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Original Research Article

Pancytopenia: A Cross-sectional Clinico-Haematological Study in a Tertiary Care Centre

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ABSTRACT

Background

Pancytopenia is the decrease in all three hematologic cell lines and is relatively a common haematological presentation. The common causes include megaloblastic anaemia, leukemia, lymphoma, myelodysplastic syndrome, aplastic anaemia and granulomatous disease of bone marrow. Pancytopenia is a distinct feature in many serious and life threatening illnesses and its severity decides the management and prognosis of the underlying disease.

Objectives

The aim of this study is to study different patterns of clinical presentation and co-relate with haematological parameters and bone marrow study in various causes of pancytopenia.

Materials and methods

It was a Cross-sectional study done in the department of pathology, VIMSAR, Burla from the period of January 2021 to April 2023. 133 pancytopenia patients were evaluated clinically and the findings were co-related with haematological parameters and bone marrow aspiration.

Results

Out of 133 cases studied, age of patient ranged from 2 to 85 years with majority of patients presenting in 3rd decade and male predominance(M:F=1.1:1). Pallor was found in all the cases. Generalized weakness is the most common presenting symptom followed by fever, bleeding manifestations, splenomegaly, lymphadenopathy and hepatomegaly. Megaloblastic anaemia was the predominant cause of pancytopenia. The commonest marrow finding was hypercellularity with megaloblastic erythropoiesis followed by hypoplastic marrow. In our study, rare cases of

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pancytopenia with gelatinous transformation of bone and pancytopenia with bone marrow necrosis in a sickle cell patient was found.

Conclusion

Pancytopenia is a common haematological presentation of various undiagnosed diseases. Hence, proper evaluation of both clinical findings and haematological parameters are necessary for diagnosis and better treatment.

Key words: Pancytopenia, megaloblastic anaemia, gelatinous transformation of marrow

INTRODUCTION

Pancytopenia is an important clinic-haematological entity characterised by a triad of laboratory findings comprising of anaemia, leucopenia and thrombocytopenia. It results from a number of disease processes and the cause of pancytopenia varies from case to case. The treatment and outcomes depend upon the underlying disease process.[1] The cause of pancytopenia may lie in the bone marrow, periphery or both. The bone marrow picture varies according to the aetiological factors.[2] Physical findings and peripheral blood picture, both are essential for proper evaluation of disease process. Along with the routine haematological investigations, examination of bone marrow by aspiration and biopsy helps in better understanding of the pathogenesis in a particular case of pancytopenia.[3]

Many diseases present with the features of pancytopenia, among which megaloblastic anaemia is the most common cause along with various haematological malignancies like leukemias, lymphomas, myelodysplastic syndrome, aplastic anaemia and granulomatous diseases of bone marrow.[4]

The essential investigations required for diagnosis of pancytopenia are-

1. Complete blood count (CBC)
2. Peripheral blood examination
3. Bone marrow examination

In some special situations radiological, microbiological, biochemical and immunological investigations are required for confirmation of diagnosis. [5]

AIMS AND OBJECTIVES

The aim of this study is to study different patterns of clinical presentation and co-relate with haematological parameters and bone marrow study in various causes of pancytopenia.

MATERIALS AND METHODS

This is a Cross-sectional study conducted in the Department of Pathology, VIMSAR, Burla from a period between January 2021 to April 2023. Data were collected from the hematology records such as age, sex, clinical presentation of the patients, food habits (vegetarian or non-vegetarian), previous exposure to any types of drugs, chemicals etc. Blood smears, CBC reports, bone marrow aspiration smears and bone marrow biopsy were studied from archived slides of all the cases of pancytopenia came to Department of pathology for diagnosis during the study period. Depending up on the complete blood count report by automated blood analyzer, criteria for pancytopenia are Hb% - <10gm%, Total leucocyte count- $<4x10^9$/L, total platelet count- <100 X

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10^9/L. Peripheral blood smear examination was done in each case of pancytopenia, followed by bone marrow aspiration study. Bone marrow biopsy was done in cases of hypoplastic marrow, granulomatous disease and few other cases of pancytopenia. Peripheral smears and bone marrow aspiration smears were stained with Leishman stain, whereas Bone marrow biopsy specimens were stained with Hematoxylin and eosin stain. Perl's Prussian blue stain done in case of hypoplastic marrow and cases of MDS. All the data are analysed and tables are formulated by descriptive statistical analysis using frequency and percentage.

