Original Research Article

Clino-hematological Evaluation and Correlation with Bone Marrow Examination in Cases of Pancytopenia in Tertiary Health Care Center

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Abstract

Introduction: Pancytopenia is a relatively common hematological entity. It is a striking feature of many serious and life threatening illnesses, ranging from simple drug-induced bone marrow hypoplasia, megaloblastic anemia to fatal bone marrow aplasias and leukemias. The severity of pancytopenia and the underlying pathology determine the management and prognosis. Thus, identification of the correct cause will help in implementing appropriate therapy.

Aim and objectives: To study the clinical presentations in pancytopenia due to various causes; and to evaluate haematological parameters, including bone marrow aspiration.

Materials and methods: In this study, a total 50 patients presenting with pancytopenia on initial work up requiring bone marrow examination were studied along with their relevant clinical history, examination findings and routine haematological findings.

Results: Among 50 cases studied, age of patients ranged from 10 to 70 years with a most common age group of 35-45 years and male predominance. Most of the patients presented with generalized weakness and fever. The commonest physical finding was pallor, followed by splenomegaly and hepatomegaly. Dimorphic anemia was the predominant blood picture. Bone marrow aspiration was conclusive in all cases. The commonest marrow finding was hypercellularity with megaloblastic erythropoiesis. The commonest cause for pancytopenia was megaloblastic anemia (80.4%), followed by sub/aleukemic anemia (8.2%).

Conclusion: The present study concluded that detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding disease process and to diagnose or to rule out the causes of cytopenia. These are also helpful in planning further investigations and management.

Key words

Bone Marrow Examination, Megaloblastic Anemia, Pancytopenia, Sub/aleukemic Leukemia.

Introduction

Pancytopenia is an important clinicohematological entity encountered in our day-to-day clinical practice. There are varying trends in its clinical pattern, treatment modalities, and outcome [1]. It is not a disease entity but a triad of findings that may result from a number of disease processes – primarily or secondarily involving the bone marrow [2]. Pancytopenia is a triad of findings characterized by reduction in all three major formed elements of blood erythrocytes, leucocytes, platelets below their reference values [3].

The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients [4]. In India, the causes of pancytopenia are not well defined, so the present study has been undertaken to evaluate the various causes and to correlate the peripheral blood findings with bone marrow aspirate [4, 5]. Thereby, this data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

Materials and methods

The study was carried out in Geetanjali Hopsital and Medical College, Udaipur, Rajasthan over a period of one year. Patients of all age groups and both sexes were included. A total of 50 cases were selected based on clinical features and supported by laboratory evidence, which include complete blood count and peripheral blood smear.

Inclusion criteria were presence of all 3 of the following: hemoglobin, <9 g/dL; total leukocyte count (TLC), <4,000/μL; platelet count, <100,000/ μL [5].

Exclusion criteria

- Patients on myelotoxic chemotherapy and radiotherapy were excluded from study.
- Follow up cases of leukemia and pregnant women were excluded from study.
- Patients who had recently received blood transfusion were excluded from study.
- Patients who had not given consent for bone marrow examination were excluded from study.
- Already diagnosed cases of pancytopenia who were taking treatment, excluded from study.

Bone marrow aspiration was done from posterior superior iliac spine using Salah bone marrow aspiration needle. Simultaneously, from same puncture site but from a different plane, bone marrow biopsy was done using Jamshidi needle, taking all aseptic precautions and consent. Peripheral blood smear and bone marrow aspirate smear were stained by Leishman Stain and trephine biopsy were processed and stained by hematoxylin and eosin stain.

Results

A total of 50 patients presented with pancytopenia and indicated for bone marrow examination during study period were studied. The study showed male predominance with 64.2 % cases in comparison with female cases which were 35.8 % (**Graph - 1**). The age of patients ranged from 10 to 70 years with a most common age group of 35-45 years. The commonest presenting complaints and physical findings in pancytopenia cases were shown in **Table - 1**.

Table - 1: Presenting complaints in cases of pancytopenia.

Presenting complaints	No. of cases out of total (n=50)	% of cases
Pallor	10	20
Fever	8	16
Generalised weakness	17	34
Hepatosplenomegaly	4	8
Dyspnoea	3	6
Jaundice	5	10
Lymphadenopathy	1	2
Weight loss	2	4

Graph - 1: Gender Distribution.

