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Research Article

Hematological Study of Pancytopenia in Patients Attending in Tertiary Care Hospital at, SKMCH, Muzaffarpur, Bihar

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ABSTRACT

Objective: The aim of present study was designed to ascertain the percentage of occurrence and cause of pancytopenia. **Materials and Methods**: A total of 232 patients fulfilled the criteria for Pancytopenia. Out of them 186 were subjected to Bone marrow examination and regular follow up and we have restricted our studies with them. **Results**: Most of the patients were ranged between 12 to 75 years of age with male preponderance and were seen in third decade of life. Commonest cause of pancytopenia was megaloblastic anemia Seen in 148 cases (79.56%) followed by hypersplenism due to kala-azar in 18 cases (9.67%) and in non-hodgkin'slymphoma 03(1.61%) cases. Pallor was seen in most cases. Massive splenomegaly was seen in kala azar, malaria. Hepatosplenomegaly was seen in many cases of megaloblastic anemia. In peripheral blood smear examination anisopoikilocytosis was the predominant finding of megaloblastic anemia, hypersplenism due to kala- azar and malaria. **Conclusion**: Bone marrow examination was of diagnostic value to the patients with pancytopenia. So, any case of anemia detailed study on physical finding, peripheral blood picture and for conformation bone marrow aspiration was done.

Key Words: *Pancytopenia, megaloblastic anemia, bone marrow examination*

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INTRODUCTION

Simultaneous presence of anemia, leucopenia and thrombocytopenia is knownas Pancytopenia, characterized byhemoglobin is less than 13.5 g/dl and 11.5 g/dl in male and female respectively, leukocyte count is less than $4x10^9$/L and the platelet count is less than $150x10^3/\mu l$[1].

Presence of pancytopenia in Peripheral blood smear is usually a manifestation of the bone marrow disorders which is may be either primary or secondary. Anemia, leucopenia or thrombocytopenia are the most common presenting complains.

Mild pancytopenia often does not cause symptoms. In severe cases symptoms including fatigue, pale skin, shortness of breath (dyspnea), weakness, dizziness, fever, easy bruising, bleeding from mucosa, petechiae, purpura, bleeding from gums and nose, cardiac symptoms, increased susceptibility to infection, confusion and loss of consciousness[1,2].

Pancytopenia starts due to the defect in bone marrow which is a spongy tissue inside bones is where blood cells are produced. Disease and exposure to certain drugs and chemicals can leads to bone marrow damage. Causes of pancytopenia are megaloblastic anemia, parasitic infection like kala azar and malaria[3]. Viral infections such as epstein bar virus (infectious mononucleosis), cmv and hiv; septicemia like disseminated tuberculosis (TB) and glycogen storage diseases (gaucher's disease) cause pancytopenia, cancers that affect bone marrow such as leukemia, multiple myeloma, myelofibrosis, Aplastic anemia, myelodysplastic syndrome (MDS), sub-leuekemic leukemia, non-hodgkin's (NHL) and hodgkin lymphoma, waldenstrom's macroglobulinemia causes pancytopenia[4], other is paroxysmal nocturnal hemoglobinuria, damage from chemotherapy or radiation, exposure to chemicals such as arsenic and benzene may lead to pancytopenia.

Nutritional deficiency is the also the common cause of pancytopenia like vitamin B_{12} and folate deficiency. Liver disease, excessive intake of alcohol and autoimmune disease like systemic lupus erthymatosus is also cause pancytopenia.

MATERIALS AND METHODS

The present study was conducted in the department of pathology Sri Krishna medical college, Muzaffarpur, during the period of April 2020 to December 2021. During this time, a total of 232 patients fulfilled criteria for pancytopenia, out of them186 were subjected to bone marrow examination and we have restricted our studies with them.

Inclusion criteria for analysis were taken as Hemoglobin (Hb) concentration <10 gms%, leukocyte count <4000/c.mm, platelets count <100,000/c.mm. Bone marrow aspirations or trephine were done using salah and jamshidi needle. A detailed clinical history and physical examination was also performed on each case.

Clinical details of age, sex, intake or exposure to chemicals or drugs, bone pain, fever, night sweats, malaise, weight loss and pruritus was taken. Symptoms of diseases causing major splenic enlargement was also ruled out. A detailed physical examination was done to look for the presence of hepatomegaly, splenomegaly, lymphadenopathy and sternal tenderness. Gum hypertrophy, evidence of hypersplenism and primary malignancy was searched for when necessary. Peripheral smears were examined for the presence of anisopoikilocytosis, circulating erythroblasts, hypo or hyper-segmented neutrophils, abnormally increased or decreased granulation in neutrophils, immature WBC, and lymphocytosis. Reticulocyte production index was also noted.

