Hematological Analysis of Pancytopenia: A Prospective Study

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Abstract

Background: Pancytopenia is manifestations of many illnesses which can be life threatening at times. The severity of pancytopenia and the underlying pathology determine the management and prognosis. This study was conducted to evaluate hematological and bone marrow findings in patients presenting with pancytopenia.

Materials and Methods: In this study, a total of 80 cases were studied by performing complete hemograms, examining peripheral smears, and bone marrow aspiration.

Results: Among the 80 cases studied the age of the patients ranged from 4 to 80, with a slight preponderance in the males. Most of the patients presented with generalized weakness and fever. The most common physical finding was pallor, followed by generalized weakness and fever. The most common cause for pancytopenia was megaloblastic anemia followed by aplastic anemia, subleukemic leukemia, and myelodysplastic syndrome. The most common bone marrow finding was hypercellularity with erythroid hyperplasia.

Conclusion: This study highlights the importance of detailed primary hematological investigations along with bone marrow aspiration in patients with pancytopenia which will help to identify the cause which is important for planning further investigation and management.

Key words: Bone marrow, Hematological parameters, Megaloblastic anemia, Pancytopenia

INTRODUCTION

Pancytopenia is a disorder in which all three major formed elements of blood (red blood cells, white blood cells [WBC] and platelets) are below normal reference. It may be a manifestation of a wide variety of disorders which primarily/secondarily affect the bone marrow. The presenting symptoms are often attributed to anemia/thrombocytopenia. Leukopenia is an uncommon cause of initial presentation but can become the most serious threat to life during the course of the disorder. ²

Pancytopenia is a serious hematological problem, the underlying cause of which is diagnosed by bone marrow

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examination.³ Underlying pathology determines management and prognosis of patients, hence it is extremely important to study the etiology of pancytopenia.

MATERIALS AND METHODS

The present prospective study was conducted spanning a period of 2-year in the Department of Pathology at Goa Medical College, Goa. The patients of all age groups with hematological diagnosis of pancytopenia on peripheral smear and followed by bone marrow aspiration were included in the study. The other inclusion criteria were presence of all 3 of the following: Hemoglobin, ≤10 g/dl; total leukocyte count, ≤4000/mm³; platelet count, ≤100,000/mm³. Relevant clinical data were collected.

About 2 ml anticoagulated blood sent for complete hemogram by the respective departments was run on a coulter counter for the following results: Hemoglobin, total count, platelet count, packed cell volume, and red blood cell indices. Peripheral smear was studied after staining

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with Wright's stain. Special stain myeloperoxidase and Perl's stain were used as indicated. Bone marrow aspirates on slides sent to department of pathology were stained with Wright's stain.

RESULTS

A total of 80 cases which presented with pancytopenia formed the study sample. The following results were recorded and analyzed. Age of patients ranged from 4 to 83 years, the most common age group was 21-30 years (20%). The incidence of pancytopenia showed slight preponderance in males, male: female ratio being 1.28:1.

Hemoglobin in the majority of the cases was in the range 5.1-7 g/dl. (41.0%) and WBC in the majority of the cases were in the range 3,100-4,000 cells/mm³ (37.5%). Platelet count in the majority of the cases was in the range 76,000-100,000/mm³ (46%).

Hypercellular marrow was noted in 67 out of 80 patients (83.75%) and the most common cause was megaloblastic anemia followed by leukemia, myelodysplastic syndrome (MDS), hypersplenism, paroxysmal nocturnal hematuria, mastocytosis, and falciparum malaria.

Hypocellular marrow was noted in 9 of 80 patients (11.25%). 1 was diagnosed as hypoplastic MDS and 8 being diagnosed as aplastic anemia. 5 of 8 had no etiological factor, thus diagnosed as idiopathic aplastic anemia and 3 of 8 gave a history of HIV receiving antiretroviral therapy (ART).

Normocellular marrow was noted in 3 of 80 patients (3.75%), 1 case was that of hypersplenism and the other 2 that of megaloblastic anemia and one with iron deficiency anemia (Tables 1 and 2).

The most common presenting complaints in the cases with pancytopenia were generalized weakness (37.5%), fever (35%), and breathlessness (30%). The most common physical findings were pallor (100%) followed by splenomegaly (32.5%) (Table 3).