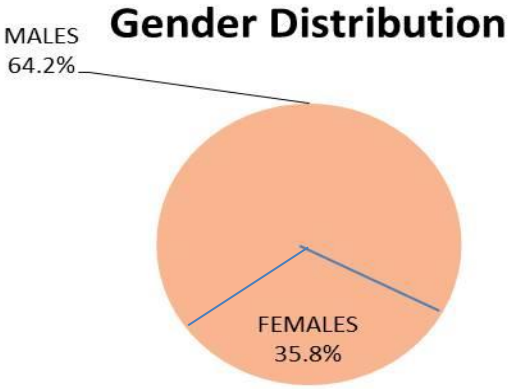
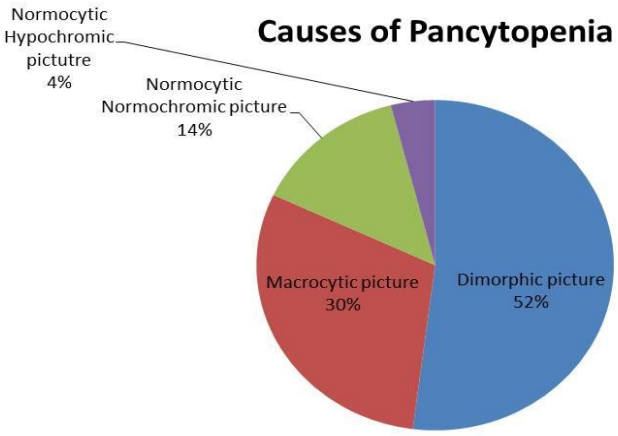


Table - 2: Causes of Pancytopenia.

Causes of Pancytopenia	No. of cases	%
Megaloblastic anemia	33	66
Sub/aleukemic leukemia	11	22
Aplastic anemia	2	4
Malaria	3	6
NHL	1	2
Total	50	100

Graph - 2: Causes of pancytopenia.



Graph - 3: Peripheral blood smear findings.

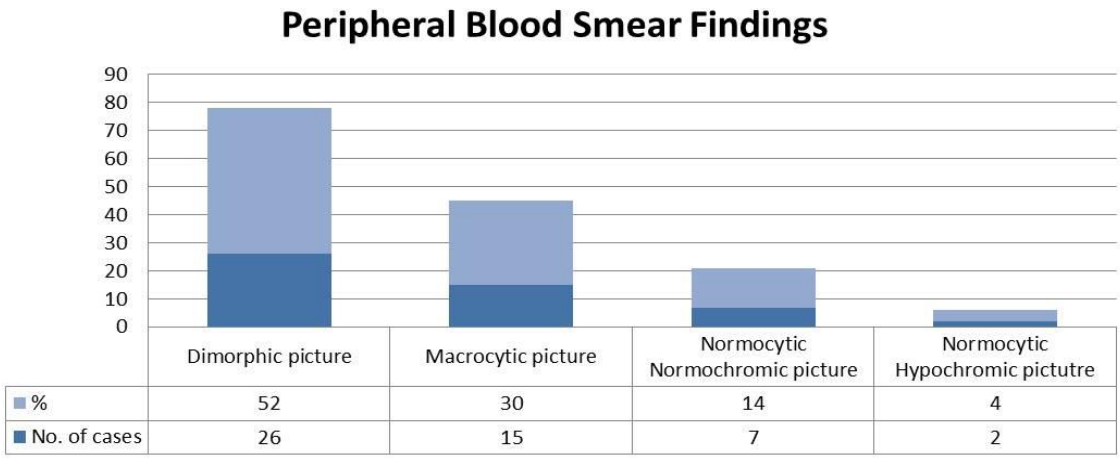


Table - 3: Bone marrow microscopic examination findings.

Bone Marrow Aspiration and Biopsy Findings	No. of cases out of total (n=47)	%
Megaloblastic erythroid hyperplasia	26	52
Normoblastic erythroid hyperplasia	5	10
Normoblastic bone marrow with megaloblastoid changes	9	18
Acute Myeloid leukemia	2	4
Hypocellular marrow with fatty replacement	2	4
Sub/Aleukemic leukemia	3	6

The commonest mode of presentation was generalized weakness (34%) and pallor (20%), followed by fever (16%) and jaundice (10%). Hepatosplenomegaly (8%) were seen mostly in cases of megaloblastic anemia followed by sub/aleukemic leukemia and malaria.

Table - 2 and **Graph - 2** showed the causes of pancytopenia in the study. The commonest cause of pancytopenia was megaloblastic anemia (66%) followed by sub/aleukemic leukemia (22%), malaria (6%), aplastic anemia (4%) and non-hodgkin's lymphoma (2%).

Graph - 3 showed predominant blood picture was dimorphic anemia (52%), followed by macrocytic anemia (13%); peripheral smear showed macro-ovalocytes with hypersegmented neutrophils. Normocytic normochromic anemia constituted 14% of the cases; and normocytic hypochromic anemia 4%. Leucopenia and thrombocytopenia were seen in all cases.

Out of 50 cases, exact cause of pancytopenia was evaluated on the basis of bone marrow microscopic examination in 47 cases. This distribution was shown in **Table - 3**. Most of the bone marrow was hypercellular 53.2%, followed by normocellular 44.5% and hypocellular 2.3%. In megaloblastic anemia, bone marrow was hypercellular in 61.2% cases followed by normocellular marrow 38.8%.