Inclusion Criteria

All the cases of pancytopenia diagnosed by CBC report and peripheral smear study were included in the study group.

Exclusion Criteria

Patients undergoing radiotherapy and Chemotherapy for treatment of malignancy, known cases of chronic liver disease and kidney disease were excluded from our study group.

RESULT

A total of 133 cases were included in our study group with male:Female ratio 1.1:1, showing slight male preponderance. Youngest patient in our study was 2 year 4 month child diagnosed as ALL-L2 and oldest patient was 85 year male diagnosed as megaloblastic anemia. Maximum number of patients (24%) presenting with pancytopenia were seen to be in 3rd decade (Table-1) followed by 6th decade (15.78%). In case of hypoplastic marrow females (56.25%) outnumbered male (43.75%). Patients were complaining of generalized weakness, fever and bleeding manifestation. Many patients show multiple symptoms together like fever with lymphadenopathy along with bleeding manifestations, while some patients show only fever and weakness. Maximum number of cases (51.12%) presented as generalized weakness (Table-2) and easy fatiguability. Splenomegaly was seen in 13.53% of cases, hepatomegaly in 6.01% cases and lymphadenopathy in 9.02% of cases. Pallor was present in all cases. Hb% ranges from 2gm% to 7 gm%, total leucocyte count varies from 500cells/cubic mm to 3800 /cubic mm. Platelet count varies from 5000/ µL to 80,000/µL. Bone marrow cellularity was categorized into hypocellular, normocellular or hypercellular marrow. Hypercellular marrow were seen in case of megaloblastic anemia, most of the cases of hypersplenism, acute leukemia, and MDS (myelodysplastic syndrome). Hypocellular marrow was seen in case of hypoplastic marrow, HIV myelopathy, gelatinous transformation of marrow, and avascular necrosis of marrow. Normocellular marrow was seen in case of nutritional anemia and two cases of hypersplenism. In our study 47 cases (35.33%) cases were diagnosed as megaloblastic anemia (Fig-1) followed by hypoplastic marrow 32(24.06%), 3 cases (2.25%) HIV patients presented with pancytopenia diagnosed as myelosuppression.(table-2). Peripheral smears of megaloblastic anemia show macro ovalocytes, hyper segmented neutrophils, leucopenia and thrombocytopenia. Bone marrow pictures showed hypercellular marrow with good numbers of megaloblasts, giant metamyelocytes and stab form. In our study a rare case of pancytopenia like gelatinous transformation of bone was found in a 20 yr. male (Fig-2). A 12 yr. female child, known case of sickle cell anemia with clinical diagnosis of sickle cell crisis with pancytopenia, bone marrow aspiration cytology done, aspirate was pus

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like. Bone marrow smear study found it to be marrow necrosis of the bone marrow(Fig-3). Granulomatous disease of bone marrow was diagnosed in a case of 33 yr. male. Bone marrow aspiration smear showed collection of epithelioid cells, biopsy study reveals granulomatous deposits in the bone marrow. In aleukemic leukemia cases of AML and AML we found pancytopenia in the peripheral smears and CBC reports but bone marrow aspiration showed hypercellular marrow with blasts more than equal to 20%. In our study we found 9 cases (6.76%) of ALL and 9 cases of AML (acute myeloid leukemia) (6.76%) presented as pancytopenia with cellular marrow. In our study we found 5 cases of MDS (myelodysplastic syndrome) (3.75%) and all are found between third to sixth decade. We found 9 cases (6.76%) of hypersplenism patients out of which (88.88%) of cases seen in case of female patients. Bone marrow findings are mostly hypercellular marrow (90%) cases, rest 10% cases showed normocellular marrow.

