

Bonemarrow Pathology in Pancytopenia



Medical science

KEYWORDS : Pathology, pancytopenia , bonemarrow

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ABSTRACT

Objective: Pancytopenia is a common hematological problem. It is the simultaneous presence of a decreased RBC, WBC & platelet count. Many disorders can cause pancytopenia. The aim of this study is to compare retrospectively, the incidence of the underlying pathology in the bone marrow in cases presenting with pancytopenia at PSGIMS&R, Coimbatore. 100 cases of pancytopenia were included in the study. The most common cause of pancytopenia as elicited by bone marrow study was Megaloblastic anemia followed by dimorphic anemia, Iron deficiency anemia, Acute leukemia, Aplastic anemia, myeloma, malarial infection, lymphoma, refractory cytopenia with multilineage dysplasia, metastatic carcinomatous deposits, HIV & drug induced pancytopenia were less common causes.

INTRODUCTION :

Pancytopenia is not a disease entity, but a triad of findings, that results from various disease processes. The criteria for diagnosis includes hemoglobin levels less than 13.5g/dl in males or 11.5g/dl in females, leukocyte count less than $4 \times 10^9/l$ & platelet count less than $150 \times 10^9/l$.

The causes of pancytopenia can vary from simple deficiency states like Megaloblastic anemia & infectious diseases to malignant conditions such as leukemia, lymphoma & myeloma. The major diagnostic problems occur when there are no specific features in the peripheral smear to point to the cause.

The aim of this study was to analyze the spectrum of bone marrow pathology in various cases of pancytopenia in our institution, to compare the frequency of these causes & to find out the most common cause.

MATERIALS & METHODS:

This study was carried out from June 2009 to September 2011 at the department of Pathology, PSGIMS&R, Coimbatore. Case files of patients who presented with pancytopenia were retrieved & the bone marrow pathology was studied in each case. The cases that satisfied the criteria of pancytopenia such as hemoglobin <13.5g/dl in males or 11.5g/dl in females, WBC < $4 \times 10^9/l$ and platelet count < $150 \times 10^9/l$ were included in the study.

RESULTS :

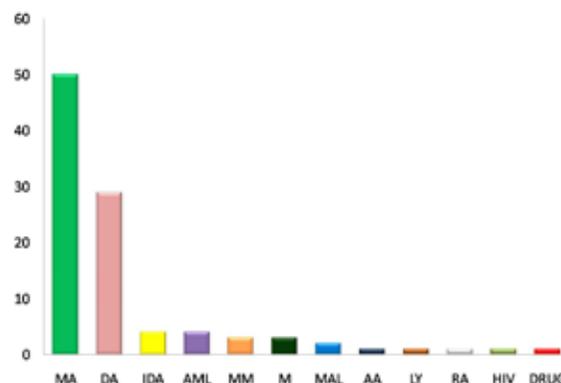
Of the 100 patients who presented with pancytopenia, 58 were males and 42 were females. The youngest in this study was a 2 1/2 month old male child & the oldest patient was an 80 year old male. Mean age at presentation was 20-60 years. The distribution of cases has been shown in Table1 & figure1

TABLE1: Showing the distribution of cases presenting with pancytopenia

PATHOLOGY IN BONE MARROW	n=100 NO OF CASES	% OF CASES
Megaloblastic anemia	50	50%
Dimorphic anemia	29	29%
Iron deficiency anemia	4	4%
Acute leukemia	4	4%
Myeloma	3	3%

Metastatic carcinomatous deposits	3	3%
Infection(Malaria)	2	2%
Aplastic anemia	1	1%
Lymphoma	1	1%
Refractory cytopenia with multilineage dysplasia	1	1%
HIV with cryptococcosis	1	1%
Drug induced	1	1%

