A prospective and retrospective study of bone marrow in patients with pancytopenia – A study of 150 cases

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Abstract
Background: Pancytopenia is one of the day to day common problem which we face. By definition pancytopenia means decrease in all the three blood forming elements like erythrocytes, leucocytes and platelets. Along with peripheral smear, bone marrow is also one of the main diagnostic test to diagnose pancytopenia.

Materials & Methods: The present study is a retrospective and prospective study done in the department of Pathology, for a period of three years. All the relevant history, clinical details, radiological details and biochemical parameters were considered.

Results: Out of 150 cases, 86 were males and 64 were females. Most of the patients were in the age group of 41-60 years (54%). Megaloblastic anemia was the most important cause of pancytopenia.

Conclusion: There are many causes of pancytopenia, among them the most common cause is Megaloblastic anemia in day to day practice. In the present study also megaloblastic anemia was the most common cause of pancytopenia which was compared with other studies also.

Keywords: Bone marrow aspiration; Pancytopenia, megaloblastic anemia.

Introduction
Pancytopenia is a medical condition in which there is reduction in the number of red and white blood cells, as well as platelets. If only two parameters from the complete blood count are low, the term bicytopenia can be used. The diagnostic approach is the same for pancytopenia. Conditions like aplastic anemia, carcinomas, autoimmune conditions, chemotherapy, infections are some of the causes of pancytopenia¹.

Our body needs all of these blood cells, pancytopenia can be very serious. It can even be life threatening if we don’t treat it. Mild pancytopenia often does not cause any symptoms. More severe pancytopenia can cause symptoms including shortness of breath, pale skin, fatigue, weakness, fever, dizziness, easy bruising, bleeding, tiny purple spots on skin called petechiae, larger purple spots on skin called purpura, bleeding gums and nose bleeds, fast heart rate².

Materials & Methods
The present study is a retrospective and prospective study done in the department of Pathology, for a period of three years. All the
relevant history, clinical details, radiological details and biochemical parameters were considered. Patients between 5-65 years age group, cases showing parameters as Hb less than 10g/dl, WBC count less than 4000 cells/cumm. Platelet count less than 1.5 lakhs/ cumm, were included and patients between <5 yrs and > 65yrs were excluded in our study. Investigations like hemoglobin estimation, RBC count, WBC count, Platelet count, Reticulocyte count and hematocrit were carried out.

Other parameters like Red cell indices, bleeding time and clotting time when required, peripheral smear study and bone marrow aspiration study were done. Three ml of blood was collected by venepuncture in all the cases.

Peripheral Smear Study

Blood counts were again cross checked with peripheral smear manually in all cases of pancytopenia. Peripheral smears were prepared, the films were air dried, and stained with Leishman’s stain. Smears were examined under microscope for following features, RBC morphology-to type morphological anemia, immature RBC’s, any inclusions. WBC morphology—for differential count, morphology of each cell, immature cells. Platelet count and its morphology and for any parasites.

Based on these basic hematological investigations in suspected cases, clinical details like age, sex, symptoms such as bone pain, fever, night sweats, malaise, weight loss and pruritis were taken. A detailed physical examination was done to look for the presence of pallor, hepatomegaly, splenomegaly, lymphadenopathy and sternal tenderness, gum hypertrophy, evidence of hypersplenism and primary malignancies were searched for, when necessary. Further bone marrow aspiration carried out in all cases.

Bone marrow aspiration stained with leishman stain and marrow aspiration smears were examined for cellularity, erythropoiesis, myelopoiesis, M:E ratio, megakaryopoiesis, plasma cells, lymphocytes, mast cells, any abnormal cells and any hemoparasites.

Compiling clinical details, hematological parameters and bone marrow study, the cases were studied. The cause for pancytopenia, age and sex distribution and other relevant details were noted and analyzed.

Pancytopenia is a serious hematological problem, the underlying cause of which is diagnosed by bone marrow aspiration and biopsy. Bone marrow examination is extremely helpful in the evaluation of pancytopenia.

Various factors encompassing geographic distribution and genetic disturbances may cause variation in the incidence of disorders causing pancytopenia. In India, the causes of pancytopenia are not well defined. Previous studies done in India, stress the importance of megaloblastic anemia as being the major cause of pancytopenia.

Results

One hundred and Fifty patients with a hematological diagnosis of pancytopenia were studied during the retrospective and prospective study.

The following data was recorded and analysed. The sex distribution of pancytopenia showed a male preponderance [Table 1]. The male to female ratio was 1.78:1. Most of the patients were in the age group of 15-25 years (32.7%) and least occurrence was seen in the age group of 45-55 years (7.3%) [Table 2].

Table 1: Incidence of Pancytopenia in different sex groups

| SNo | SEX  | No of cases(%) |
|-----|------|----------------|
| 1   | MALE | 96 (64%)       |
| 2   | FEMALE | 54 (36%)     |
| TOTAL | 150(100%) |

Table 2: Age and Sex wise distribution of incidence of Pancytopenia

| Age (in years) | Male % | Female % | Total % |
|---------------|--------|----------|---------|
| 5 to 15       | 15.6   | 24.1     | 28.1    |
| 15 to 25      | 33.3   | 31.5     | 32.7    |
| 25 to 35      | 19.8   | 18.5     | 19.3    |
| 35 to 45      | 13.5   | 7.4      | 11.3    |
| 45 to 55      | 6.3    | 9.3      | 7.3     |
| 55 to 65      | 11.5   | 9.3      | 10.7    |
| TOTAL         | 100.0  | 100.0    | 100.0   |

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The commonest symptom was General Weakness (86%). The other main symptoms were fever (59.3%) dyspnoea (44.7%), and bleeding (2.7%). Pallor being most commonest finding in (83.3%) cases. Varying degrees of hepatomegaly (24%) and splenomegaly (18%) were also noted. 9.3% of patients had lymphadenopathy. Pancytopenia is a serious haematological problem, which makes the patient prone to anaemic manifestations, infections and bleeding tendency. Underlying it are many diseases, which are diagnosed by means of bone marrow aspiration and trephine biopsy. In the present study megaloblastic anaemia was the commonest cause of pancytopenia.

