

Pancytopenia: A Clinico-Haematological Evaluation and Correlation with Bone Marrow Examination

Nitin Gupta, Arvind Khajuria

Abstract

The present study was carried out in the Post Graduate Department of Pathology, Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu (J&K) over a period of one year. During this period, bone marrow examination was carried out in all the 50 cases studied. The commonest cause of Pancytopenia as revealed by bone marrow examination was Megaloblastic anaemia (70%) followed by Aplastic anaemia (16%) and others

Key Words

Pancytopenia, Haematological, Bone Marrow Examination

Introduction

Pancytopenia is a reduction in the number of RBCs, WBCs, and platelets in the peripheral blood below the lower limits of the age-adjusted normal range for healthy people. It is therefore the combination of anaemia, leukopenia, and thrombocytopenia. The presenting symptoms are usually related to anaemia, leucopenia or thrombocytopenia. Anaemia leads to fatigue, dyspnea and cardiac symptoms. Thrombocytopenia leads to bruising and mucosal bleeding and neutropenia leads to increase susceptibility to infection. It is not a disease entity but a triad of findings that may result from a number of disease processes - primarily or secondarily involving the bone marrow (1,2). Delineation of etiologies & severity of pancytopenia determine the management and prognosis of the patients (3,4).

Material and Methods

The present study was carried out in the Post Graduate Department of Pathology, Acharya Shri Chander College

of Medical Sciences and Hospital, Sidhra, Jammu (J&K) over a period of one year. Patients of all age groups and both sexes were included. A total of 50 cases were selected based on clinical features and supported by laboratory evidence, which included peripheral blood counts, hemoglobin, leukocytes and platelets. Inclusion criteria were presence of all 3 of the following: hemoglobin, <9 g/dL; total leukocyte count (TLC), $<4,000/\mu\text{L}$; platelet count, $<100,000/\mu\text{L}$. (3) Peripheral smear was stained by Leishman stain for all the cases and examined in detail. Bone marrow aspiration was subsequently carried out under aseptic precaution using Salah's bone marrow aspiration needle after obtaining written consent from the patient or guardian.

Results

A total of 50 cases who presented with pancytopenia were studied. They consisted of 40 males and 10 females with a male to female ratio of 4:1. The age of patients

From the Department of Pathology, ASCOMS Sidhra, Jammu- J&K India

Correspondence to : Dr. Arvind Khajuria Prof and Head Department of Pathology, ASCOMS, Sidhra, Jammu - 180005- J&K India

ranged from 10-80 years.(mean age, 40 years).Out of the 50 cases, pancytopenia was observed in 10 pediatric patients(10-18 years). *Table no 1* shows the causes of pancytopenia in the study. The commonest cause of pancytopenia was Megaloblastic anaemia(70%) followed by Aplastic anaemia(16%), Subleukemic leukemia(6%), Hypersplenism due to malaria (4%),Non Hodgkin's lymphoma(2%) and one case of Multiple myeloma(2%).. *Table no 2* shows the physical findings in the study

The commonest mode of presentation was generalized weakness; other main symptoms were dyspnea, fever, weight loss. Pallor was noted in all cases. Hepatomegaly was present in 71.4 % and splenomegaly was present in 68.5 % of the cases of megaloblastic anaemia followed by Subleukemic leukemia and Malaria.Lymphadenopathy was predominant in all the cases of subleukemic leukemia

Table 1. Causes of Pancytopenia in our Study

Causes	No of cases	Percentage
Megaloblastic anaemia	35	70%
Aplastic anaemia	8	16%
Sub-leukemic leukemia	3	6%
Malaria	2	4%
NHL	1	2%
Multiple myeloma	1	2%

and NHL.Sternal tenderness was also present in subleukemic leukemia followed by NHL and multiple myeloma.

A detailed Peripheral smear examination was done on all the patients. Anisopoikilocytosis was the predominant finding in Megaloblastic anaemia and malaria.The predominant blood picture was dimorphic anaemia(60%), followed by macrocytic anaemia (20%).Normocytic normochromic anaemia constituted 15% of the cases and normocytic hypochromic anaemia constituted 5 % of the cases.Leukopenia and thrombocytopenia were seen in all the cases. *Fig.1* shows haematological parameters in the 3 subgroups of pancytopenia

Other findings included were the presence of hypersegmented neutrophils in all the cases (100%) of megaloblastic anaemia and presence of circulating megaloblast in 40% of the cases of megaloblastic anaemia.

Fig. 1 The Commonest Cause of Pancytopenia

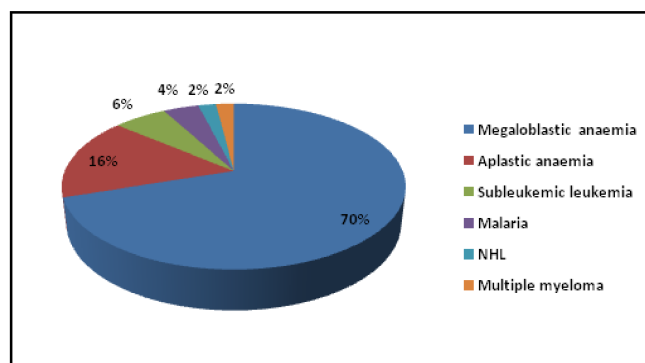


Table 2. Physical Findings in Pancytopenia Patients

		Hepatomegaly	Splenomegaly	Lymphadenopathy	Sternal Tenderness
Megaloblastic anaemia	35	25 (71.4%)	24(68.5%)	-	-
Aplastic anaemia	8	3 (37.5%)	-	1	-
Subleukemic leukemia	3	2	1	3(100%)	3(100%)
Malaria	2	1	2(100%)	-	-
NHL	1	-	-	1(100%)	1(100%)
Multiple myeloma	1	1	-	-	1(100%)

Bone marrow aspiration showed megaloblastic erythroid hyperplasia. Megaloblasts had the characteristic feature of sieved nuclear chromatin, asynchronous nuclear maturation and bluish cytoplasm with cytoplasmic blebs. Giant metamyelocytes and band forms were predominant in granulocyte series.

