Original Article

Pathology

Pancytopenia: A Clinico-Haematologic Analysis of 100 Cases At Tertiary Care Hospital

1. Farzana Memon 2. Tanweer Ahmed Shaikh 3. Jawaid Hussain Memon 4. Rasheed Ahmed Soomro

1. Assoc. Prof. of Pathology, LUM&HS, Jamshoro 2. Asstt. Prof. of Pathology, LUM&HS, Jamshoro 3. Asstt. Prof. of Pathology, PUM&HSW, Benazirabad 4. Asstt. Prof. of Pathology, LUM&HS, Jamshoro

ABSTRACT

Object: Pancytopenia is a serious haematological problem, which makes the patient prone to anaemic manifestations, infections and bleeding tandency. Underlying it are many diseases, which are diagnosed by bone marrow aspiration & trephine biopsy. This study was done to describe different etiological causes of pancytopenia in adults population of lower Sindh.

Study Design: Cross sectional study.

Place & duration: The study was carried out in the department of pathology and diagnostic & research laboratory, Liaquat University of Medical & Health Sciences (LUMHS) Hyderabad in collaboration with medical units of LUMHS Jamshoro from January 2009 to June 2010.

Materials and Methods: A total of 100 adult patients with Pancytopenia diagnosed on peripheral blood smear examination were admitted in four medical units of LUMHS Jamshoro during study period, were followed by bone marrow examination and trephine biopsy wherever required.

Results: Megaloblastic anaemia was diagnosed in 46% cases, followed by aplastic anaemia in 22% and Acute leukaemia in 10% cases and 5% cases each were diagnosed as hyperspleenism and disseminated tuberculosis. Multiple myelomas were diagnosed in 4% cases, Meylodysplastic syndrome in 3% and Non-Hodgkins lymphoma is seen in 3% and Myelo-fibrosis in 2% cases.

Conclusion: It is concluded that Megaloblastic anaemia is most common cause of Pancytopenia in our series followed by aplastic anaemia and acute leukaemia.

Key Words: Pancytopenia, Megaloblastic anaemia, Aplastic anaemia.

INTRODUCTION

Pancytopenia is a reduction in the number in any of the three types of peripheral blood cell. A reduction in all three types of cellular components is termed pancytopenia and this involves anemia, leucopoenia, and thrombocytopenia.[1]

The spectrum of disorders primarily or secondarily affecting the bone marrow may manifest with peripheral pancytopenia.[2]. Patient usually presents with complaints ascribed to anaemia, thrombocytopenia, and rarely leucopenia which in later stages is responsible for the downhill course. Various factors encompassing geographic distribution and genetic disturbances may cause variation in the incidence of disorders causing pancytopenia.[2]

Pancytopenia can be due to decrease in hematopoietic cell production in the bone marrow e.g. by infections, toxins, malignant cell infiltration or suppression or can have normocellular or even hypercellular marrow, without any abnormal cells, e.g. ineffective hematopoiesis and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells.[1]

The basic investigations in a suspected case of pancytopenia include Complete Blood Count with peripheral blood film and Reticulocyte count. In peripheral film, blast cells may be evident in patients where pancytopenia is due to malignant infiltration. Neutrophils might show absent granulation and nuclear abnormalities suggestive of pre-leukemic or myelodysplastic states. Bone marrow examination is indicated in all cases of pancytopenia where the underlying cause is not obvious. This is particularly needed to exclude leukemia or other malignant infiltration.

Megaloblastic anemia has been found to be the most common cause of pancytopenia worldwide. Diagnosis of megaloblasitc anemia requires only complete blood count, peripheral blood smear and bone marrow cytology, which is cost effective. Nutritional factors, recurrent infection and deficiencies of vitamin B_{12} and folate seem to be associated strongly with megaloblastic anemia.[3]

Megaloblstic anaemia results from abnormal maturation of haematopoietic cells due to faulty DNA synthesis. Two vitamins, cobalamin (vitamin B_{12}) and folic acid are essential for DNA biosynthesis. Deficiency of either vitamin results in asynchrony in the maturation of the nucleus and cytoplasm of rapidly regenerating cells. In the haematopoietic system this asynchrony results in abnormal nuclear maturation with normal cytoplasmic maturation, apoptosis, ineffective erythropoiesis,

intramedullary haemolysis, pancytopenia and typical morphological abnormalities in the blood and marrow cells.[4,5]

Pancytopenia is an important clinicohaematological entity encountered in our day-to-day clinical practice. There are varying trends in its clinical pattern, treatment modalities, and outcome. The aim of this study was to evaluate the etiological spectrum of pancytopenias on the basis of bone marrow examination.