FIGURE 1 SHOWING THE RELATIVE FREQUENCY OF BONE MARROW PATHOLOGY IN PANCYTOPENIA CASES



MA- MEGALOBLASTIC ANEMIA DA - DIMORPHIC ANEMIA IDA-IRON DFICIENCY ANEMIA

AML- ACUTE LEUKEMIA MM - MULTIPLE MYELOMA M - METASTATIC DEPOSITS

MAL- INFECTION (MALARIA) AA - APLASTIC ANEMIA LY- LYMPHOMA

RA- REFRACTORY CYTOPENIA WITH MULTILINEAGE DYSPLASIA

HIV- HUMAN IMMUNODEFICIENCY VIRUS DRUG- DRUG INDUCED

Megaloblastic anemia, dimorphic anemia & iron deficiency anemia were seen in the age group of 16 to 62 years. The age at presentation for leukemia, myeloma, aplastic anemia, metastatic deposits, malarial infection, lymphoma, refractory cytopenia with multilineage dysplasia, HIV, drug (azathioprine) induced pancytopenia were 2 1/2 months, 48 years, 20 years, 80 years, 55 years, 40 years, 52 years, 65 years & 43 years respectively.

The additional peripheral smear findings that were appreciated in these cases were macro ovalocytes, hypersegmented neutrophils & giant platelets in Megaloblastic & dimorphic anemia; prominent rouleaux formation in myeloma (fig2), gametocytes of *Plasmodium falciparum* in the cases of malaria, presence of bilobed neutrophils, few nucleated RBCs and giant platelets in Refractory cytopenia with multilineage dysplasia.

The marrow in refractory anemia showed dyspoiesis in the erythroid, myeloid & megakaryocytic series. Multilobated erythroid precursors, hypogranular myelocytes & metamyelocytes, megakaryocytes with separation of nuclear lobes were seen.

The marrow in the HIV case showed budding yeast forms of cryptococci. CSF and blood culture were positive for cryptococci in this case. Gametocytes of *P.falciparum* were seen in the Bonemarrow of the case with malarial infection. The metastatic deposits in one of the cases were of adenocarcinoma from breast (fig3) and in the other from the melanoma of unknown primary site (fig4). The 2 cases of lymphoma were anaplastic large cell lymphoma and diffuse large B cell lymphoma as typed by lymph node biopsy and immunohistochemical studies. The cases of acute leukemia were acute myeloid leukemia and Hairy cell leukemia (fig 5).

DISCUSSION:

The spectrum of hematological disorders resulting in pancytopenia both in children & in adults is very wide. Bone marrow examination is a useful test in reaching the final diagnosis.

In the present study of 100 cases of pancytopenia, the most common bone marrow pathology was Megaloblastic anemia (50%), followed by dimorphic anemia (29%) & Iron deficiency anemia (4%). Similarly, 24.29% micronutrient deficiency anemia like Megaloblastic anemia & 15% mixed deficiency anemia was reported by Rahim et al in a study in Pakistan¹. In other studies, the incidence of these deficiency disorders ranged from 24%² to 68%³. It is a common problem in developing countries. The usual presenting age in developed countries is in infancy, but in developing countries like India, it can occur at any age.

The less common causes in the present study were acute leukemia, metastatic deposits, myeloma, aplastic anemia, malarial infection, refractory cytopenia with multilineage dysplasia, HIV with cryptococcal infection & Drug induced pancytopenia. These disorders together constituted 17% of cases & are second to deficiency disorders as causes of pancytopenia. These findings are supported by other studies.^(4,5)

Infections causing pancytopenia has been reported. Kala-azar, falciparum malaria & enteric fever were common causes of pancytopenia⁶ In the recent decades, HIV has been found to be an important cause. In the present study, a case of plasmodium falciparum infection and a case of HIV with cryptococcosis causing pancytopenia were found. HIV acts synergistically with cryptococci to cause pancytopenia. Many of the HIV cases noted during our retrieval of records presented with bicytopenia.