In this study, megaloblastic anemia was the major cause of pancytopenia, constituting 60% (48) of the cases of which 28 were males and 20 females. The highest incidence was found in the age group 21-30 years (25.8%), least were in the age group of more than 80 years (2%) and <10 years (2%). 21/48 cases were pure megaloblastic anemia. 27/48 cases were megaloblastic anemia associated with iron deficiency anemia (Figure 1).

The second most common causes were aplastic anemia 8 cases (10%) and subleukemic leukemia 8 cases (10%).

Table 1: Age and sex wise distribution of patients with pancytopenia

| Age group | Female | Male | Number of cases (%) |
|-----------|--------|------|---------------------|
| ≤10 | 1 | 5 | 6 (7.5) |
| 11-20 | 7 | 3 | 10 (12.5) |
| 21-30 | 6 | 10 | 16 (20) |
| 31-40 | 5 | 8 | 13 (16.25) |
| 41-50 | 5 | 8 | 13 (16.25) |
| 51-60 | 5 | 4 | 9 (11.25) |
| 61-70 | 3 | 4 | 7 (8.75) |
| 71-80 | 3 | 2 | 5 (6.25) |
| >80 | 0 | 1 | 1 (1.25) |
| Total | 35 | 45 | 80 (100) |

Table 2: Clinical features of pancytopenia

| Clinical features | Number of cases (%) |
|---------------------------|---------------------|
| Pallor | 80 (100) |
| General weakness/fatigue | 30 (37.5) |
| Fever | 28 (35) |
| Splenomegaly | 26 (32.5) |
| Dyspnea/breathlessness | 24 (30) |
| Weight loss/appetite loss | 14 (17.5) |
| Bleeding | 12 (15) |
| Hepatomegaly | 16 (20) |
| Abdominal pain | 6 (7.5) |
| Lymphadenopathy | 6 (7.5) |
| Jaundice | 8 (6.25) |
| Pedal edema | 3 (3.75) |
| Rash | 2 (2.5) |
| Ascites | 2 (2.5) |
| Sore tongue/ulcers | 1 (1.25) |

Table 3: Distribution of the various etiological causes of pancytopenia

| Etiological causes | Number of cases | Males | Females | Percentage |
|-----------------------------------|-----------------|-------|---------|------------|
| Megaloblastic anemia | 48 | 28 | 20 | 60 |
| Aplastic anemia | 8 | 5 | 3 | 10 |
| Subleukemic leukemia | 8 | 6 | 2 | 10 |
| MDS | 7 | 4 | 3 | 8.75 |
| Hypersplenism | 5 | 2 | 3 | 6.25 |
| Paroxysmal Nocturnal Hematuria | 1 | 1 | 0 | 2.5 |
| Mastocytosis | 1 | 0 | 1 | 2.5 |
| Falciparum malaria | 1 | 1 | 0 | 2.5 |
| Hemophagocytosis syndrome | 1 | 1 | 0 | 2.5 |
| Total | 80 | | | 100 |

MDS: Myelodysplastic syndrome

There were 5 males and 3 females. The highest incidence was found in the age group 31-40 years. In 5/8 cases etiology was not known and grouped under idiopathic aplastic anemia and 3/8 cases gave a history of HIV on ART (Figure 2).

There were 6 males and 2 females with subleukemic leukemia with the highest incidence being in the age group <10 years (37.5%). 4/8 cases were diagnosed as acute

myeloid leukemia (AML) and 4/8 cases were diagnosed as acute lymphoblastic leukemia (ALL) (Figure 3).

MDS was the third most common diagnosis with 7 cases (8.75%). There were 4 males and 3 females and the highest incidence was found in the age group 61-70 years (43%). 1/7 case was diagnosed as hypoplastic MDS and 6/7 cases were diagnosed as refractory cytopenia with multilineage dysplasia.

There were 5 cases of hypersplenism and one case each of paroxysmal nocturnal hematuria, mastocytosis, falciparum malaria and hemophagocytosis syndrome.

DISCUSSION

In this study done at the Goa Medical College over a period of 2 years, a total number of hemograms were 62,698 and bone marrow aspirations sent was 764; pancytopenia was found in 80 cases.

