Original Article

Role of Bone Marrow Profile in Cytopenias

Neelima Bahal, Brijesh Thakur, Aparna Bhardwaj*, Sandip Kudesia, Seema Acharya and Sanjeev Kishore

Department of Pathology, SGRR Institute of Medical & Health Sciences, Patel Nagar, Dehradun, India

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ABSTRACT

Background: Cytopenia occurs usually due to some underlying haematological medical disorder. There is a long list of causes for pancytopenia and bicytopenia. Bone marrow examination is an effective way of evaluating various causes of cytopenia.

Method: Relevant clinical history and examination findings along with routine hematological, serological and biochemical investigations were recorded in all included 129 cases. Bone marrow aspiration smears and biopsy slides were studied. Special stains like Reticulin, PAS, Perl's stain were used when required.

Results: Megaloblastic anemia was the commonest cause of pancytopenia as well as bicytopenia. Other significant causes were leukemia, lymphoproliferative disorders, hypoplastic marrow and metastatic lesions.

Conclusion: Both bone marrow aspiration and biopsy are complementary to each other to give the correct diagnosis.

***Corresponding author:**
Dr. Aparna Bhardwaj, Professor, Department of Pathology, SGRR Institute of Medical & Health Sciences, Patel Nagar, Dehradun, India- 248001.
Phone: +91 9411718270, 11 352760439
Email: aparnapande1977@gmail.com

Introduction

Cytopenia occurs due to failure of normal hematopoiesis. It is a presentation of some underlying medical disorder most of which are primarily haematological.[1] Pancytopenia is defined as the decrease in the number of all the three formed elements of the blood below their normal reference values while bicytopenia is a disorder in which any two cell lineages are suppressed.[2] There is a considerable overlap between the causes of pancytopenia and bicytopenia in India as well as other countries, which may be attributable to geographical factors, socioeconomic status, diagnostic criteria, genetic causes and various cultural taboos. Bone marrow examination involving the study of bone marrow aspirates, imprint smears and trephine biopsy is an effective way of diagnosing and evaluating hematologic and metastatic neoplasm as well as non hematological disorders responsible for cytopenia. These three procedures are complementary to each other and superiority of one method over the other depends on the specific disease process.[3] The current study is intended to evaluate the various causes of bicytopenia and pancytopenia in adult and pediatric patients as well as their clinico-hematological correlations in a tertiary care centre of Uttarakhand.

Materials and Methods

This study was carried out in haematology section of the department of Pathology and included all cases diagnosed as bicytopenia or pancytopenia by routine hematological investigations. The inclusion criteria (all three or any two) used for selection of cases were-

1. Hb < 10gm/dl
2. TLC < 4000 cells/µl
3. Platelet count < 1.0 lac/µl

Relevant clinical history and examination findings along with routine hematological, serological and biochemical investigations were recorded. Bone marrow aspiration was done in all included 129 cases using Salah needle from posterior superior iliac spine. All the aspirate smears were stained with May-Grunwald-Giemsa stain (MGG) and special stains like Myeloperoxidase (MPO), Periodic-acid Schiff (PAS), Perl's Prussian blue stain were done as required. Bone marrow trephine biopsy was done in 90 cases from posterior superior iliac spine by using Jamshidi needle. Core biopsy was then used to make imprint smears, before placing it in Bouin's fluid for fixation. Routine histopathological processing was done after decalcification in 5% nitric acid for 24 hours. Trephine biopsy sections were stained with haematoxylin and eosin (H&E) and special stains like Reticulin, PAS, Perl's stain were used when required.

Results

A total of 129 cases of cytopenia (bicytopenia and pancytopenia) were included in the present study. The age of the patients ranged from 7 months to 93 years with maximum number of cases observed in the 2nd and 3rd decade. There were just 13 cases (10.07%) presenting at the age of more than 60 years. Males accounted for 73 (56.59%) cases, females for 56 (43.41%) cases and the male to female ratio was 1.3:1. (Table 1)

Most of the cases presented with a combination of two to three or more clinical features. As per the frequency, pallor was seen in 82.0% cases followed by fever in 50.38% cases, splenomegaly in 24.8% cases, weakness in 23.25% cases and hepatomegaly in 16.6% cases (fig. 1). Hemoglobin values in the present study varied from 2.2 gm/dl to 12.7 gm/dl. Majority of cases (87 cases, 67.43%) had hemoglobin values less than 8 gm/dl with 33.33% (43 cases) having hemoglobin less than 6 gm/dl. The lowest hemoglobin was 2.2 gm/dl seen in a case of acute leukemia.