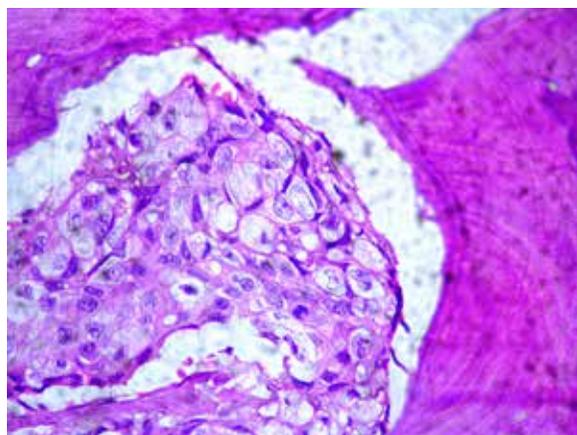
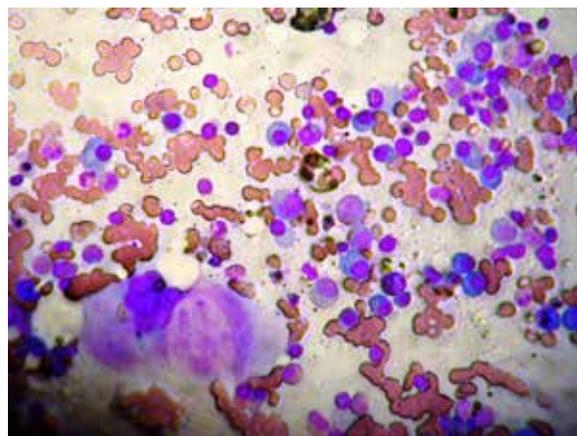
Myelodysplastic syndrome as a cause of pancytopenia is seen in the elderly (70 years)⁸. The case in our study was a 65 yr male who presented with anemia not responding to Iron, folate & vit B12 supplements. Dyspoietic features were seen in 10% of cell of all lineages. However cytogenetic study for trisomy 8, monosomy 7, del 5q translocation commonly encountered genetic aberrations in Refractory cytopenia with multilineage dysplasia, for confirmation was not done⁸.

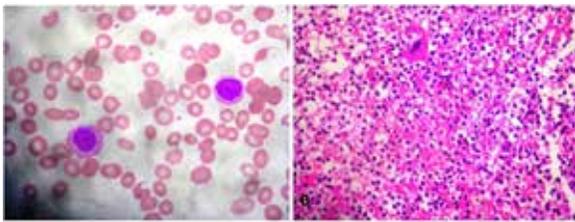
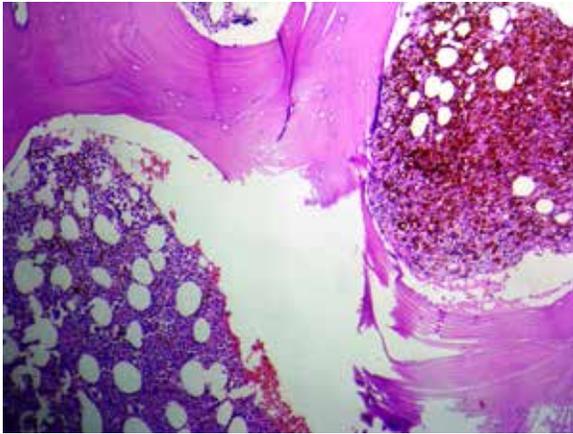
Bone marrow involvement is frequently seen in non Hodgkin's lymphomas such as diffuse large B-cell lymphoma, follicular lymphoma, small lymphocytic lymphoma (SLL), Peripheral T-cell (PTC) lymphoma, unspecified, enteropathy-associated T-cell lymphoma and mantle cell lymphoma⁹. In the present study, BM involvement was seen in anaplastic large cell lymphoma and diffuse large B cell lymphoma.

There is a long list of drugs causing pancytopenia. Of these the important ones include, cytotoxic drugs, Chloramphenicol, NSAIDs, Colchicine, Sulfonamides, Phenothiazines, Anti-epileptics, Anti-diabetics etc^{10,11}. In the present study, a case of rheumatoid arthritis on Azathioprine presented with pancytopenia.

CONCLUSION :

Bone marrow examination plays a very important role in the investigation of pancytopenia. Megaloblastic anemia, dimorphic anemia, Iron deficiency anemia & acute leukemia are the most common causes of pancytopenia, but other less common causes such as aplastic anemia, metastatic deposits, myeloma, malarial infection, lymphoma, Myelodysplastic syndrome, HIV & drug induced pancytopenia should also be kept in mind.





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LEGENDS:

13. Fig2 Bonemarrow with increase in plasma cells Leishman stain 400X
14. Fig3 Bonemarrow with adenocarcinomatous deposits from breast carcinoma H&E 400X
15. Fig4 Bonemarrow with hemopoietic cells and metastatic deposits from melanoma H&E 100X
16. Fig5A Hairy cells in peripheral smear Leishman stain 400X B Bonemarrow with cells having fried egg appearance H&E 100X