Symptoms	No. of cases	Frequency (%)
Generalized weakness	68	51.12
Fever	50	37.59
Bleeding manifestations	41	30.83
Splenomegaly	18	13.53
Lymphadenopathy	12	9.02
Hepatomegaly	08	6.01

Table -1: Clinical presentations

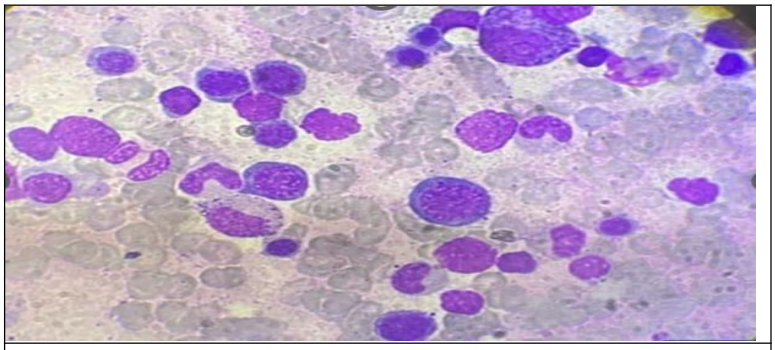

Figure-1: Bone marrow showing megaloblasts with sieve-like chromatin pattern (Leishman, x 1000)

Diagnosis	Age group (years)									Total (%)
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
ALL	4	3	0	0	0	2	0	0	0	9(6.76%)
AML	0	3	1	1	3	0	1	0	0	9(6.76%)
BM necrosis (SCD)	1	0	0	0	0	0	0	0	0	1(0.75%)
Gelatinous transformation	0	1	0	0	0	0	0	0	0	1(0.75%)

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Granulomatous disease	0	0	0	1	0	0	0	0	0	1(0.75%)
HIV (Myelosuppression)	0	0	2	1	0	0	0	0	0	3(2.25%)
Hypersplenism	0	0	3	2	2	2	0	0	0	9(6.76%)
Hypoplastic marrow	0	2	4	4	2	9	9	2	0	32 (24.06%)
MDS	0	0	1	2	1	1	0	0	0	5(3.75%)
Megaloblastic anaemia	0	8	18	5	7	3	5	0	1	47 (35.33%)
Nutritional anemia	0	1	3	1	1	0	1	1	1	9(6.76%)
Plasma cell dyscrasias	0	0	0	0	3	4	0	0	0	7(5.26%)
Total per age group (%)	5 (3.76)	18 (13.53)	32 (24.06)	17 (12.78)	19 (14.29)	21 (15.78)	16 (12.03)	3 (2.25)	2 (1.5)	133(100 %)

Table-2: Distribution of cases according to age group

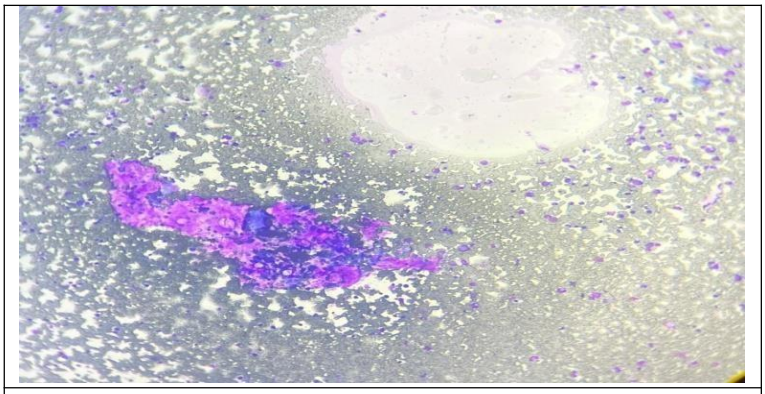

Figure 2: Bone marrow showing gelatinous transformation (Leishman, x 100)

