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EVALUATION OF CAUSES OF PANCYTOPENIA ON THE BASIS OF BONE MARROW EXAMINATION AT TERTIARY HEALTH CENTER IN CENTRAL INDIA

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Abstract:

Introduction:

Pancytopenia is reduction in all the three major cellular elements of blood; hence it is the simultaneous presence of anemia, leucopenia and thrombocytopenia. The causes of pancytopenia can be (a) ineffective hematopoiesis with cell death in the marrow, (b) formation of defective cells which are rapidly removed from circulation, (c) sequestration and/or destruction of cells by the action of antibodies or, (d) trapping of normal cells in a hypertrophied and over-reactive reticuloendothelial system.[5] The pattern of diseases leading to pancytopenia is expected to vary in different population groups with their difference in age pattern, nutritional status, and prevalence of infective disorders. The severity of pancytopenia and the underlying pathology determines the management and prognosis of these patients.

Material & Methods:

The present study was carried out in the department of pathology in a tertiary care hospital in central India, from September 2018 to October 2020 from the patients fulfilling the inclusion and exclusion criteria. The cases were selected on the basis of clinical features and laboratory results. Bone marrow aspiration was carried out after getting a written consent from the patient or the guardian.

Result:

The most common etiology noted was megaloblastic anemia (52%), followed by dimorphic anemia (19%), hypersplenism (10%), leukemia and others.

Key words:

Pancytopenia, Bone Marrow Examination

Introduction:

Pancytopenia is reduction in all the three major cellular elements of blood; hence it is the simultaneous presence of anemia, leucopenia and thrombocytopenia. It is not a disease entity but a triad of findings that may result from various disease processes, primarily or secondarily involving the bone marrow.[1] The complete hematological work up with good clinical correlation is of utmost importance to evaluate the cause of pancytopenia and planning further investigations.[2] Bone marrow aspiration and biopsy are indispensable adjunct to the study of hematopoetic

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disorders. The final interpretation requires the integration of peripheral blood findings, bone marrow aspirate and trephine biopsy evaluation, together with the results of supplementary tests such as immunophenotyping, cytogenetic analysis and molecular genetic studies as appropriate.[3] Bone marrow examination is indicated in all cases of pancytopenia where the underlying cause is not quite obvious. This is particularly needed in case of hypoplasia/aplasia and to exclude leukemia or other malignant infiltration.[4] Routine aspiration smears may have to be combined with trephine biopsies as quite often aspiration might yield dry or bloody tap.

The causes of pancytopenia can be (a) ineffective hematopoiesis with cell death in the marrow, (b) formation of defective cells which are rapidly removed from circulation, (c) sequestration and/or destruction of cells by the action of antibodies or, (d) trapping of normal cells in a hypertrophied and over-reactive reticuloendothelial system.[5] The pattern of diseases leading to pancytopenia is expected to vary in different population groups with their difference in age pattern, nutritional status, and prevalence of infective disorders. The severity of pancytopenia and the underlying pathology determines the management and prognosis of these patients. The etiology of pancytopenia can vary from treatable disorders-such as megaloblastic anemia to more serious conditions such as the myelodysplastic syndromes which increase the likelihood of developing hematological malignancies in future.[6] With this background present study was planned to assess causes of pancytopenia on the basis of bone marrow findings.

Objective: To study causes of pancytopenia on the basis of bone marrow findings.

Material & Methods:

The present study was carried out in the department of pathology in a tertiary care hospital in central India, from September 2018 to October 2020 from the patients fulfilling the inclusion and exclusion criteria.

The cases were selected on the basis of clinical features and laboratory results. Bone marrow aspiration was carried out after getting a written consent from the patient or the guardian.

INCLUSION CRITERIA:

Presence of all three of the following:

Hemoglobin < 10gm/dl

Total leukocyte count (TLC) < 4000/microL

Platelet count < 1,50,000/ microL

EXCLUSION CRITERIA:

Patients who have recently received blood transfusions

Patients on radiotherapy

Patients on cytotoxic drugs

Pregnant patients

Patients with psychiatric illness

FOLLOWING INVESTIGATIONS WERE CARRIED OUT:

1. Hemoglobin
2. RBC count
3. WBC count

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4. Platelet count
5. HIV, HBsAg
6. Bleeding time and clotting time when required
7. Peripheral smear study
8. Bone marrow study

SAMPLE COLLECTION:

Two ml of blood was collected by venepuncture under aseptic precaution in a dry bulb containing ethylene di-amine tetra acetic acid (EDTA) anticoagulant. Samples were processed by an automated autoanalyzer and blood counts with other details were obtained.