In this study, age of patients with pancytopenia ranged from 4 to 83 years. Most of the studies by Tilak and Jain⁴ Tariq *et al.*,⁵ Mussarrat *et al.*,⁶ Qamar and Aijaz⁷ Khodke *et al.*,⁸ and Gayathri and Rao⁹ reported patients to be in the same age range. Pancytopenia showed its highest incidence in the age group 21-30 years similar to the studies by Mussarrat *et al.*⁶ and Qamar and Aijaz.⁷

The most common cause of pancytopenia reported from various studies worldwide has been aplastic anemia. This is in sharp contrast with the results of the present study where the most common cause of pancytopenia was megaloblastic anemia. This seems to reflect the higher prevalence of nutritional anemia in Indian subjects as well as in developing countries³ (Table 4).

In this study, megaloblastic anemia was the most common cause of pancytopenia, the incidence being 60%. Incidence of 72% was reported by Khunger *et al.*, ²⁰ 68% by Tilak and Jain⁴ and 74% by Gayathri and Rao, ⁹ 49% by Rangaswamy *et al.*, ²⁷ 62% by Khanduri and Sharma, ³⁰ 72.6% by Javalgi and Dombale, ²⁸ and 26.42% by Subrahmanyam and Padma. ²⁹

All the above-mentioned studies have been done in India, and they stress the importance of megaloblastic anemia as the major cause of pancytopenia. 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.³¹

Age and Sex Distribution

The age of the patients with megaloblastic anemia ranged from 4 to 83 years and male:female ratio was 1.4:1. This

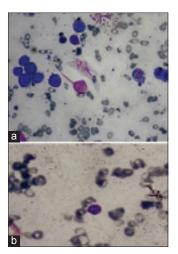


Figure 1: Megeloblastic anemia. (a) Bone marrow aspiration of a case of megaloblastic anemia showing erythroid hyperplasia with magaloblastic maturation (x100), (b) peripheral smear case of megaloblastic anemia showing hypersegmented neutrophil (x40)

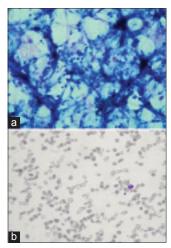


Figure 2: Aplastic anemia. (a) Bone marrow aspirate of a case of aplastic anemia showing markedly hypocellular marrow (x100), (b) peripheral smear of a case aplastic anemia (x40)

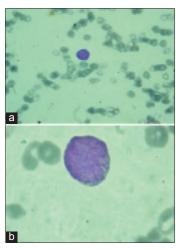


Figure 3: Subleukemic leukemia. (a) Peripheral smear of a case of subleukemic leukemia presenting as pancytopenia (×40), (b) myeloblast showing auer rods (×100)

