ORIGINAL RESEARCH PAPER

Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY TO EVALUATE THE ETIOLOGY OF PANCYTOPENIA BY BONE MARROW ASPIRATION AND BONE MARROW BIOPSY AT TERTIARY CARE CENTER JAIPUR (RAJASTHAN)

Pathology

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ABSTRACT

Background :- Pancytopenia is an important clinico-haematological entity encountered in our day-today clinical practice. Pancytopenia is the simultaneous presence of anemia, leucopenia and thrombocytopenia. Bone Marrow Aspiration and biopsy plays a major role in the diagnosis of its underlying pathology and determine the implementation of correct management and prognosis.

Method :- Seventy pancytopenic patients with diagnosed with various haematological disorders by bone marrow aspiration and bone marrow biopsy were studied during October 2017 to December 2019 in Department of Pathology, SMS medical college, Jaipur (Rajasthan). A combined evaluation of presenting symptoms and sign, primary haematological investigations, biochemical investigations and bone marrow examination were done.

Results:- 45 cases (64%) male and 25 cases (36 %) female with M:F ratio of 1.8:1. 19 cases (27%) patients were in age group 21-30 years. A commonest presenting symptom was fever, followed by generalized weakness and bleeding. Commonest clinical sign was pallor, followed by splenomegaly, hepatomegaly and lymphadenopathy. Megaloblastic anemia (33%) was commonest cause of pancytopenia, followed by Myelodysplastic syndrome (29%) ,Hypoplastic marrow (7%),Aplastic anemia (6%),Acute leukemia (4%) and Plasma cell dyscrasia (3%).18% cases were non-conclusive.

Conclusion :- Pancytopenia is a common hematological entity that we come across in routine practices. Clinical finding, peripheral smear finding, aspiration and biopsy should go hand in hand to work-up of the patient of pancytopenia to reach to a concrete diagnosis.

KEYWORDS

INTRODUCTION

Pancytopenia is defined as reduction of all the three formed elements of blood below the normal reference range.[1]The presenting symptoms are often attributable either to the anaemia or thrombocytopenia.[2] Leucopenia is often seen in the subsequent course of the disorder. Varieties of hematopoietic and non-hematopoietic conditions manifest with features of pancytopenia.[3] Anemia leads to fatigue, dyspnea and cardiac symptoms. Thrombocytopenia leads to bruising, mucosal bleeding and neutropenia to sharply increased susceptibility to infection.[4] The mechanism contributing to pancytopenia include, decrease in haematopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective hematopoiesis with cell death, defective cell formation, antibody mediated sequestration or destruction of cells in a hypertrophied and overactive reticuloendothelial system.[5]

The complete haematological work up with good clinical correlation is of utmost importance to evaluate the cause of pancytopenia and planning further investigations. Bone marrow aspiration and biopsy are indispensable adjunct to the study of hematopoietic disorders. The spectrum of disorders primarily or secondarily affecting the bone marrow may manifest with peripheral pancytopenia.[6] Various factors encompassing geographic distribution and genetic disturbances may cause variation in the incidence of disorders causing Pancytopenia.[7] It is recommended that Bone Marrow Aspiration and Biopsy can be done simultaneously in cases of pancytopenia. Aspiration smears are superior for morphological details while biopsy provides a more reliable index of cellularity and often reveals bone marrow infiltration, fibrosis and granulomas.[8] Present study has been undertaken to evaluate the etiology, clinical profile and bone marrow morphology of pancytopenia. There by, this data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

AIM AND OBEJECTIVE

To evaluate the etiology of pancytopenia by bone marrow examination (bone marrow aspiration and bone marrow biopsy). To analyzes the clinical and haematological findings in the patients who present with pancytopenia.

MATERIALS AND METHODS

Total 70 patients were evaluated those presenting with pancytopenia on initial work up requiring bone marrow aspirate and bone marrow biopsy at S.M.S. Hospital and Medical College, Jaipur. All patient who fulfilled inclusion criteria for diagnosis of pancytopenia were haemoglobin less than 10.5 gm/dl in female and 12.5 gm/dl in male , total leucocyte count less than 3500/cumm and platelet count less than 100000/cumm.[9] The exclusion criteria were patient on chemotherapy and radiotherapy causing pancytopenia, those patient who do not give consent and inadequate sample. Bone marrow aspiration were performed using Salah needle and Bone marrow biopsy were performed using Jamshadi needle .