PERIPHERAL SMEAR STUDY

The peripheral smear was studied after staining with Leishman's stain. Special stains like periodic acid schiff reagent stain, myeloperoxidase, sudan black and perl's iron stain were used wherever indicated.

Smears were examined under microscope for following features

• RBC morphology- type, morphological anemia, immature RBC's, any inclusions.
• WBC morphology – for differential count, morphology of each cell, immature cells.
• Platelet count and its morphology.
• Any parasites.

BONE MARROW ASPIRATION:

A written consent from the patient or the patent's guardians were obtained prior to the procedure.

Needle used: Salah needle

The aspiration site was posterior iliac crest.

PROCEDURE:

Patient was given left or right lateral decubitus position.

The posterior superior iliac spine was located.

The site was prepared, cleaned with antiseptic betadine and spirit. The surrounding area was draped exposing only the aspiration area.

Intramuscular atropine was given and xylocaine skin sensitivity test was done prior to the procedure.

Skin, subcutaneous tissue and periosteum overlying the selected site was infiltrated with a local anesthetic such as 2-5 ml 2% lignocaine.

Waited until anesthesia has been achieved.

Bone marrow aspiration was performed using salah needle.

With a boring movement bone marrow aspiration needle with a sty-let in place was passed perpendicularly into the cavity of the ilium at the center of the oval posterior superior iliac spine.

When the bone had been penetrated sty-let was removed.

2 ml syringe was attached and marrow contents were sucked up for making films.

About 0.2 to 0.5 ml of fluid was aspirated.

Aspiration needle was then removed and pressure was applied to the site with cotton pads until bleeding stopped.

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Preparing the films from bone marrow aspirates: The films were made 3-5 cm in length of aspirated marrow using a smooth-edged glass spreader of not more than 2cm width. The marrow fragments were dragged behind the spreader by leaving behind a trail of cells.
After procedure was completed pressure bandage was done and patient was instructed to check the site frequently and to report in case of any bleeding.
These aspiration smears were dried and stained with Leishman or MGG stain

BONE MARROW BIOPSY

Biopsy, whenever required was done along with aspiration in the same setting. Bone marrow biopsy needle inserted at bone with stylet then stylet was withdrawn from the needle and the cap was closed, and then was further pushed into the cavity by rotating movements for about 0.5-1cm. The needle was then withdrawn in the reverse rotating direction. A wire probe was inserted at the needle hub on to a sterile gauge. The specimen was fixed in 10% formalin overnight and decalcified in 6% EDTA for 72 hrs. It is then processed similar to histopathological sample and H and E section were studied.

Statistical analysis:

The statistical analysis was performed through SPSS for windows (version 16.0). The Chi square test procedure tabulates a variable into categories and computes chi square statistics. This test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user specified portion of values.

Result:

Fifty patients with hematological diagnosis of pancytopenia were studied during the period of September 2018 to October 2020, in the department of pathology at tertiary care teaching hospital in central India.

Table No.1: Age And Sex Distribution In Patients With Pancytopenia

Age	Female	Male	Total cases	Percentage
18-20	0	1	1	2
21-30	3	5	8	16
31-40	4	8	12	24
41-50	4	10	14	28
51-60	5	8	13	26
61-70	0	2	2	4
Total	16	34	50	100

$X2= 3.362$, $p<10$, $df=5$

Most of the patients were in the age group of 41-60 years (54%) and least occurrence was seen in the age group of 18-20(2%). There was a male predominance and the male to female ratio was 2.1:1

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Table No.2: Incidence of Pancytopenia in Leukemia, MDS, Dengue Fever, Hemolytic Anemia, Malaria

	No. of Patients	Percentage
Malignant diseases- Acute myeloblastic leukemia	3	37.5
Myelodysplastic syndrome	1	12.5
Dengue fever	1	12.5
Hemolytic anemia	1	12.5
Malaria	1	12.5
Multiple myeloma	1	12.5
Total	**8**	**100**

Pancytopenia was observed in 3 patients with Acute myeloblastic leukemia followed by 1 patients each with myelodysplastic syndrome, dengue fever, hemolytic anemia, malaria & multiple myeloma.