Table 4: Causes of pancytopenia in various studies

| Name of the study | Place and year | Number of cases | Most common cause | 2 nd common cause |
|-----------------------------------------------------------------------------|-------------------|-----------------|-------------------------------|---------------------------------------|
| Retief and Heyns ¹⁰ | South Africa 1976 | 195 | Bone marrow failure 67.7% | Severe infections 9.7% |
| International agranulocytosis and aplastic anemia study group ¹¹ | Europe 1987 | 389 | Aplastic anemia 52.7% | MDS 10.5% |
| Imbert et al. ¹² | Europe 1989 | 213 | Malignant myeloid disease 42% | Malignant lymphoid disease 18% |
| Keisu and Ost ¹³ | Sweden 1990 | 100 | Neoplastic disease 32% | Aplastic anemia 16% |
| Hossain et al.14 | Bangladesh 1992 | 50 | Aplastic anemia | Chronic malaria, Kala Azar |
| Varma and Dash ¹⁵ | India 1992 | 202 | Aplastic anemia 40.6% | Megaloblastic anemia 23.26% |
| Tilak and Jain⁴ | India 1998 | 77 | Megaloblastic anemia 68% | Aplastic anemia 7.7% |
| Savage et al. 16 | Zimbabwe 1999 | 134 | Megaloblastic anemia | Aplastic anemia |
| Khodke et al.8 | India 2000 | 166 | Hypoplastic anemia 29.5% | Megaloblastic anemia 23.3% |
| Khan et al.17 | Pakistan 2001 | 30 | Aplastic anemia 20% | Megaloblastic anemia 16.7% |
| Kumar and Raghupathi ¹⁸ | India 2001 | 166 | Aplastic anemia 29.5% | Megaloblastic anemia 22.3% |
| Ishtiaq et al.19 | Pakistan 2002 | 100 | Megaloblastic anemia 39% | Hypersplenism 19% |
| Khunger et al.20 | India 2002 | 200 | Megaloblastic anemia 72% | Aplastic anemia 14% |
| Mussarrat et al.6 | Pakistan 2004 | 89 | Aplastic anemia 38.3% | Megaloblastic anemia 27.7% |
| Dodhy et al.21 | Pakistan 2005 | 392 | Megaloblastic anemia 35.95% | Hypersplenism 16.3% |
| Rahim et al.22 | Pakistan 2005 | 424 | Megaloblastic anemia 24.92% | Aplastic anemia 14.15% |
| Memon et al.23 | Pakistan 2008 | 230 | Aplastic anemia 23.9% | Megaloblastic anemia 13.04% |
| Jha et al.24 | Nepal 2008 | 148 | Hypoplastic anemia 29.5% | Megaloblastic anemia 23.64% |
| Gayathri and Rao9 | India 2008 | 104 | Megaloblastic anemia 74.04% | Aplastic anemia 18.26% |
| Tariq et al.⁵ | Pakistan 2010 | 50 | Aplastic anemia 36% | Megaloblastic anemia 16% |
| Santra and Das ²⁵ | India 2010 | 111 | Aplastic anemia 20% | Hypersplenism 11.7% |
| Kumar et al.17 | India 2011 | 48 | Hypoplastic marrow 16% | |
| Qamar and Aijaz ⁷ | Pakistan 2011 | 150 | Aplastic anemia 50.67% | Megaloblastic anemia 36.6% |
| Lakhey et al.26 | Nepal 2012 | 54 | Hypoplastic anemia 29.6% | Hematological Malignancy 27.78% |
| Rangaswamy et al.27 | India 2012 | 100 | Megaloblastic anemia 49% | Aplastic anemia 14% |
| Javalgi and Dombale ²⁸ | India 2013 | 106 | Megaloblastic anemia 72.6% | Iron deficiency anemia 12.2% |
| Subrahmanyam and Padma ²⁹ | India 2015 | 106 | Megaloblastic anemia 26.42% | Hypersplenism 24.53% |
| Present study | India 2015 | 80 | Megaloblastic anemia 60% | Aplastic anemia and leukemia 10% each |

finding is in accordance with the studies by Jha *et al.*²⁴ wherein the age of the patients ranged from 10 to 79 years with a male preponderance (male:female = 1.5:1) and Rangaswamy *et al.*²⁷ wherein the age ranged from 12 to 85 years with a male preponderance, male:female = 3.4:1.

Hematological Parameters

The hemoglobin percentage varied from 1.6 to 9.9, the total leukocyte count was in the range of 1000-3900 cells/mm³ and the range of platelet count varied from 20,000 to 90,000/mm³. This finding is in agreement with that of Jha *et al.*,²⁴ Kumar and Raghupathi,¹⁸ and Rangaswamy *et al.*²⁷

On peripheral smear, 21 of 48 cases were found to be pure megaloblastic anemia where macro ovalocytosis with anisopoikilocytosis (seen in all cases) and hypersegmented neutrophils (17/21, 81%) were found to be the main features. Prabhu *et al.*²⁸ also found macro ovalocytosis with anisopoikilocytosis in all cases. Khodke *et al.*⁸ found anisocytosis in 20/22 cases, Tilak and Jain⁴ in 51/53 cases. Khodke *et al.*⁸ found hypersegmented neutrophils in 20/22 cases (91%), Tilak and Jain⁴ in 45/53 cases (84.9%), Gayathri and Rao⁹ in 51.35% cases.

62% (13/21) showed relative lymphocytosis comparable to Tilak and Jain⁴ (50%), Gayathri and Rao⁹ (52.63%) and Khunger *et al.*²⁰

Mean corpuscular volume was found to be more than 100 fl in 70% of our cases compared to Prabhu *et al.*²⁸ in 57.5% cases.