Diagnosis	No. of Cases	Male	Frequency (%)	female	Frequency (%)
ALL	9	6	66.66	3	33.33
AML	9	4	44.44	5	55.56
BM necrosis (SCD)	1	0	0	1	100
Gelatinous transformation	1	1	100	0	0
Granulomatous disease	1	1	100	0	0
HIV(Myelosuppression)	3	3	100	0	0
Hypersplenism	9	1	11.11	8	88.88
Hypoplastic marrow	32	14	43.75	18	56.25
MDS	5	2	40	3	60
Megaloblastic anemia	47	27	57.44	20	42.55
Nutritional anemia	9	4	44.44	5	55.55
Plasma cell dyscrasias	7	5	71.43	2	28.57

Table 3: Distribution of cases according to Sex

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Study	Total number of cases	Most common cause	Percentage (%)
Gayatri et al.	104	Megaloblastic anaemia	74.04%
Jalbani et al.	40	Aplastic anaemia	32%
Mohanty B et al	100	Megaloblastic anaemia	44%
Present study	133	Megaloblastic anaemia	35.33%

Table 4: Most common cause of pancytopenia in different studies

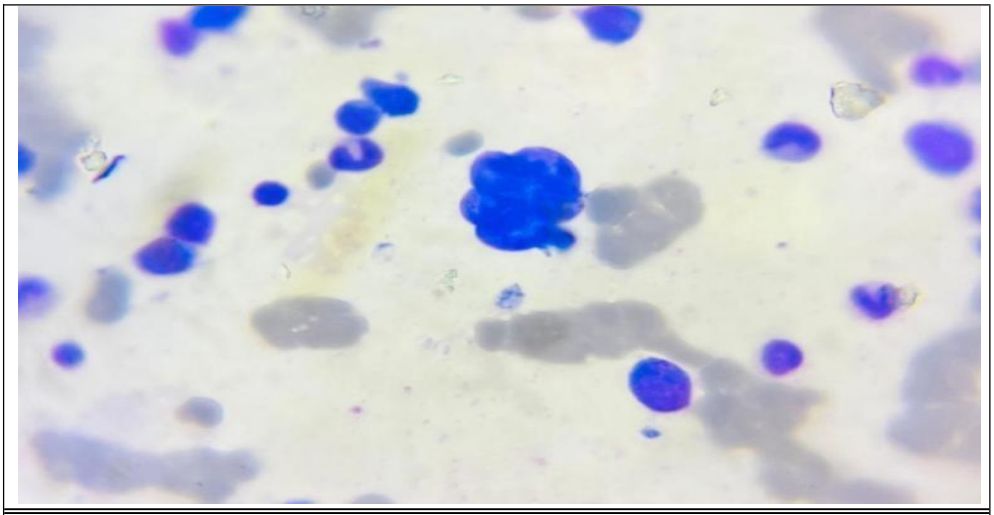

Figure 3: Bone marrow showing naked megakaryocyte in HIV myelosuppression (Leishman, x 400)

DISCUSSION

A total number of 133 cases of pancytopenia were studied with M:F ratio 1.1:1. In the present study age group ranges from 2.4 years to 85 years. B N Gayathri et al [6] observed a M:F ratio 1.2:1 in their study with age group ranging from 2 to 80 years, which correlates with our study. In Jha A et al [7] study, they observed pancytopenia in the age group of 1 to 79 yrs. with M:F ratio of 1.5:1. Commonest symptoms in our study is generalized weakness. In the present study most common age group presenting as pancytopenia is 3rd decade followed by 5th decade. In Study of Kalpana Chandra et al.[5] and Sahay S and Ramesh ST[3] and Tilak et al[8], they found generalized weakness is the most common symptom. In our study megaloblastic anaemia is most commonly seen in 3rd decade. In the study of Khunger et al.[9] they found 72% of cases as megaloblastic anaemia and it was most common cause of pancytopenia in their study. In Indian scenario most common cause of pancytopenia is megaloblastic anaemia. In our present study megaloblastic anaemia is the most common cause (35.33%) followed by hypoplastic marrow (24.06%), nutritional anaemia seen in 6.76% of cases. Study of Kumar and Karla et al.[10], Nafil H et al.[11] and many other authors studies megaloblastic anaemia is the most common cause of pancytopenia.