MATERIALS AND METHODS

This cross sectional study was carried out in the department of pathology, Liaquat University of Medical and Health Sciences Jamshoro and Diagnostic Research Laboratory Liaquat University Hospital Hyderabad in collaboration with all Medical wards of Liaquat University Hospital Jamshoro from 1st January 2009 to 30th June 2010. A total of 100 cases above 14 years of age, of either sex with diagnosis of pancytopenia on peripheral blood smear were included in this study; those who were already diagnosed by bone marrow examination, received blood transfusion, patients on cancer chemotherapy were excluded from this study.

Pancytopenia was diagnosed in the presence of anemia (hematocrit value <0.35 in women, <0.40 in men), leucopenia (WBC <3.5x10/L) and thrombocytopenia, (platelets <150x10/L).

In all patients, a detailed relevant history including the treatment history, history of drug intake, radiation exposure. Meticulous clinical examination of every patient was done for pallor, jaundice, hepatomegaly, splenomegaly and lymphadenopathy. After history and examination basic investigations were performed for each patient including Haemoglobin, hematocrit value, Total leukocyte count, Platelet count, Reticulocyte count. Absolute values including packed cell volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated for every patient, Blood film examination after staining with giemsa's stain for red cell morphology and malarial parasite (MP) was performed, Chest radiograph and abdominal ultrasonography was done in selected patients. Bone marrow examination was done in all patients and wherever required, a trephine biopsy were also performed.

Data Analysis: The data were evaluated in statistical program for social sciences version 16.0. Qualitative data (frequency and percentages) such as age (in groups), physical and blood findings, causes etc. were presented as n(%). No statistical test was applied.

RESULTS

Total 100 cases of pancytopenia were included in this study based on inclusion and exclusion criteria. Male female ratio was 1.5:1. Minimum age for patients wit pancytopenia was 15 years and maximum age was 70 years (Table No.1).

Majority of the patients 40 (40.0%, n = 100) were ranged from 31 to 40 years of age group. Sixty (60.0%), n = 100) were males and 40 (40.0%, n = 100) were females.

Table No.1: Age Distribution of Patients (n = 100)

Age group	No. of cases	(%)
15 – 20	10	10.0%
21 – 30	20	20.0%
31 – 40	40	40.0%
41 – 50	15	15.0%
51 – 60	10	10.0%
61 – 70	05	5.0%

Table No. 2: Physical findings in pancytopenic patients (n = 100)

Causes	Number	Hepatomegally	Spleemegally	Lymphadenopathy	Sternal tenderness
Megaloblasti anaemia	46	20	22	02	2
Aplastic anaemia	22	12	06	04	-
Subleukaemic leukaemia:	10	03	03	04	4
- Acute lymphoblastic leukaemia = 6)	-	-	-	-	-
- Acute myeloblastic leukaemia = 4)	-	-	-	-	-
Hyperspleenism	05	01	05	-	-
Myelodysplastic syndrome	03	03	03	-	3
Myelo fibrosis	02	-	02	-	2
Non-hodgkins lymphoma	03	02	01	03	2
Multiple myeloma	04	-	01	-	-
Disseminated tuberculosis	05	-	-	03	-

Megaloblastic anaemia was diagnosed in 46 (46.0%, n= 100), 20 (43.4%, n = 46) clinically presented with hepatomegaly, 22 (47.8%, n – 46) with spleenomegally and 2 (4.3%, n = 46) with Lymphadenopathy and Sternal tenderness respectively. Aplastic anaemia was noted in 22 (22.0%, n = 100), 12 (26.0%, n = 22) presented with hepatomegaly, 06 (27.0%, n = 22) with

spleenomegally and 4 (18.18%, n = 22) cases had lymphadenopathy.

Table No.3: Causes of pancytopenia as seen on bone marrow examination (n = 100)

Causes	No. of cases	(%)
Megaloblasti anaemia	46	46.0%
Aplastic anaemia	22	22.0%
Subleukaemic leukaemia:	10	10.0%
- Acute lymphoblastic leukaemia = 6)	-	-
- Acute myeloblastic leukaemia = 4)	-	-
Hyperspleenism	05	5.0%
Myelodysplastic syndrome	03	3.0%
Myelo fibrosis	02	2.0%
Non-hodgkins lymphoma	03	3.0%
Multiple myeloma	04	4.0%
Disseminated tuberculosis	05	5.0%

Table No.4: Peripheral Blood Findings In Pancytopenic Patients (n = 100)