On bone marrow examination, marrows were found to be hypercellular, with erythroid hyperplasia, megaloblastic maturation, and reversal of M:E ratio. All cases showed shift to the left in myeloid series and 47.6% showed hyperplasia. Rangaswamy *et al.*²⁷ found 87.8% of the marrows to be hypercellular.

Around 27 of 48 (56.25%) cases were megaloblastic associated with IDA with dimorphic blood picture. Most had hypochromia with both microcytes and macrocytes. Khodke *et al.*⁸ reported dimorphic blood picture in 10/22 (45.5%) and Gayathri and Rao⁹ reported 39/72 cases, (54.2%).

Aplastic anemia was the second most common cause and constituted 10% cases of pancytopenia which is comparable to the studies of Tilak and Jain⁴ 7.7%,

Khunger et al.²⁰ 14%, Rahim et al.²² 14.15%, Rangaswamy, Rangaswamy et al.²⁷ 14% and Khodke et al.⁸ 14%.

The incidence of aplastic anemia quoted from the West is much higher than that observed by US. The increased incidence may be related to environmental factors. ¹⁰ A few studies that quote aplastic anemia to be the most common cause in India as well as elsewhere are International Agranulocytosis and Aplastic Anemia study group ¹¹ 52.7%, Varma and Dash ¹⁵ 40.6%, Khodke *et al.* ⁸ 29.5%, Khan *et al.* ¹⁷ 20%, Kumar *et al.* ³² 29.5%, Mussarrat *et al.* ⁶ 38.3%, Memon *et al.* ²⁵ 23.9%, Jha *et al.* ²⁴ 29.5%, Mohammad Tariq *et al.* ⁵ 36%, Lakhey *et al.* ²⁶ 29.6%, Santra and Das ²⁵ 50.67%, Kumar and Raghupathi ¹⁸ 16%, Qamar and Aijaz ⁷ 20%.

Age and Sex Distribution

Age of patients with aplastic anemia ranged from 7 to 67 years and male: female being 1.7:1. studies by Kumar and Raghupathi¹⁸ Jha *et al.*,²⁴ Rangaswamy *et al.*²⁷ and Tilak and Jain⁴ reported similar age range and male:female ratio.

Hematological Parameters

Hemoglobin varied from 3.2 to 8.6 g/dl, total WBC count varied from 400 to 3900 cells/mm³ and platelet count varied from 20,000 to 90,000/mm³. Similar hematological parameters were reported by Tilak and Jain⁴ Jha *et al.*,²⁴ Kumar and Raghupathi¹8 and Rangaswamy *et al.*²¬

Peripheral Smear and Bone Marrow Aspiration Findings

In our study, five of the eight patients showed anisocytosis and three of eight showed relative lymphocytosis. In a study by Khodke *et al.*, three of seven patients showed anisocytosis and one of three showed relative lymphocytosis. In a study by Tilak and Jain, two of six patients showed anisocytosis and three of six showed relative lymphocytosis.

Bone marrow findings were the following: Markedly hypocellular with increased fat spaces, marked depression of all 3 series and increase in plasma cells, lymphocytes, and reticular cells. Mohler³³ in their analysis of 50 cases reported 74% patients with hypocellular marrow, 16% with normocellular marrow which later became hypocellular and 10% were acellular.

5/8 cases etiology was not known, grouped under Idiopathic aplastic anemia.

3/8 cases gave a history of HIV on ART. Khodke *et al.*⁸ reported 1 case of HIV (50 cases). Ishtiaq *et al.*¹⁹ reported 1 case of AIDS presenting with pancytopenia, so did Rangaswamy *et al.*²⁷

Leukemia was also the second most common cause and constituted 10% of the cases of our study, which is comparable to the studies of Tariq *et al.*⁵ (14%), Mussarrat *et al.*⁶ (13.6%) and Qamar and Aijaz⁷ 11%.

Khoo and Keihani³³ in a study of 188 cases of pancytopenia found leukemia to be the most common cause, most of the cases being AML.