Total leucocyte count ranged from 400 to 95000 cells/µl and 60.46% (78 cases) had leucocyte count between 1000 and 4000/µl. Lowest count of 400/µl and highest count of 95000/µl were noted in case of acute leukemia. Platelet count ranged from 5000 to 2.2 lac/µl. The lowest platelet count of 5000/µl was seen in three cases of hypoplastic marrow.

Anemia was seen 96.12% (124) cases followed by thrombocytopenia in 83.73% (108) cases and leucopenia in 69.76% (90) cases. Pancytopenia was noted in 60 (46.51%) cases and bicytopenia in 69 (53.49%) cases of cytopenia. Thrombocytopenia and anemia were the commonest form of bicytopenia seen in 40 cases (57.97%) followed by anemia and leucopenia in 25 cases (36.26%) and thrombocytopenia and leucopenia only in 4 cases (05.79%).

Megaloblastic anemia was the commonest cause of pancytopenia seen in 46.66% (28) cases followed by leukemia in 20.00% (12) cases and hypoplastic marrow in 18.33% (11) cases in the present study. Megaloblastic anemia and leukemia were also the most common causes of bicytopenia seen in 28.98% (20) and 23.18% (16) cases respectively. Myelofibrosis, multiple myeloma, lymphoproliferative disorders, infections and metastasis were among the occasional and isolated causes of

pancytopenia and bicytopenia. Among the cases of megaloblastic anemia, pancytopenia was seen in 58.33% cases and bicytopenia in 41.67 % cases and among the cases of leukemia, pancytopenia was seen in 42.85% cases and bicytopenia in 57.15% cases. (Table 2)

Discussion

This incidence of cytopenia was 55.6% (129/232) during the study peroid. This correlated with the studies done by Naseem et al. and Bushra et al. from Pakistan, where the incidence of cytopenia was observed to be 53.3% and

Table I: Distribution of the cases of cytopenia according to age and sex (n=129).

Age	Pancytopenia		Bicytopenia		Total (129)
	Male	Female	Male	Female	
0 - 10	06	01	04	06	17
11 - 20	11	07	06	06	30
21 - 30	08	04	08	07	27
31 - 40	06	01	02	05	14
41 - 50	03	01	04	05	13
51 - 60	03	03	04	05	15
61 - 70	03	02	02	02	9
71 - 80	00	00	01	01	2
81 - 90	01	00	00	00	1
91 - 100	00	00	01	00	1

Table II: Distribution of cases of cytopenia according to the causes (n = 129) diagnosed on bone marrow aspiration and/or biopsy.

Causes	Pancytopenia		Bicytopenia	
	BMA	BMB	BMA	BMB
Megaloblastic anemia	28	15	20	13
Leukemia	12	07	16	06
Normoblastic	01	02	07	06
Hypoplastic marrow	11	10	07	04
Multiple myeloma	01	01	06	06
Lymphoproliferative disorders	02	03	06	06
Megakaryocytic thrombocytopenia with nutritional anemia	02	01	02	02
Myelofibrosis	01	01	01	01
Metastasis	01	01	01	01
Others (Leishmaniasis & Haemophagocytosis)	01	01	01	01
No opinion possible	00	00	02	02