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In present study male (57.44%) out numbered female 42.55%) in megaloblastic anaemia, but in nutritional anaemia, hypoplastic marrow female out numbers male. (Table-3). Bone marrow examination of HIV patients are done for evaluation of pancytopenia, systemic infections or to rule out malignancy. Abnormalities are found in both cellular elements as well as in the matrix. Marrow cellularity may be hypocellular, normocellular or hypercellular according to disease progression. Marrow findings are either dysplasia in single lineage or multiple lineage. Erythroid dysplasia is the most common abnormalities followed by dysplasia in myeloid series of cells and dysplastic changes in megakaryocytes.[12] We found 3 cases of severe myelosuppression in HIV patient, characterised by hypocellular marrow, mild erythroid dysplasia, naked megakaryocytes, hypo segmented and micromega karyocytes (fig-3)[13].

Gelatinous transformation of bone marrow was seen in a 20 year old orphan male (Fig-2). The main feature is atrophy of adipocytes, eosinophilic deposition of substances and hypoplastic marrow. Eosinophilic substances are hyaluronic acid and mucopolysaccharides.[14] Single case of avascular necrosis of marrow seen in a 12 year female child of sickle cell disease case. Bone marrow aspiration yielded pus-like material. Bone marrow necrosis is very rare findings seen in sickle cell disease patients. Bone marrow pictures in sickle cell disease is mainly necrotic cells in an amorphous eosinophilic background. Bone marrow necrosis is found in only 2% cases of sickle cell disease (SCD), whereas the most common cause is neoplastic[15]. The present study was conducted in western Odisha which is a sickle cell disease belt [16]. Bone marrow necrosis is very rarely seen in SCD. We found (6.76%) of nutritional anaemia and 35.33% cases of megaloblastic anaemia. Nutritional anaemia may be due to combined deficiency of iron, folic acid and vitamin B12 deficiency[17]. In most of the Indian studies megaloblastic anaemia is the most common cause of pancytopenia due to poverty, vegetarian diet, and parasitic infestations[18]. In this present study we found only one case of granulomatous disease. Bodem CR et al.[19] in their 20 yrs. study they found 50 cases of granulomatous disease in the bone marrow. Hypersplenism is characterised by splenomegaly, peripheral pancytopenia with hypercellular marrow and correction of cytopenia after splenectomy.

Hypersplenism causes pancytopenia due to rapid destruction of premature red cells, retention of large number of blood cells up to more than 20% of initial volume. Blood cells are captured in the spleen, phagocytosed and destroyed causing peripheral pancytopenia.[20] found 9 cases (6.76%) of hypersplenism in our study. Anita P et al.[1] found only one case(0.9%) of hypersplenism in their study out of total 106 cases of pancytopenia patients. MDS is a disorder of stem cells diagnosed in elderly patients considering degree of dysplasia and blast percentage in peripheral blood and bone marrow. Most common presentation is refractory anaemia. Many patients show bi-cytopenia or pancytopenia. Disease course of MDS varies from patient to patient and it may progresses to acute leukemia.[21] In this present study we found 5 cases(3.75%) of MDS. Though it is a disease of elderly people we found MDS cases in third, fourth, fifth and sixth decades. In our studies rare causes of pancytopenia are marrow necrosis, gelatinous transformation of marrow, bone marrow suppression due to HIV, and granulomatous deposits in the marrow. It correlates with study of many authors.

CONCLUSION

Pancytopenia is a common clinical presentation of various underlying undiagnosed diseases, it should be properly evaluated as treatment protocol is different according to aetiology.

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Megaloblastic anaemia is the most common cause of pancytopenia in Indian scenario, most probably due to food habits and nutritional deficiencies. Keeping these factors in mind we have to take proper clinical history, peripheral blood smear examination and bone marrow study for evaluation of disease aetiology. The findings of this study will help us in better understanding of such cases as well as their demographic variability for better patient management.

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