In the study by Jha *et al.*²⁴ acute leukemia alone constituted 19.59% of the total cases of pancytopenia, in contrast to the studies by Khodke *et al.*⁸ and Tilak and Jain⁴ where one case of AML was detected as a cause of pancytopenia. Khunger *et al.*²⁰ reported incidence of 5% and so did Rangaswamy *et al.*²⁷ Santra and Das²⁵ reported incidence of 1.8% and Ishtiaq *et al.*¹⁹ 1.8%.

Nevertheless, in the study of Bashawri³⁴ the main indication for bone marrow examination in cases of pancytopenia was acute leukemia.

Pancytopenia can be seen in 30% of acute leukemia at the time of presentation.⁸

The highest incidence was found in the age group <10 years (37.5%) and the age ranged from 5 to 57 years with a male: female = 3:1, which is in agreement to that reported by Jha *et al.*²⁴ years and Rangaswamy *et al.*²⁷

Hemoglobin varied from 3.7 to 8.1 g/dl. Total WBC count varied from 400 to 3800 cells/mm³. Platelet count varied from 20,000 to 94,000/mm³ similar to the hematological parameters reported by Jha *et al.*,²⁴ Kumar and Raghupathi¹⁸ and Rangaswamy *et al.*²⁷

Bone marrow aspiration revealed all cases to be hypercellular, with decreased fat spaces and marked suppression of megakaryocytic and myeloid series. 4/8 cases were diagnosed as AML, showed presence of myeloblast and were myeloperoxidase positive. 4/8 cases were diagnosed as ALL, showed presence of lymphoblast and were myeloperoxidase negative. In the study by Rangaswamy *et al.*²⁷ 80% marrows were hypercellular and 20% hypocellular.

In the study by Tariq *et al.*⁵ ALL constituted 12% cases and AML 2% cases whereas Varma and Dash¹⁵ reported AML to be 12.8%. Gayathri and Rao⁹ reported 4 cases of leukemia, 3 being AML and 1 ALL and Kumar and Raghupathi¹⁸ reported 13 cases of AML and 5 cases of ALL.

The incidence of MDS in our study was 8.75%. Lakhey et al.²⁶ reported an incidence of 7.4%, Kumar and

Raghupathi¹⁸ 8.3% which is comparable to our study. Qamar and Aijaz⁷ reported incidence of 5.3%, Mussarrat *et al.*⁶ 2.4%, Khunger *et al.*²⁰ 2%, Jha *et al.*²⁴ 0.94% and Tariq *et al.*⁵ 14%.

In a study of 118 patients with MDS by Juneja *et al.*,³⁵ age ranged from 48 to 95 years, study by Lakhey *et al.*²⁶ age ranged from 30 to 79 years. In the present study, highest incidence was found in the age group 61-70 years (43%) and age of patients ranged from 28 to 65 years, male:female=1.3:1

6/5 cases showed hypochromia, anisocytosis, microcytes, macrocytes. Anemia associated with MDS can be microcytic, normocytic, or, most commonly, macrocytic.³⁶

Six of seven cases were diagnosed as refractory cytopenia with multilineage dysplasia. Marrow was hypercellular, showed dysplastic features in erythroid series ranging from increased mitotic activity in normoblasts, abnormal mitosis, megaloblastoid change, nuclear hypoblasts, irregular hypersegmentation, ringed nuclei and abnormal segmentation. Dysgranulopoeis and dysmegakaryopoiesis were also noted.

In a study by Kumar and Raghupathi¹⁸ of the four cases of MDS, one was refractory anemia, two refractory cytopenia with multilineage dysplasia and one MDS unclassified.

Hypersplenism constituted 6.25% cases of pancytopenia. Age of patients ranged from 21 to 63 years male:female = 3:4.

Retief and Heyns¹⁰ found hypersplenism to be the cause of pancytopenia in 7.7% cases, which is comparable to our finding.

Rangaswamy *et al.*²⁷ found hypersplenism to be a cause of pancytopenia in 10% cases, with male:female ratio of 1:1.5. Ishtiaq *et al.*¹⁹ in 12% with a female preponderance being 1:1.3.). In a study of 195 patients, Kumar and Raghupathi¹⁸ reported incidence of hypersplenism in 11%, age ranging 14-49 years. Momen *et al.*³⁶ in 4.34%, Santra and Das²⁵ 11.7%, Tariq *et al.*⁵ in 10%.