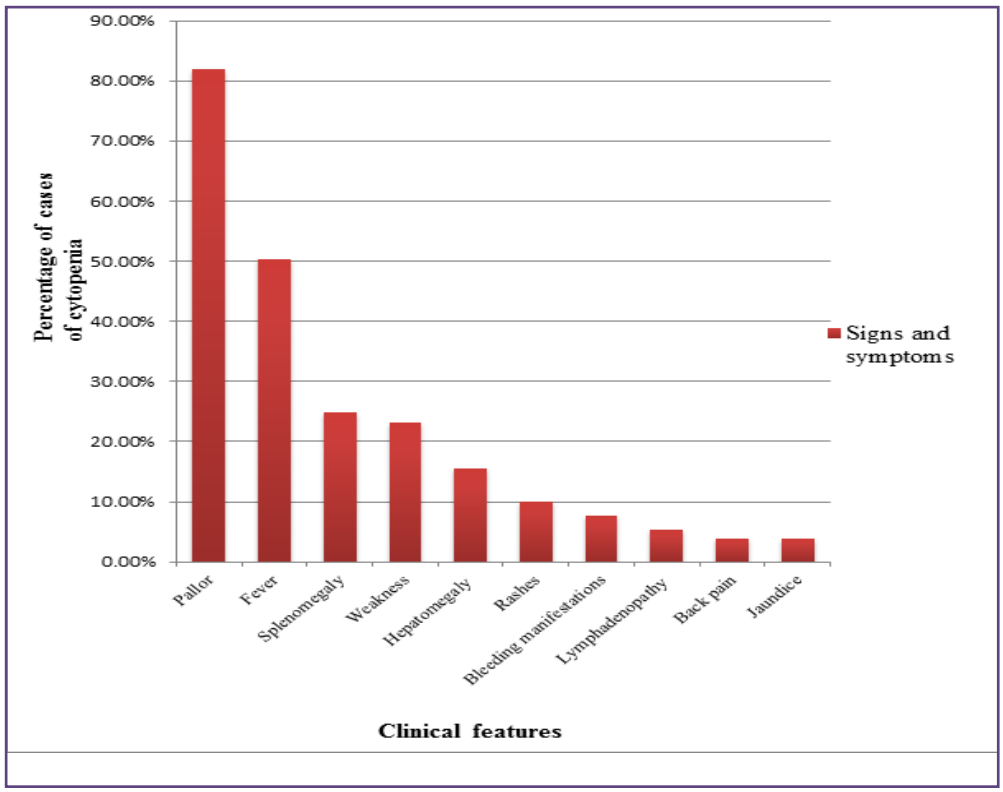

Fig. 1: Bar diagram showing distribution of cases of cytopenias according to clinical features.