OBSERVATIONS AND RESULTS

70 patients who presented with pancytopenia were studied. Following results were recorded and analyzed.

1 .Gender - There was a male preponderance (M:F = 1.8:1),

Table 1: Gender distribution of cases of pancytopenia in present study.

S. No.	Gender	Present study	Percentage (%)
1.	Male	45	64
2.	Female	25	36

2. Age group distribution - The study group includes age 2 month to 82 years. Majority of patients belonged to the age group 21-30years (19 cases, 27%) followed by 11-20years (16 cases, 22%).

Table 2: Sex and Age distributions of cases of pancytopenia in present study.

S. No.	Age group (in years)	No. of cases	Percentage	Male	Female
1.	<10	6	9	4	2
2.	11-20	16	22	7	9
3.	21-30	19	27	12	7
4.	31-40	9	13	7	2
5.	41-50	6	9	3	3
6.	51-60	6	9	6	0
7.	>60	8	11	6	2
8.	Total	70	100	45	25

3. Chief complaints - Chief complaints fever (57%) common presenting feature followed by Generalized weakness and Bleeding manifestations.

Table 3: Chief complaints in cases of pancytopenia in present study.

S. No.	Clinical features	Cases	Percentage (%)
1.	Generalized weakness	37	53
2.	Fever	40	57
3.	Bleeding	10	14

4. Clinical finding - Pallor was noted in 66 cases (94%) among 70 cases followed by splenomegaly (27%) and hepatomegaly (14%).

Table 4: Clinical finding in cases in pancytopenia in present study.

S. No.	Clinical sign	Cases	Percentage
1.	Pallor	66	94
2.	Hepatomegaly	10	14
3.	Splenomegaly	19	27
4.	Lymphadenopathy	4	6

5. Etiology in pancytopenia in present study- The most common cause of pancytopenia is Megaloblastic anemia (23 cases, 33%) in present study. Second common cause was MDS {Myelodysplastic syndrome} (20 cases, 29%). In present study, 13 cases (18%) were non-conclusive on bone marrow examination.

Table 5: Etiology in pancytopenia in present study

S. No.	Diagnosis based on bone marrow examination	Cases	Percentage
1.	Megaloblastic anemia	23	33
2.	MDS	20	29
3.	Hypoplastic marrow	5	7
4.	Aplastic anemia	4	6
5.	Acute leukemia	3	4
6.	Plasma cell dyscrasia	2	3
7.	Non-conclusive	13	18
8.	Total	70	100

6. Peripheral blood finding in present study.

Table 6: Peripheral blood finding in various etiology of pancytopenia in

S. No.	Disorder	No. of Cases	Anisocytosis	Tear drop cells	Polychromasia	NRBCs	Hyperseg. Neutrophils	Immature cells	Relative lymphocytosis
1.	Megaloblastic anemia	23	20	15	8	15	19	3	1
2.	MDS	20	17	13	2	2	8	7	2
3.	Hypoplastic marrow	5	3	4	0	0	1	1	1
4.	Aplastic anemia	4	4	3	0	1	0	0	1
5.	Acute leukemia	3	2	2	1	2	1	1	1
6.	Plasma cell dyscrasia	2	0	1	0	1	1	1	1
7.	Non-conclusive	13	11	8	4	4	2	2	0
8.	Total	70	57	46	15	24	32	15	7

DISCUSSION

Pancytopenia is a clinico-haematological entity encountered in our day to day practice in which all the three major formed elements of blood (RBCs, WBCs and platelets) are diminished in number. There are varying trends in its clinical pattern, treatment modalities, and outcome. Bone marrow examination is a frequently requested investigation to determine the cause of pancytopenia. In present study around 70 cases of pancytopenia were studied. Various clinical and hematological parameters were evaluated and final diagnosis for pancytopenia was made. Peripheral smear examination and bone marrow examination (Bone marrow aspiration and biopsy) were also evaluated in each case.

In present study out of 70 cases, 45 patients were males and 25 were females. Thus males formed the majority of patients, similar in other studies done by Biradar et al[13], showed a male predominance with male to female ratio of 2.1:1. Similar male predominance were found in other studies Katti et al[16] as well in Singh P et al[12]. Male to female ratio was 2.18:1 in this study group. In contrast of other study done by Roopali et al[17] found female predominance. Patients were predominantly in the age group of 21-30 years (27 %). Mean age was 32 years in our study population. Similar age group (21-30 years) were found in other studies by Reddy et al[14] and Goyal et al.[15]

The most common presenting complain in the present study was fever (57 %), generalized weakness (54%) and bleeding (14%). A study done by kishor khodke et al found similar most presenting complain fever (40%). Pallor was present in most of cases (94%). Clinical finding were comparable with other studies, pallor was most common presenting sign. Splenomegaly were second most presenting sign (27%) followed by hepatomegaly (14%) and least common was lymphadenopathy (6%) as similar in a study done by Khunger et al[4] and Kumar et al[11].