Hemoglobin varied from 5.4 to 9.9 m/dl, total WBC count varied from 1100 to 3600 cells/mm³ and platelet count varied from 50,000 to 90,000/mm³. This is in conformity with the findings of Kumar and Raghupathi¹8 and Gayathri and Rao.9

A single case of paroxysmal nocturnal hematuria was encountered. Santra and Das²⁵ in a study of 111 cases of pancytopenia encountered one case and so did Khan *et al.*¹⁷ in a study of 30 cases of pancytopenia.

A 55-year-old male presented with hematuria, jaundice and splenomegaly. Laboratory investigations revealed elevated lactic acid dehydrogenase levels, raised erythrocyte sedimentation rate and C-reactive protein, mildly elevated fetal hemoglobin, serum ferritin 37 μ g/L, and total iron binding capacity 289/ μ g/dl.

We encountered a single case of falciparum malaria causing pancytopenia.

In the study of Hossain *et al.*,¹⁴ chronic malaria was the second most common cause of pancytopenia. In the study of Khunger *et al.*,²⁰ incidence was 1%, Gayathri and Rao⁹ 1.93%, Tilak and Jain⁴ 3.9%, Kumar and Raghupathi¹⁸ 3%, and Santra and Das²⁵ 1.8%.

We encountered a single case of mastocytosis causing pancytopenia.

None of the above studies of pancytopenia have encountered a case of mastocytosis. Systemic mast cell disease is characterized by bone marrow involvement by mast cells and frequently by peripheral blood cytopenias and may result in pancytopenia.^{37,38}

A 16-year-old female presented with fever, macular-papular rash on face. Hemoglobin 5.4 g/dl total count 1900/mm³ platelet count: 48,000/mm³. Peripheral smear revealed moderate hypochromia, moderate anisocytosis. Bone marrow was hypercellular. Fat content was decreased. M:E ratio was reversed to 1:3.

Erythroid series were hyperplastic at all levels. Most showing megaloblastoid change. Myeloid series showed shift to left with mild increase in eosinophilic precursors. A Large number of mature mast cells, precursors were seen scattered in marrow, forming 40% of the nonerythroid cells. Megakaryocytic series were normal and iron staining was mildly increased +4.

A single case of hemophagocytosis was encountered in our study. Tilak and Jain⁴ also encountered one such case in a study of 77 cases of pancytopenia.

A 4-year-old boy presented with fever, breathlessness, bleeding and was found to have hepatomegaly. Erythrocyte sedimentation rate was raised.

Hemoglobin was 1.9 g/dl, the total count of 3500/mm³ and platelet count of 90,000/mm³. Peripheral smear examination revealed moderate hypochromia and moderate anisocytosis, 2 normoblasts/100 WBC' S. Differential count showed shift to left and presence of toxic granules.

Bone marrow aspiration revealed the following: No marrow fragments were aspirated, mainly sinusoidal blood. Few myeloid and erythroid cells seen which show normal morphology. Occasional megakaryocytes seen. Scattered among the marrow cells are few histiocytes showing phagocytosis of WBC's.

We were not able to determine the exact etiology of hemophagocytosis syndrome.

CONCLUSION

Pancytopenia is not an uncommon hematological problem encountered in clinical practice and should be suspected on clinical grounds when a patient presents with unexplained anemia, prolonged fever and tendency to bleed.

Physical findings and peripheral blood picture provide valuable information in the workup of cytopenic patients.

Bone marrow aspiration is an important diagnostic tool in hematology which helps to evaluate various causes of cytopenia and to plan further investigations and management of the patients.

Since a large number of causes for pancytopenia are remediable and reversible, accurate diagnoses and timely intervention may be lifesaving and will definitely have an influence on the morbidity and mortality in these patients.

The early detection of the underlying conditions would also help to enhance the prognosis of a patient with pancytopenia.

Thus, a comprehensive, clinical, and hematological study of patients with pancytopenia will usually help in identifying the underlying cause.

Further research with a larger sample size is required to replicate the findings of this study.

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