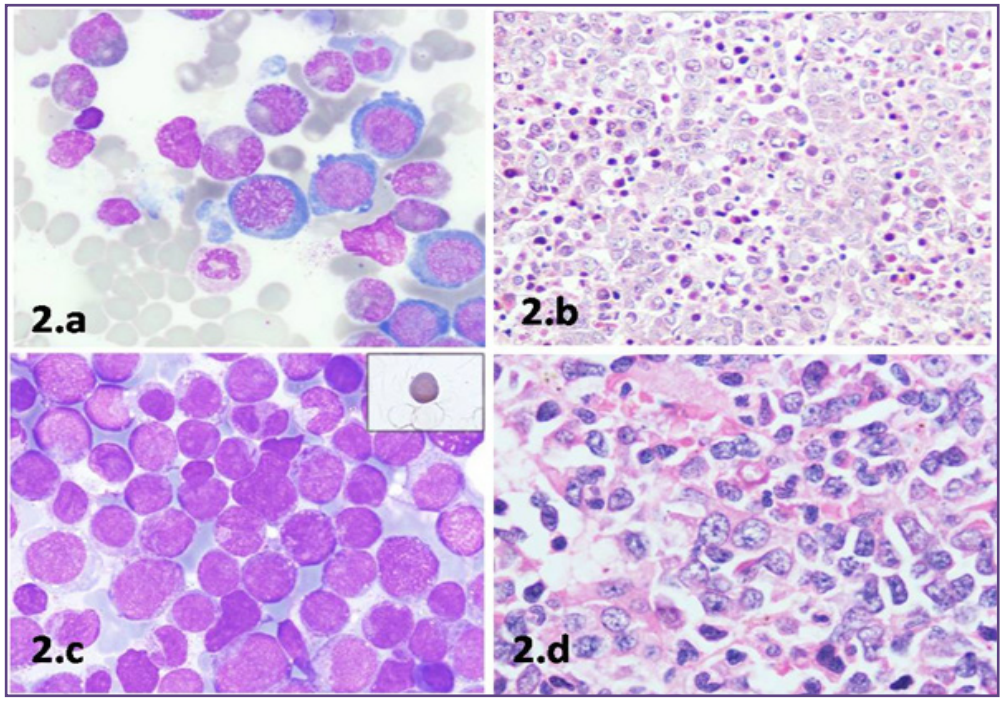

Fig. 2 a: Bone marrow aspiration smears showing megaloblasts with sieve like chromatin. (MGG 1000x) b)Bone marrow biopsy showing megaloblastic erythroid hyperplasia. (H&E 400x) c) Bone marrow aspiration smears comprising large no. of blasts with inset showing myeloperoxidase positivity in blast. (MGG 1000x) d) Bone marrow biopsy showing blasts. (H&E 1000x)

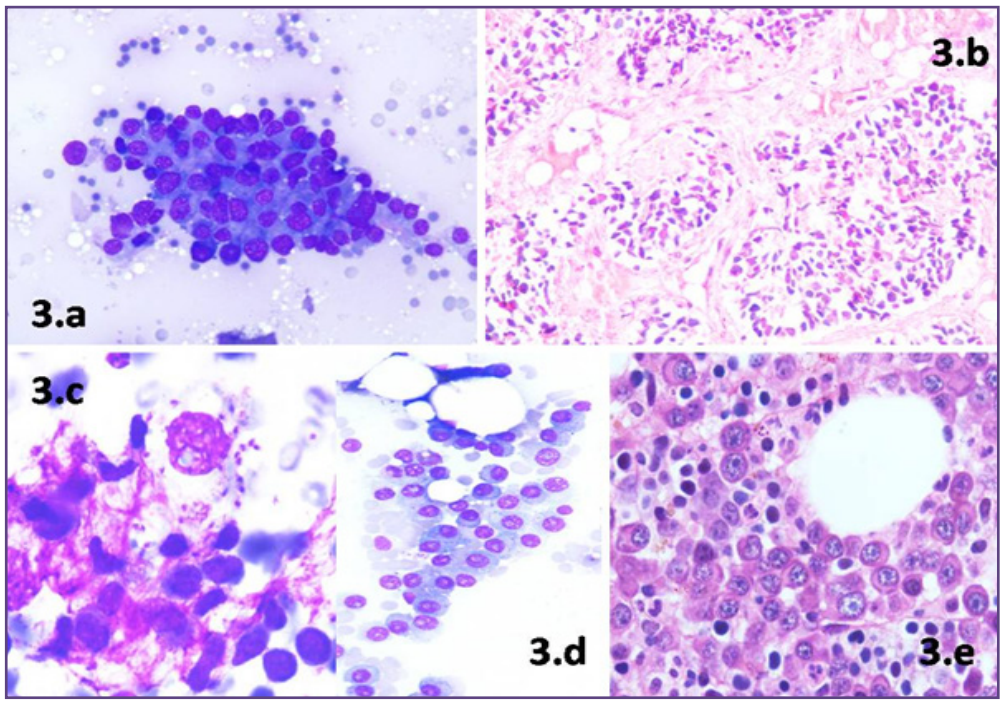

Fig. 3 a: Bone marrow aspiration smears showing sheets of tumor cells exhibiting an ill defined glandular pattern. (MGG 400x) b) Bone marrow biopsy showing infiltration of marrow by the tumor cells forming glands & tubules. (H&E 400x) c) Bone marrow aspiration smears showing Leishman Donovan bodies within macrophage. (MGG 1000x) d) Bone marrow aspiration smears showing numerous plasma cells. (MGG 400x) e) Bone marrow biopsy showing a cluster of myeloma cells with eccentric nucleus & prominent nucleoli. (H&E 1000x).

57.7% respectively.[1,4] However, studies conducted in India show a lower incidence of cytopenia varying from 20.0% to 37.6%. [3,5,6,7] The higher incidence of cytopenia in the study can be explained by the fact that the cases included were mainly referred cases from remote hilly areas, the study center being a tertiary care hospital. Moreover, the cases reached the centre after a considerable time gap, possibly due to lack of awareness about the urgency of the disease entities.