In the present study, commonest cause of pancytopenia was megaloblastic anemia (33%). A study done by Tilak et al[9], Khunger et al[4] and Biradar et al[13] were Megaloblastic anemia most common cause of pancytopenia. Similar finding were observed in other studies which were conduct in different part of India.

In present study, Myelodysplastic syndrome (29%) were second most cause of pancytopenic patients. In Israel and Europe [10] a study done, there were similar second leading cause of pancytopenia was MDS (Myelodysplastic syndrome). Aplastic anemia were second most common cause of pancytopenia in the studies by Tilak V et al[9] and Reddy et al[14]. Acute Leukemia second leading cause of pancytopenia in the study by Roopali et al.[17]

In present study, 13 cases (18%) were non-conclusive on bone marrow biopsy. Patients with plasma cell dyscrasia (multiple myeloma) can develop pancytopenia due to replacement of marrow element by the myeloma cells. Tilak V et al[9] reported one case in their study. Our study had 3% cases of pancytopenia due to plasma cell dyscrasia.

Aplastic anemia was the main etiology of pancytopenia accounting to 52.7% by international study of agranulocytosis and aplastic anemia in Israel and Europe[11]. Aplastic anemia was 29.5% by kumar R et al.[13] It was 31.4% by Goyal et al.[15] Our present study found 6% cases of aplastic anemia. Hypoplastic anemia accounted 7% of pancytopenia and acute leukemia to 4% of cases.

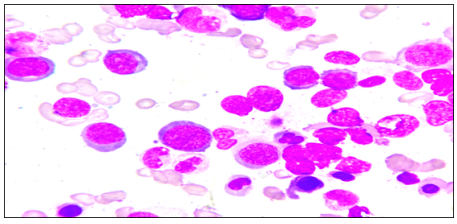
Table 6: Comparative studies showing the etiology of pancytopenia.

S. No.	Study	Country	Year	Cases	M:F	Commonest cause	Second common
1.	International agranulocytosis and aplastic anemia study[10]	Israel and Europe	1987	389	1.3:1	Aplastic anemia (52.7%)	MDS (10.5%)
2.	Tilak et al[9]	India	1999	77		Megaloblastic anemia (68%)	Aplastic anemia (7.7%)
3.	Khodke et al[5]	India	2000	166	1.2:1	Hypoplastic anemia (29.51%)	Megaloblastic anemia (22.3%)
4.	Kumar et al[11]	India	2001	166	2.1:1	Aplastic anemia (29.5%)	Megaloblastic anemia (22.3%)
5.	Khunger et al[4]	India	2002	200		Megaloblastic anemia (72%)	Aplastic anemia (28%)
6.	Singh P et al[12]	India	2016	50	2.1:1	Aplastic anemia (44%)	Megaloblastic anemia (20%)
7.	Biradar et al[13]	India	2016	30	2:1	Megaloblastic anemia (46.6%)	Iron deficiency anemia (16.6%)
8.	Reddy et al[14]	India	2016	42	1.2:1	Megaloblastic anemia (38.1%)	Aplastic anemia (26.2%)
9.	Goyal et al[15]	India	2017	140	1.37:1	Aplastic anemia (31.4%)	Megaloblastic anemia (22.1%)
10.	Katti et al[16]	India	2018	136	2.1:1	Megaloblastic anemia (68.4%)	Dengue fever (10.3%)
11.	Roopali et al[17]	India	2019	79	1:1.19	Megaloblastic anemia (74.1%)	Acute leukemia (11.3%)
12.	Present study	India	2019	70	2.1:1	Megaloblastic anemia (33%)	MDS (29%)