Results

The male: female ratio, in our studies was 1.2:1. The age ranged between 12 to 75 years Maximum number of patients was seen in the third decade of life, with a slight male preponderance.

The commonest cause as megaloblastic anemia seen in 148 Cases (79.56%), This was followed by aplastic anemia in 02 cases (1.07%), subleukemic leukemia in 02 cases(1.07 %), mylodysplastic syndrome in 01case (0.53%), hypersplenism due to kala-azar in 18 cases (9.67%), hypersplenism due to malaria in 09 cases (4.83%) , non-hodgkins Lymphoma in 03 cases (1.61%), myelofibrosis in 01 cases(0.53 %), multiple myeloma in 01 cases (0.53%), no any cases of waldenstrom's macroglobulinemia and disseminated tuberculosis in 01 case (0.53%).

Pallor was noted in all cases, splenomegaly was massive in cases of kala azar, malaria and myelofibrosis.Hepatosplenomegaly was seen in many of the cases of megaloblastic anemia followed by subleukemic leukemia and MDS. Lymphadenopathy was seen predominantly in cases of subleukemic leukemia, NHL and in disseminated koch's. Sternal tenderness was an important manifestation of subleukemic neukemia, followed by cases of MDS, NHL and myelofibrosis.

A detailed peripheral smear examination was done on all patients. Anisopoikilocytosis was the predominant finding in megaloblastic anemia, kala-azar, malaria, myelofibrosis and multiple myeloma.Other findings in megaloblastic anemia were hyper segmented neutrophils and few cases having increased reticulocytes and mild lymphocytosis. Lymphocytosis was predominantly noted among cases of aplastic anemia. Immature WBC's were noted in all cases of subleukemic leukemia and in most cases of MDS and NHL. Circulating erythroblasts were also noted in most cases of subleukemic leukemia and MDS, multiple myeloma and waldenstrom's macroglobulinemia had rouleaux formation.

Bone marrow aspiration was of diagnostic value to the patients with pancytopenia. Megaloblastic anemia has typical megaloblasts, with sieved chromatin and a synchronic N: C ratio. Hypoplasia of the marrow was noted in aplastic anemia. Hypercellular marrow was noted in cases of MDS, multiple myeloma, NHL, subleukemic leukemia and in inflammatory conditions. Dysplastic cells were evident in all cases of MDS.

DISCUSSION

The incidence of megaloblastic anemia varies from 0.8% to 32.26% of all pancytopenic patients. Our incidence of megaloblastic anemia was 79. 56%. This correlated with the studies done by Tilak et al., in 1999, whose incidence for the same was 68%[2]. Kumar et al also showed the incidence of 37%, in megaloblastic anemia among pancytopenia patients[5]. All the above studies done in India, stresses the importance of megaloblastic anemia being the major cause of pancytopenia, which may present acutely in the critically ill patients should be rapidly corrected.

Aplastic anemia varies from 10 to 52.7% in incidence among pan cytopenicpatients. In aplastic anemia, due to failing of hematopoiesisblood cell counts are very low, and the bone marrow seems to be empty. Aplastic anemia is an immune mediated disease, and may be due to active destruction of blood forming cells by lymphocytes. The bizarre immune response may be triggered by environmental exposures, like chemicals, drugs, viral infections and endogenous antigens activated by genetically altered bone marrow cells.

This underlying mechanism is similar to other human disorders of lymphocyte - mediated tissue specific organ destruction (diabetes, multiple scleroses, uveitis, colitis etc.). Aplastic anemia varies in the prevalence, in causes of pancytopenia. It is the predominant cause, as seen in studies of Kumar et al., whereas it is the least cause in our studies and studies of Tilak et al.[2,5].

Subleukemic leukemia was noted in 02 cases of pancytopenia (1.07%). Bone marrow was of diagnostic value in these cases, besides the sternal tenderness. There are few interesting cases in the literature, giving proof for the initial pancytopenic phase, which turned out to be acute lymphocytic leukemia (AML) and chronic lymphocytic leukemia (CML) in due course.