Causes	No. of cases	A	B	C	D	E
Megaloblasti anaemia	46	38	10	08	-	05
Aplastic anaemia	22	04	-	-	-	16
Subleukaemic leukaemia:	10	02	-	-	06	04
- Acute lymphoblastic leukaemia = 6)	-	-	-	-	-	-
- Acute myeloblastic leukaemia = 4)	-	-	-	-	-	-
Hyperspleenism	05	03	02	-	-	02
Myelodysplastic syndrome	03	01	02	-	-	02
Myelo fibrosis	02	01	-	-	-	01
Non-hodgkins lymphoma	03	-	-	-	-	03
Multiple myeloma	04	01	-	-	-	-
Disseminated tuberculosis	05	02	-	-	-	04

A = Anisopoiklocytosis. B = Immature RBC
C = Hypersemented neutrophils D =Immature WBC
E = Lymphocytosis

Ten (10.0%, n = 100) patients had subleukaemic leukaemia, out of them, 03 (30.0%, n = 100) had hepatmegally and spleenomegally respectively, 05 (5.0%, n = 100) cases were diagnosed with Hyperspleenism and presented with spleenomegally and lymphadenopathy. Disseminated tuberculosis was diagnosed in 05 (5.0%, n= 100). Multiple myeloma was diagnosed in 4 (4.0%, n=100) cases (Table No. 2&3).

The results of this study showed that the Megaloblastic anaemia was most common cause and showed Anisopoiklocytosis in 38 (82.60%, n = 46), immature RBC in 10 (21.7%, n = 46), Hypersegmented neutrophils in 8 (17.3%, n = 46) and Lymphocytosis in 5(10.8%, n=46) on peripheral blood smear examination. While cases of Aplastic anaemia showed increase number of lymphocytes on peripheral blood smear examination (Table No.4).

DISCUSSION

Pancytopenia is not an uncommon hematological problem encountered in our clinical practice and should be suspected on clinical grounds when a patient presents with unexplained anemia, prolonged fever and tendency to bleed. Underlying it are many diseases, which are diagnosed by bone marrow aspiration and trephine biopsy.[6]

The mechanism by which pancytopenia develops appears to be either associate with decrease in haematopoietic cell production as a result of destruction of the marrow tissue by toxins, replacement by abnormal or malignant tissue, or perhaps suppression of normal growth and differentiation.

In all cases, megaloblastic anemia constituted the largest group. Megaloblastic anemia is the most common disorder in our patients. The incidence of megaloblstic anaemia varies from 0.8% to 32.26% of all pancytopenic patients.[7]

In our study the incidence of megaloblastic anaemia was 46%. In a local study conducted by Aziz T et al.[1] in Karachi, he reported that megaloblastic anemia was the most common cause of Pancytopenia at 40.9% which falls in the wide range of results reported in other local studies that vary from 38% to 72%.[8-11] Megaloblastic anemia due to vitamin B12 or folic acid deficiency is now a well-recognized and established cause of cytopenias.[12]

The second most common cause of pancytopenia in our study was aplastic anemia (22.0% patients) whereas Aziz T et al. and his colleagues showed 31.8%. In other similar studies it varied from 38% to 41%[11,12,13,18] although it was higher than Aplastic Anemia in the West which is reported to be between 10-25%. Aplastic anemia is thought to be more common in the Orient than in western world which may be related to environmental factors such as increased exposure to toxic chemicals rather than genetic factors as this increase is not seen in people of oriental ancestry presently living in US.[14,15]

The incidence of acute lymphoblastic leukemia at our setup is lower as compared to develop countries. In our study, acute leukemia 10(10.0%, n = 100) was found to be the third most common cause of Pancytopenia which is similar to a study conducted by Aziz T et al.[1] who

observed 9.99% in his study whereas Savage et al[17] who reported that the most common cause of pacytopenia was megaloblastic anemia followed by aplastic anemia, acute leukemia, AIDS and hypersplenism while in another local study conducted by Tariq M et al.[16] in Peshawar, in their study leukemias were noted, with acute lymphoblastic leukemia as the commonest malignancy in their patients (12%). These results correlate well to our findings

CONCLUSION

Megaloblastic anaemia and Aplastic anaemia are the major causes of pancytopenia in our patients. Physical findings and peripheral blood picture provide valuable information in workup of pancytopenic patients. However some un-common cause like myelodysplastic syndreome, multiple myeloma, myelofibrosis and hyperspleenism should also be kept in mind while planning the investigations for complete workup of pancytopenic patients. Bone marrow aspiration and trephine biopsy were followed to be useful diagnostic tool for evaluating the etioilogy of pancytopenia.

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Address for Corresponding Author:
Dr. Farzana Memon
House No. A-15, Sajjadabad Housing Soceity
Behind NLC Dryport Jamshoro Road Hyderabad.
Ph: 022-2620516, Cell: 0300-3021088
Email: drfarzana_memon@hotmail.com