Table No.3: Bone Marrow cellularity in Patients with Pancytopenia

Cellularity	No. of cases	Percentage
Hypercellular	41	82
Hypocellular	4	8
Normocellular	5	10
Total cases	50	100

$X2= 18.777$, $p < 0.000$

Majority of the patients had hypercellular marrow (82%) and the least number of patients had hypocellular marrow (8%).

Table No. 4: Causes of Pancytopenia in study Participants

Etiology	Total no. cases	
	No.	Percentage
Megaloblastic anemia	24	52.17
Dimorphic anemia	9	19.56
Hypersplenism	5	10.8

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Leukemia	3	6.52
Myelodysplastic syndrome	1	2.17
Dengue	1	2.17
Hemolytic anemia	1	2.17
Malaria	1	2.17
Multiple myeloma	1	2.17
Total	46	100

The most common etiology noted was megaloblastic anemia (52%), followed by dimorphic anemia (19%), hypersplenism (10%), leukemia and others.

Discussion:

Pancytopenia is commonly seen in various clinical settings all over the world. The recognition of the cause of the pancytopenia is important in order to come to the accurate diagnosis and proper treatment planning. A total of 50 cases were studied from September 2018 to October 2020, at tertiary care hospital in central India.

Age of the patients in the present study ranged from 18-70 years with the mean age of 45 years and there was male predominance with the M:F ratio being 2.1:1. Most common age group affected in Tilak et al[7] was between 5-20 years, in Khodke et al[5] it was 12-30 years, in Khunger et al[8] it was in the third decade and in Yadav et al[9] it was in the range of 41-50 years. In the present study, it was in the range of 41-50 years, which is in accordance with Yadav et al.[9]

Pancytopenia has many diverse etiological factors, and the occurrence of particular pathology as the entity causing pancytopenia may depend on various factors like genetic constitution, geographical distribution, dietary habits etc.

The present study shows megaloblastic anemia as the most common cause of pancytopenia with 24 cases, constituting 48% of all the pancytopenia cases, and findings was similar with the studies conducted by Khunger et al[8] and Tilak et al[7] where in the megaloblastic anemia constituted 72% and 68% of all the pancytopenia cases. Recently, Gayathri et al[10] Reddy et al[11] and Varma et al[12] found 74%, 38% and 39% of the megaloblastic anemia cases in their studies.

Present study revealed Dimorphic anemia in 18% of the total pancytopenia cases, similar to the studies done by Yadav et al[9] where the incidence was 17%.

Present study revealed hypersplenism as cause of Pancytopenia in 10.8% of patients. In contrast to the findings in the present study Gayathri et al[10] and Reddy et al[11] showed 35% and 28% of the splenomegaly cases in pancytopenia. Aplastic anemia contributed to about 8% of the total pancytopenia cases in the present study. It was the second most common cause in the studies done

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by Tilak et al[7], Khunger et al[8] here it constituted to about 7% and 29% of the total pancytopenia cases respectively. Yadav et al[9] reported aplastic anemia with 12.8% cases, while Khodke et al[5] with 14% of the total pancytopenia cases. Our findings were similar to the studies conducted by Graham et al[13] and Varma et al[12], where aplastic anemia contributed to total of 6% and 8% of all the pancytopenia cases. In the present study, we encountered one case(2%) of malaria. Our findings are in accordance with studies conducted by Khunger et al[8], Tilak et al[7], Gayathri et al[10] and Reddy et al[11] where they found two and three cases of malaria among all the pancytopenia cases.

A study done by Khunger et al[8], found four cases of myelodysplastic syndrome, constituting about 4.14% of the total pancytopenia cases. In present study, there was one case of myelodysplastic syndrome, constituting2% of the total pancytopenia cases.

Conclusion:

Pancytopenia is a frequently encountered hematological problem in the clinical practice. Megaloblastic anemia was the commonest cause followed by dimorphic anemia and aplastic anemia. However, uncommon and rare causes such as multiple myeloma, dengue fever, hemolytic anemia and malaria infection should be kept in mind while planning investigation for complete work up of cytopenic patients.

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