Hypersplenism was the cause pancytopenia in 14.5 % of cases (out of which 9.67% was due to Kala azar and 4.83% due to Malaria). Leishmania donovani bodies seen in the bone marrow aspirate and, malarial parasites seen in the peripheral, blood smear were diagnostic of kala azar and Malaria respectively. Tilak has reported on a similar kala azar related pancytopenia andmalaria related cytopenia's was also noted in studies done by Canard et al and Aruba et al[6,3].

Pancytopenia with few abnormal cells as seen in MDS, was noted in 0.53% of our cases. Hypercellularity of the bone marrow and presence of abnormal cells confirmed the cases. Myelodysplastic syndrome is presented by ineffective hematopoiesis. It differs from AML, by its increased apoptosis in early and mature hematopoietic cells. MDS may thus be suspected in cases of pancytopenia, as also revealed in various other studies

Pancytopenia related to hon-hodgkin's lymphoma was noted in 1.61% of our cases. Bone marrow infiltrate of hypercellular abnormal lymphoid cells was diagnostic of NHL. Studies of ma et al has also described pancytopenia in a case of lymphoma[7].

Myelofibrosis was seen in 0.53% of our cases of pancytopenia. Literature also reveals pancytopenia in studies done by kiss et al in a case of myelofibrosis[8].

Pancytopenia was seen in multiple myeloma (0.53% of our cases) and no any case of waldenstrom's macroglobulinemia. Besides rouleaux's formation and bone marrow examination, bone x-ray, serum electrophoresis and urinary bence Jones protein aided in their diagnosis.

Disseminated tuberculosis related to pancytopenia was noted in 0.53% of our cases. Chest x-ray, needle biopsy of liver and mantoux test was done in them. Dalugama and Gawarammana also reported that various cases of pancytopenia in disseminated TB[9]. The above studies prove the prevalence of TB in India, and it is necessary to be aware of its manifestation as pancytopenia.

CONCLUSION

Complete blood count (CBC), Bone marrow aspiration and biopsy are gold standard tests for the diagnosis of pancytopenia. It is not a preventable disease but any drug causing pancytopenia, abrupt taking off or stopping the drug and avoid to exposure to chemicals and with good hygienic practice. Pancytopenia may be treated as drugs to stimulate blood cell production in bone marrow, blood transfusion, antibiotics to treat infection and bone marrow transplantation.

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Table – 1

Causes of Pancytopenia	Hepatomegaly	Splenomegaly	Lymphadenopathy	Sternal tender	Anisopoikilocytosis	Immature RBC	Hyper Segmented Neutrophil	Immature WBC	Lymphocytosis	Increased retics
Megaloblastic anemia n = 148(79.56%)	40	38	01	-	138	14	-	13	09	-
Aplastic anemia n = 02 (1.07%)	01	-	-	-	01	-	-	-	02	-
Subleukaemic leukemia n=02 (1.07%)	02	01	01	02	01	01	-	02	-	-
Myelodysplastic syndrome n =01 (0.53%)	01	01	-	01	-	01	01	01	-	-
Hypersplenism due to kala-azar n=18(9.67%)	18	18	-	-	17	-	-	-	-	-
Hypersplenism due to malaria n=09 (4.83%)	04	09	-	-	09	-	-	-	-	-
Non-hodgkins lymphoma n=03 (1.61%)	03	03	-	-	-	-	-	-	-	-
Myelofibrosis n=01 (0.53%)	01	01	-	01	01	-	-	-	-	-
Multiple myeloma n=01(0.53%)	-	01	-	-	01	-	-	-	-	-
Waldenstrom's macroglobulinemia n=00 (0.00%)	-	-	-	-	-	-	-	-	-	-
Disseminated tuberculosis n= 01 (0.54%)	01	01	01	-	-	-	-	-	-	-

Table-1 shows cause, physical finding and peripheral blood picture of pancytopenia

Megaloblastic anemia seen in 148 Cases (79.56%), this was followed by aplastic anemia in 02 cases (1.07%), subleukemic leukemia in 02 cases(1.07%), mylodysplastic syndrome in 01case (0.53%), hypersplenism due to kala azar in 18 cases (9.67%), hypersplenism due to malaria in 09 cases (4.83%), non-hodgkins lymphoma in 03 cases (1.61%), myelofibrosis in 01 cases (0.53 %), multiple myeloma in 01 cases (0.53%), no any cases of waldenstrom's macroglobulinemia and disseminated tuberculosis in 01 case (0.53%).