Pancytopenia: A Tertiary Care Institutional Study

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Abstract

Background: Pancytopenia means decrease in all three cell lines .It is the striking feature of many illness ranging from megaloblastic anaemia to leukaemias. The underlying pathology of pancytopenia will determine the management and prognosis. *Objective:* To identify the various etiologies of Pancytopenia. *Materials and Methods:* The present study was undertaken at BRIMS Bidar. *Results:* 100 cases were studied, 57 males and 43 females with age ranging from 3 yrs to 90 yrs .Most of the cases presented with generalized weakness, followed by pallor, hepatosplenomegaly and bleeding manifestations. *Conclusion:* The present study were helpful in understanding the various causes of diseases process with bone marrow aspiration done in few of the pancytopenic patients along with support of biochemical investigations which were helpful in planning further investigations and management .

Keywords: Pancytopenia; Bone Marrow Aspiration; Megaloblastic Anaemia; Leukaemia.

Introduction

The hypoproliferative anemias are normochromic, normocytic,or macrocytic and are characterized by a low reticulocyte count. Hypoproliferative anemia is also a prominent feature of hematologic diseases that are described as bone marrow failure states; these include aplastic anemia, myelodysplastic syndrome (MDS), pure red cell aplasia (PRCA), and myelophthisis. Anemia in these disorders is often not a solitary or even the major hematologic finding. More frequent in bone marrow failure is *pancytopenia*: anemia, leukopenia, and thrombocytopenia. Low blood counts in the marrow failure diseases result from deficient hematopoiesis, as distinguished from blood count depression due to peripheral destruction of red cells (hemolytic anemias), platelets (idiopathic thrombocytopenic purpura [ITP] or due to splenomegaly), and granulocytes (as in the immune leukopenias).

Marrow damage and dysfunction also may be secondary to infection, inflammation, or cancer.

Hematopoietic failure syndromes are classified by dominant morphologic features of the bone marrow Although practical distinction among these syndromes usually is clear, some processes are so closely related that the diagnosis may be complex. Patients may seem to suffer from two or three related diseases simultaneously, or one diagnosis may appear to evolve into another. Many of these syndromes share an immune-mediated mechanism of marrow destruction and some element of genomic instability resulting in a higher rate of malignant transformation.

Pancytopenia is an important clinico-hematological entity encountered in our day to day clinical practice. It is a disorder in which all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number [1]. 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 [2]. There are varying trends in its clinical pattern, treatment modalities and outcome [3]. The severity of pancytopenia and underlying pathology determine the management and prognosis of the patients [4] . In present study we have evaluated the various

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causes of pancytopenia with peripheral blood , bone marrow findings along with Vit B12 and Lactate Dehydrogenase levels (LDH) .

There are incidences of pancytopenia which are a direct result of drug intake. All patients do not respond to this in a similar manner. One of the most extensively studied phase II polymorphisms is the PM trait for thiopurine S-methyltransferase (TPMT). TPMT bioinactivates the antileukemic drug 6-mercaptopurine. Further, 6-mercaptopurine is itself an active metabolite of the immunosuppressive azathioprine. Homozygotes for alleles encoding the inactive TPMT (1 in 300 individuals) predictably exhibit severe and potentially fatal pancytopenia on standard doses of azathioprine or 6-mercaptopurine. On the other hand, homozygotes for fully functional alleles may display less anti-inflammatory or antileukemic effectwith the drugs.

Materials and Methods

100 patients of pancytopenia patients were

evaluated with bone marrow aspiration in Private lab. Patients from all age groups from both sexes were included. Inclusion criteria was hemoglobin < 10 g/dl, total leukocyte count (TLC) < 4000 /μl, platelet count < 100,000/ μl. [5].

Patients blood was collected in EDTA (ethylene diamine tetra–acetic acid) and processed through Sysmex automated hematology analyzer. Peripheral smear was stained with Giemsa stain for all cases and examined thoroughly. Bone marrow aspiration was done in 26 patients after taking written consent and VitB12 and LDH levels in 35 cases.