Discussion

Pancytopenia is a common hematological finding with variable clinical presentations. It often creates diagnostic challenge to physician and the knowledge of accurate etiology of this condition is crucial in the management of the patient [6]. 50 cases of pancytopenia were studied regarding age, gender wise distribution, presenting complaints, peripheral smear examination, bone marrow microscopic examination findings and final various causes of pancytopenia were evaluated and the results were compared with previous similar studies done in India and abroad (**Table - 4**).

Table - 4: Comparison of pancytopenia in various studies.

Study	Country	No. of cases of pancytopenia	Commonest cause	Second most common cause
Keisu M, et al. [7] (1990)	Israel and Europe	100	Neoplastic diseases and radiation (32%)	Hypoplastic anemia (19%)
Tilak, et al. [8] (1999)	Chandigarh, India	77	Megaloblastic anemia (68%)	Aplstic anemia (7.70%)
Kumar, et al. [5] (2001)	India	166	Aplastic anemia (29.5%)	Megaloblastic anemia (22.3%)
Khunger, et al. [9] (2002)	New Delhi, India	200	Megaloblastic anemia (72%)	Aplastic anemia (14%)
Gayathri and Rao, et al. [10] (2011)	Karnataka, India	104	Megaloblastic anemia (74.04%)	Aplastic anemia (18.26%)
Jha A, et al. [6] (2012)	Nepal	102	Hypoplastic anemia (29.05%)	Megaloblastic anemia (23.64%)
Chandra K, et al. [11] (2014)	India	83	Megaloblastic anemia (25.03%)	Sub/aleukemic leukemia (15.67%)
Bahal D, et al. [12] (2016)	Deharadun, India	60	Megaloblastic anemia (46.66%)	Sub/aleukemic leukemia (20%)
Mallik, et al. [13] (2016)	Bihar, India	1318	Megaloblastic anemia (31.9%)	Sub/aleukemic leukemia (30.5%)
Singhal, et al. [14] (2019)	Rajasthan, India	60	Megaloblastic anemia (62.79%)	Sub/aleukemic leukemia (25.57%)
Present study	Rajasthan, India	50	Megaloblastic anemia (66%)	Sub/Aleukemic leukemia (22%)

Most studies conducted in India have also reported megaloblastic anemia as a major cause of pancytopenia similar to this study. Higher incidence of megaloblastic anemia in Indian subcontinent can be attributed to low socioeconomic status, poor hygiene, inadequate nutrition and some cultural taboos. Pancytopenia related to Non-Hodgkins Lymphoma was noted in 2% of our cases which was comparable to the study done by Santra and Das [15] who also described 1 case (0.90%) of NHL presenting with pancytopenia which was diagnosed by bone marrow examination. Jain and Naniwadekar [16] reported 5 cases (11.9%) of pancytopenia related to NHL in their study. The higher incidence of sub/aleukemic leukemia in this study can be attributed to the inclusion of referred and high risk cases in the study, as the study center is a tertiary care hospital. In this study, malaria (6%) is also the cause of pancytopenia which was similar with Gayathri and Rao [10] who reported an incidence of 1.9% of the cases of malaria in their study. Jain and Naniwadekar [16] reported an incidence of 20.5% cases of malaria out of the total pancytopenia cases. Malaria related cytopenias was also noted in studies done by Cannard, et al. [17] in (2%) cases and Albaker [18] one case. Santra and Das [15] reported two cases (1.8%) of pancytopenia due to malaria in their study.

The wide variation in incidence of causes of pancytopenia in different studies published from India as well as other countries can be attributed to the differences in methodology, selection of diagnostic criteria, nutritional status, prevalence of infective disorders and genetic differences in the population as well as varying exposure to myelotoxic agents. Predominant blood picture was dimorphic anemia 52% on peripheral blood smear which is comparable to Gayateri and Rao, et al. [10]. The commonest physical findings

were generalized weakness (34%), pallor (20%), followed by fever (16%) and jaundice (10%). Hepatosplenomegaly (8%) were seen mostly in cases of megaloblastic anemia followed by sub/aleukemic leukemia and malaria. Similar clinical findings have been reported in other studies, although their frequency varies. The differences in the frequency of clinical features can be attributed to geographic variations, genetic make-up of the patients and the hematological parameter being predominantly affected in pancytopenia cases. As the reliability of bone marrow biopsy in assessing cellularity of bone marrow is more than bone marrow aspiration, marrow cellularity was evaluated only in cases where bone marrow aspiration and biopsy both were available after comparing them. There is variation in results regarding marrow cellularity in different studies, as bone marrow cellularity depends upon cause of pancytopenia and extend of bone marrow involvement by that cause. The causes of pancytopenia were treatable in 70% of the patients, who fully recovered from cytopenia. Death occurred in 20% of the cases, which was due to severe pancytopenia and overwhelming infections.

Conclusion

Pancytopenia is a relatively common hematological entity. It is a striking feature of many serious and life threatening illnesses, ranging from megaloblastic anemia to fatal bone marrow aplasias and leukemias. The present study concludes that detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding disease process and to diagnose or to rule out the causes of cytopenia. These are also helpful in planning further investigations and management.

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