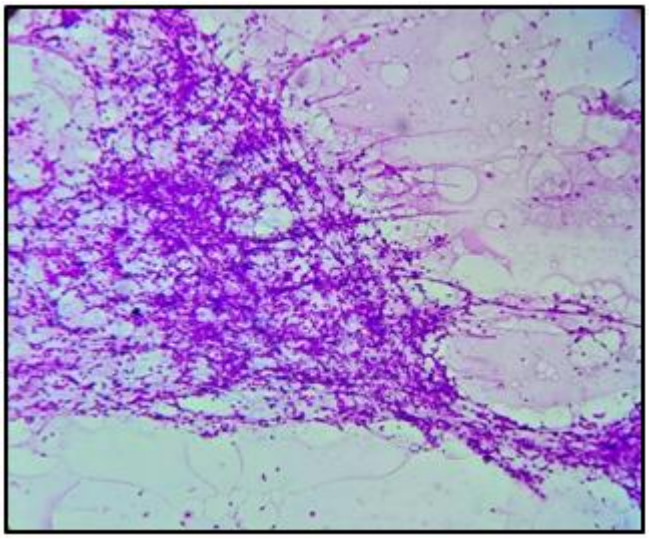

Figure 7: Bone marrow aspiration of Aplastic Anemia (400x, Leishman stain)

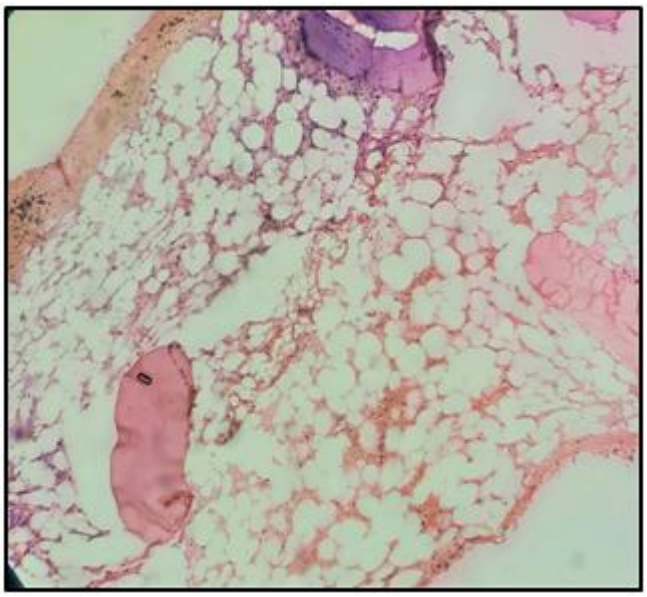

Figure 8: Bone marrow biopsy of Aplastic Anemia showing paucity of hematopoietic stem cells and marrow largely replaced by fat cells (400x, H&E stain)

4. Discussion

Pancytopenia is a common finding with variable clinical presentations such as unexplained pallor, prolonged fever, and a tendency to bleed. Diagnosis and accurate etiology are necessary for the management of the patient. Patients are subjected to peripheral blood film examination and bone marrow examination. A total of 55 cases of pancytopenia were studied. The majority of the study population was from the age group of 41-60 years with male preponderance.

In this study, the most common presentation was a generalized weakness which included 62.8% of the patients and similar observations were made by Sahay et al[1] and Gayatri et al[10]. The age of the patients ranged from 4 to 75 years with a mean age of 40 years. These findings were compared with other studies (Table 4). The male predominance observed in this study was reported by many other similar studies.

Table 4: Comparison of age and sex distribution

Authors	Age range	M: F
Sahay et al[1]	15 - 83yrs	1.02: 1
Gayatri et al[10]	2 - 80yrs	1.2: 1
Shah et al1[11]	4 - 75yrs	1.1: 1
Present study	4 - 75yrs	1.6: 1

The predominant blood picture was normocytic in 29 patients (52.8%) followed by microcytic in 13 patients (23.6%1) and macrocytic in 9 patients (16.3%). The study conducted by Patel et al[12] showed similar findings with a normocytic picture as the predominant picture but the second most dimorphic picture which was in contrast to the present study.

In this study, the maximum number of patients i. e.21 (38.2%) showed hypercellular bone marrow followed by hypocellular in 19 patients (34.5%). Bone marrow was normocellular in 27.3% of patients similar to the study conducted by Sharma A et al [13] which reported normocellular marrow in 24% of patients. Normal bone marrow can be seen in pancytopenia patients as a result of the sequestration or destruction of normal cells by the action of antibodies or trapping of normal cells in a hypertrophied and over - reactive reticuloendothelial system.3Erythroid hyperplasia is a common finding in bone marrow accounting for 32.7% of total cases. This is contrary to the study conducted by Raina JS et al[8] which constituted about 76.67% of cases.

Megaloblastic anemia is the most common cause of pancytopenia in the present study (23.7%) similar to the study by Vaidya et al[14] (34.9%) and Shah et al[11] (32%). Hypersegmented neutrophils were seen in 69.2% (9 out of 13 cases) of megaloblastic anemia cases similar to the findings reported by Raina JS et al[8] constituting 76% of megaloblastic anemia cases. The second most common cause of pancytopenia in the present study was aplastic anemia constituting about 14.5% of total cases similar to the study by Khodke et al[7] and Shah et al[11].

Table 5: Comparison of causes of pancytopenia

Study	Year	Cases	Commonest cause	Second most common cause
Khodke et al[7]	2000	50	Megaloblastic anemia (44%)	Aplastic anemia (14%)
Gayatri et al[10]	2011	104	Megaloblastic anemia (74.0%)	Aplastic anemia (18.3%)
Vidya S et al[14]	2015	83	Megaloblastic anemia (34.94%)	Aplastic anemia (31.32%)
Bahal N et al[15]	2016	129	Megaloblastic anemia (37%)	Hematological malignancy (21%)
Sahay et al [1]	2018	85	Combined deficiency anemia (51.8%)	Megaloblastic anemia (31.8%)
Shah et al [11]	2020	145	Megaloblastic anemia (32%)	Hypoplastic marrow (16%)
Present Study	2022	55	Megaloblastic anemia (23.7%)	Aplastic anemia (14.5%)

Acute leukemia was the most commonest hematological malignancy accounting for 5 out of 12 cases (41.67%) and 9.1% of total cases which showed similar findings in studies conducted by Agarwal et al[2] and Vaidya Set al[14]with 11.25% and 9.64% of total cases respectively. Hypersplenism shows peripheral pooling of cells with destruction in the enlarged spleen resulting in pancytopenia and splenomegaly. The present study had three cases (3 cases; 5.5%) of congestive splenomegaly presented with pancytopenia compared to the study by Shah et al[11] which reported 2 cases (1%).

5. Conclusion

In the present study, the major diagnostic consideration of pancytopenia was megaloblastic anemia followed by hematological malignancies with acute leukemia, being the most common malignancy and aplastic anemia. Bone marrow aspiration and biopsy complement each other. Bone marrow aspiration and biopsy is an established diagnostic modality in the evaluation of pancytopenia. The complete blood picture and bone marrow findings provided valuable information in diagnosing and managing patients with pancytopenia. Megaloblastic anemia can be prevented by improving the socioeconomic and nutritional status of our population.

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