Similar to our study, clinical features have been reported by other authors also, although the frequency varies. In a recent study by Javalgi et al. generalized weakness was the most common symptom seen in 92% cases followed by pallor in 83% cases, splenomegaly in 17% cases and lymphadenopathy in 6% cases.[8] In another report by Hasan et al. from Pakistan, pallor was seen in 82% cases, hepatomegaly in 44.8%, splenomegaly in 37.2% and lymphadenopathy in 22.2% cases.[9]

A study by Bhatnagar et al. from India reported incidence of pancytopenia seen in 54.5% cases and bicytopenia seen in 45.5% cases which is almost similar to our study.[10] However, the observations of Naseem et al. from Pakistan in their study were very different from the results of present study with pancytopenia seen in 40% cases and bicytopenia seen in 17% cases.[1] This difference in the incidence of cytopenia can be attributed to difference in methodology, selection of diagnostic criteria, socio-economic status and nutritional status of cases included in the study.

There are very few studies in the literature which have considered pancytopenia and bicytopenia as different entities. Most of the studies have been done for pancytopenia. In this study pancytopenia and bicytopenia were separately evaluated. The commonest cause of pancytopenia reported in various studies throughout the world is aplastic anemia.[11,12,13,14] However, we observed megaloblastic anemia as the commonest cause of pancytopenia followed by leukemia and hypoplastic marrow in the study. Some studies conducted in India have also reported megaloblastic anemia to be the major cause of pancytopenia.[15] The incidence of megaloblastic anemia as a cause of pancytopenia has been reported to be 44% and 40.3% in reports by Khodke et al. and Verma et al. which is correlating with the findings of this study.[4,6] In the present study, megaloblastic anemia was the commonest cause of bicytopenia followed by leukemia. Only 8.69% cases of hypoplastic marrow were seen to present as bicytopenia.

Neoplastic conditions, as the most common cause of pancytopenia, are seen more commonly in western

countries. Higher incidence of megaloblastic anemia in Indian subcontinent can be attributed to low socioeconomic status, poor hygiene, inadequate nutrition and some cultural taboos. A high frequency of aplastic anemia can be related to environmental factors such as exposure to toxic chemicals rather than genetic factors. Farming being a major occupation in Indian subcontinent leading to increased exposure to pesticides also contributes to aplastic anemia. Easy availaibility of over the counter medicines can also lead to increased risk of aplastic anemia. All these risk factors are not seen in the western countries making neoplastic conditions as a common cause of pancytopenia rather than megaloblastic anemia or aplastic anemia. The higher incidence of leukemia and other marrow infiltrative disorders 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.

The interpretation of this study is that megaloblastic anemia, leukemia and hypoplastic marrow can present either as pancytopenia or bicytopenia. However, it was observed that megaloblastic anemia and hypoplastic marrow present more commonly as pancytopenia while leukemia usually presents as bicytopenia. More frequent association of leukemia with bicytopenia was also observed by Nassem et al. in their study from Pakistan where bicytopenia was associated with malignant conditions in 69.5% cases as compared to 26.6% cases of pancytopenia, which is relatively higher as compared to findings in our study.[1] This signifies that although pancytopenia is taken with greater clinical concern than bicytopenia, timely evaluation of bicytopenia is also very important. Another Indian study by Bhatnagar et al. observed similar results regarding the frequent association of leukemia with bicytopenia.[10]

Gupta et al. in their study have reported that bone marrow aspiration and trephine biopsy are complementary to each other to arrive at a definitive diagnosis.[2] This was observed in our study also and was evident in the following cases: A case of Plasmodium falciparum infection presenting as pancytopenia was diagnosed by peripheral blood film examination. It was not evident on the bone marrow examination, signifying the complementary role of peripheral blood film examination to arrive at a diagnosis. Similarly a case diagnosed as metastasis on trephine biopsy was later found to be case of leukemia on immunohistochemistry, which correlated with the aspiration findings. Thus both bone marrow aspiration and biopsy are complementary to each other to give the correct diagnosis.

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