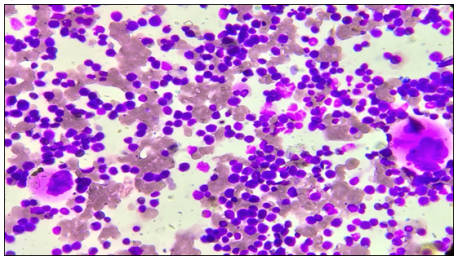
CONCLUSION

Pancytopenia is a common hematological entity that we come across in routine practices. Clinical finding, peripheral smear finding, aspiration and biopsy should go hand in hand to work-up of the patient of pancytopenia to reach to a concrete diagnosis. Bone marrow aspirated coupled with biopsy can diagnose majority of cases of pancytopenia but not all the cases. In our study megaloblastic anemia is commonest cause of pancytopenia in our centre. This seems to reflect high prevalence of nutritional anemia in Indian subject. Second most common cause in our study is MDS (Myelodysplastic syndrome). As these lesions may progress to acute leukemias, close follow-up is requested and pancytopenia in such cases should be dealt seriously.

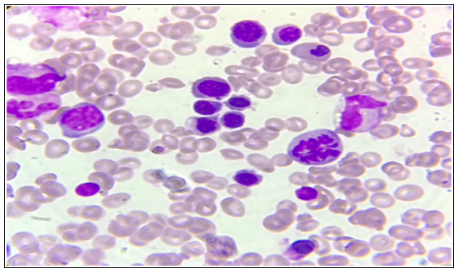
1. Megaloblastic anemia



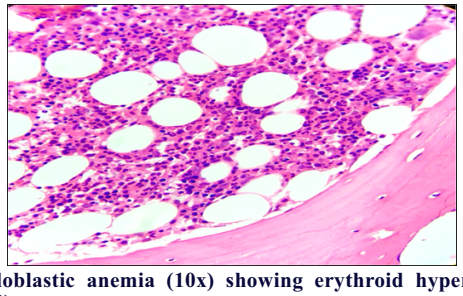
Megaloblasts with sieve like chromatin and blue cytoplasm. (10x100)



Erythroid hyperplasia with dysmegakaryopoiesis in megaloblastic anemia (10x40)

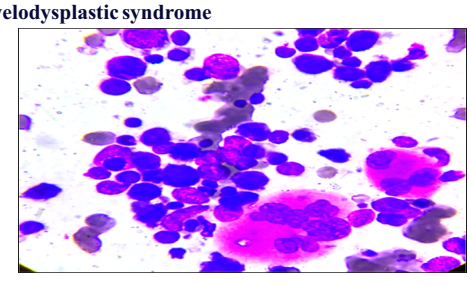


Dyserythropoiesis with megaloblasts in megaloblastic anemia. (40X)

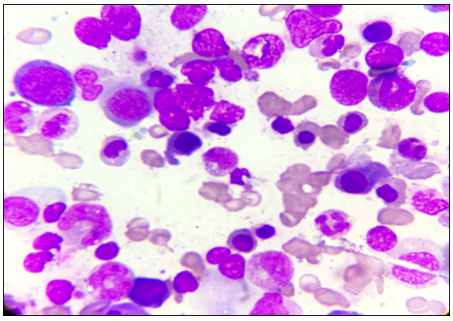


Megaloblastic anemia (10x) showing erythroid hyperplasia. (10x10)

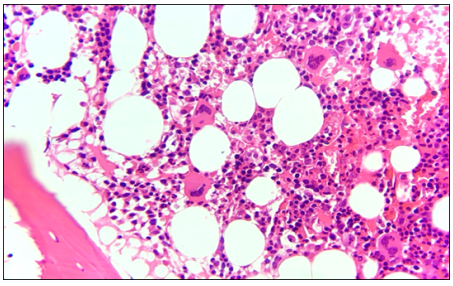
2. Myelodysplastic syndrome



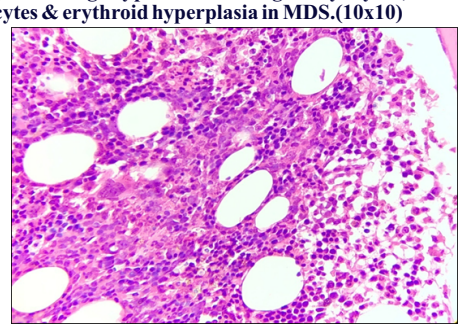
Megakaryopoiesis showing megakaryocytes having separate nuclei. (10x100)



MDS – megaloblast and ring neutrophils seen.(10x40)



Biopsy showing hypolobated megakaryocytes, micromega karyocytes & erythroid hyperplasia in MDS.(10x10)



ALIP (Abnormal localization of immature precursor) in MDS.(10x40)

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