In megaloblastic anaemia, peripheral smear may show pancytopenia. Oval omacrocyes, usually with considerable anisopoikilocytosis, are the main features. Mean corpuscular volume (MCV) is more than 100 fl. In others MCV may be normal due to excess fragmentation of red cells. Polychromatophilic cells are reduced. Reticulocyte count may be less than 1%.

Figure 1: Peripheral smear showing macroovalocytes and hyper segmented neutrophils [Leishman, x40]

Figure 2- Bone marrow aspiration shows hyper cellular smears with predominance of megaloblastoid changes with giant metamyelocytes

Figure 3- Mixed deficiency anemia- BMA showing Megaloblastic and Micronormoblastic reaction with mitotic figure, Leishman’s stain (40x)

Discussion

The present study was conducted to analyze the various causes of pancytopenia, its age distribution, sex distribution with their clinical manifestations. The statistical data obtained were compared to the previous studies published in the literature.

In present study, (15-25 yrs) years age group was most commonly affected. Age distribution were comparable with Khunger JM, et al³, Gayatri and Rao, et al⁴, Nigam RK, et al⁵, Sunkesula SB, et al⁶ studies of pancytopenia. In all studies males are affected more than females. Present study also shows male
Sex distribution was comparable with Desalphine M, et al\textsuperscript{7} (1.8:1) and Rangaswamy M, et al\textsuperscript{8} (1.63:1) showing male preponderance. Common age group affected was 10-30yrs in the studies done by Khodke K, et al\textsuperscript{9}, Khunger JM, et al\textsuperscript{3}, Niazi, et al\textsuperscript{10}, Rangaswamy M, et al\textsuperscript{8} comparable to present study where 15-25yrs age group was most commonly affected.

In the present study, most common clinical manifestation was generalized weakness (86%) followed and fever (59.3%) comparable with Gayatri and Rao, et al\textsuperscript{4}, Sunkesula SB et al\textsuperscript{6}. Other clinical manifestations included dyspnea (44.7%) and bleeding disorders (2.7%).

The most common physical finding was pallor (83.3%) followed by hepatomegaly (24%) and splenomegaly (18%) comparable to Gayatri and Rao, et al\textsuperscript{4}, Rangaswamy M, et al\textsuperscript{8}, Nigam RK, et al\textsuperscript{5}.

The variations in the frequency of various diagnostic entities causing pancytopenia has been attributed to, difference in methodology and stringency of diagnostic criteria, geographic area, period of observation, genetic differences and varying exposure to myelotoxic agents, etc. In the present study, Megaloblastic Anemia (MA) (64%) was the commonest cause of pancytopenia, comparable with Gayatri and Rao, et al\textsuperscript{4}, Sunkesula SB, et al\textsuperscript{6} followed by Nutritional(mixed) anemia (20%), Aplastic Anemia (7.33%), Leukemia (6%), MDS (1.33%) and Multiple Myeloma (1.33%) comparable with Gayatri and Rao, et al\textsuperscript{4}, Sunkesula SB, et al\textsuperscript{6}.

Second most common cause of pancytopenia in our study was Nutritional (mixed deficiency) anemia which was in sharp contrast with the studies done by other authors.

Pancytopenia is an important Clinicohaematological entity encountered in our day-today clinical practice. The possible underlying etiologies range from transient viral marrow suppression to left-threatening malignant neoplasm. The etiological diagnosis is essential for the clinical management and prognosis of the patient. Evaluation of peripheral blood film reveals the most probable cause of anemia, presence of immature myeloid cells may suggest marrow infiltration of hematologic disorder. Bone marrow examination – aspiration and biopsy is an important diagnostic tool in hematology to evaluate various causes of pancytopenia.

Bone marrow aspiration is sufficient in making diagnosis of megaloblastic anemia, mixed nutritional anemia and initial diagnosis of leukemia. Megaloblastic anemia was commonest cause of pancytopenia in the present study; this reflects the higher prevalence of nutritional anaemia in Indian subjects.

Conclusion
A combined evaluation of physical findings, primary haematological investigations and bone marrow aspiration were done in diagnosed cases of pancytopenia. The age of the patients ranged from 5 to 65 years with a mean age of 30 years. Males accounted for 96 cases (64%) and female 54 cases (36%) with a M:F ratio of 1.7:1. Megaloblastic anemia (64%) was the commonest cause of Pancytopenia followed by Nutritional (Mixed deficiency) anemia (20%), AA(7.33%), Leukemia(6%), MDS (1.33%) and MM(1.33%). Pancytopenia is a common hematological problem encountered in day to day practice commonly presenting as generalized weakness, fever and bleeding manifestations. The physical findings and peripheral blood picture provides valuable information in the work of Pancytopenia patients. Evaluation of peripheral blood film reveals the most probable cause of anemia, presence of nucleated RBC's and/or immature myeloid cells may suggest marrow infiltration or primary haematologic disorder.

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