Lymphocytosis as predominantly noted among cases of Aplastic anaemia. Bone marrow aspiration showed hypocellular marrow in all the cases of aplastic anaemia with increased fat and reactive lymphoplasmacytosis. Of the three cases of Subleukemic leukemia 2 were of AML-M2 (acute myeloblastic leukemia) and 1 case was of ALL-L2 (acute lymphoblastic leukemia). Bone marrow was hypercellular in all cases. Erythroid and megakaryocytic series were reduced. Majority of cells were myeloblasts, and lymphoblasts, constituting more than 70% and 60% of cells in marrow, respectively. Bone marrow aspirate showed myeloblasts with Auer rods. Both the cases of Malaria showed pancytopenia, and trophozoites of plasmodium vivax on peripheral blood film. Bone marrow was hypercellular with megaloblastic change. No malarial parasites were seen on bone marrow smears. In one case of NHL, bone marrow examination showed infiltration by abnormal lymphoid cells. In one case of multiple myeloma, peripheral blood film showed marked rouleaux formation. Bone marrow examination showed sheets of plasma cells and plasmablasts replacing normal marrow elements. ESR was 90 mm in first hr which also supported the diagnosis.

Discussion

The incidence of megaloblastic anaemia was 70% in our study. This correlated with the study done by Gayathri and Rao (3) whose incidence for the same was 74.04%. Rangaswamy *et al* (5) reported Megaloblastic anaemia to be the commonest cause of pancytopenia in their study with an incidence of 33%. Doshi *et al* (6) also showed the incidence of 45% in megaloblastic anaemias among pancytopenia patients. Dasgupta *et al* (7) showed

megaloblastic anaemia to be the second most common cause of pancytopenia in their study with an incidence of 20.97%. It is a rapidly correctable disorder and should be promptly notified. Although bone marrow aspiration studies are uncommon in suspected cases of megaloblastic anemia, if the diagnosis does not appear straightforward or if the patient requires urgent treatment and haematological assays are not available, bone marrow aspiration is indicated. As facilities for estimating folic acid and vitamin B12 levels are not routinely available in most centers in India, the exact deficiency is usually not identified.

The incidence of aplastic anemia in our study was 16%, which correlated with the studies done by Gayathri and Rao (3) with an incidence of 8.26% and Rangaswamy *et al* (5) with an incidence of 14%. A higher incidence of 33.47% was reported by Dasgupta *et al* (7). Similarly Jha *et al* (8) in their study found aplastic anaemia to be the most common cause of pancytopenia with 43 cases (29%). Gupta *et al* (9) reported Aplastic anaemia to be the most common cause of pancytopenia (43%) in their study.

Subleukemic leukemia was noted in 3 cases of pancytopenia (6%) in our study which included 2 cases of AML-M2 and 1 case of ALL-L2. Bone marrow was of diagnostic value in these cases. Desalphine *et al* (1) reported 7 cases (14%) of subleukemic leukemia in their study. Out of seven patients in their study, five presented as AML and 2 patients presented as ALL. The diagnosis of AML was based on bone marrow aspiration study. Gayathri and Rao (3) reported 4 patients (3.85%) of subleukemic leukemia. Three cases were of AML-M2 (acute myeloblastic leukemia) and 1 case was of ALL-L2 (acute lymphoblastic leukemia).

Hypersplenism due to malaria was present in 4% of our cases. Gayathri and Rao (3) reported an incidence of 1.9% of the cases of malaria in their study. Jain and Naniwadekar (4) reported an incidence of 20.5% cases

of malaria out of the total pancytopenia cases. Malaria related cytopenias was also noted in studies done by Cannard *et al* (10) in (2%) cases and Albaker (11) one case. Santra and Das (12) reported two cases (1.8%) of pancytopenia due to malaria in their study

Pancytopenia related to Non Hodgkins Lymphoma was noted in 2% of our cases which was comparable to the study done by Santra and Das (12) who also described 1 case (0.90%) of NHL presenting with pancytopenia which was diagnosed by bone marrow examination. Jain and Naniwadekar (4) reported 5 cases (11.9%) of pancytopenia related to NHL in their study.

We encountered 1 case of multiple myeloma, constituting 2% of total cases. In our study, the patients presented with generalized weakness, fever and bony tenderness. ESR was 90 mm at the end of 1 hour by Westergren's method. Plasmablasts with increased N:C (nuclear- cytoplasmic) ratio, multinuclearity and nuclear lobulation were seen by bone marrow examination. Gayathri and Rao (3) reported an incidence of 0.96% cases of pancytopenia due to multiple myeloma. Jain and Naniwadekar (4) reported an incidence of 0.8% of cases and Santra and Das (12) reported an incidence of 0.90% of cases of multiple myeloma presenting with pancytopenia in their studies

Conclusion

Pancytopenia is a relatively common haematological entity. It is a striking feature of many serious and life-threatening illnesses, ranging from, megaloblastic anemia to fatal bone marrow aplasias and leukemias. It should be suspected on clinical grounds when a patient presents with unexplained anemia, prolonged fever and tendency to bleed. The present study concludes that detailed primary haematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding disease process and to diagnose or to rule out the causes of cytopenia. These are also helpful in planning further investigations and management. Severe

pancytopenia has significant relation with the clinical outcome and can be used as a prognostic indicator.

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