All the statistics were done using the latest SPSS software 2015 (California).

Results

A total of 100 patients who presented with pancytopenia were studied. They consisted of 57 males and 43 females with male to female ratio of 1.3:1. The age of patients ranged from 3yrs to 90 yrs.

The commonest mode of presentation was

Table 1: Presenting complaints and physical findings

Sl. No	Presenting complaints and physical findings	No. of cases	Percentage
1	Generalized weakness	52	52
2	Dyspnea	3	3
3	Fever	2	2
4	Bleeding manifestations	2	2
5	Weight loss	7	7
6	Pallor	26	26
7	Splenomegaly	7	7
8	Hepatomegaly	7	7
9	Fatigue	7	7

Table 2: Test for Significance. Association of complaints

Complaint	P – value (< 0.05)	Significance
Generalized weakness	0.0041	Significantly associated
Pallor	0.078	Significantly associated

generalized weakness followed by pallor. Hepatosplenomegaly was seen in subleukaemic

leukemia of myeloid type.

Megaloblastic anaemia was seen as main cause of

Table 3: Distribution of various causes of Pancytopenia

Causes of Pancytopenia	No. of cases	Percentage
Megaloblastic anaemia	47	47
HIV	17	17
Malaria	9	9
Dengue	9	9
Subleukemic leukemia	2	2
Iron deficiency anaemia	5	5
Idiopathic thrombocytopenic purpura	2	2
Aplastic anaemia	9	9

pancytopenia in 47cases (47%). The peripheral blood picture showed macrocytes, macro ovalocytes ,hyper segmented neutrophils, and bone marrow showed erythroid hyperplasia megaloblastic type (Figure 1). In our study we saw in 20 cases of megaloblastic anaemia, LDH (lactate dehydrogenase) was raised and Vit B12 was reduced. In all cases of megaloblastic anaemia patients improved with vit B 12 and folic acid therapy.

Malaria was observed in 9 cases (9%) presenting with pancytopenia, it was P. Falciparum species.

We also came across 9 cases (9%) of Dengue who presented with pancytopenia in our study.

Sub leukaemic leukemia was seen in 2 cases (2%), out of which after bone marrow aspiration we came to a conclusion of acute myelocytic leukaemia in 2 cases (2%).

Iron deficiency anaemia seen in 5 cases (5%) having microcytic hypochromic anaemia along with tear drop cells in peripheral smear and showed micronormoblastic hyperplasia in bone marrow aspirations .

Idiopathic thrombocytopenic purpura seen in 2 case (2%) and bone marrow showed increased megakaryocytes with hypolobulated and hypogranular appearance.

HIV was the cause of pancytopenia in 17 cases (17%). Bone marrow aspiration was not done in these patients.

Aplastic anaemia were seen in 9 cases (9%).

Discussion

A total of 100 cases were studied. We did a detailed study of patients of Pancytopenia . Peripheral smear in 100 cases, bone marrow aspirations for 26 cases and LDH and Vit B12 for 35 cases were done. Age, gender –wise incidence, presenting complaints were studied and compared with other studies.

The age of patients ranged from 3 yrs to 90 yrs. Male to female ratio was 1.3:1. Age and sex distribution were studied and we compared it with study of other authors in Table 3.

Table 4: Age, sex distribution in various studies

Sl. No.	Authors	No. of Cases	Age Range(y)	M:F
1	KhungerJM et al.[6](2002)	200	2-70	1.2:1
2	Kumar R et al.[5](2001)	166	12-73	2.1:1
3	Khodke K et al.[7](2001)	50	3-69	1.3:1
4	Tilak V et al.[4](1999)	77	5-70	1.14:1
5	Phurailatpam Madhubala Devi et al.[10] (2008)	50	3-80	1.5:1
6	Soma Yadav et al.[9] (2013)	60	<30	1:1.2
7	S Pudasaini et al.[8](2012)	57	9 mon-75y	1:1.1
8	Present study	100	3-90	1.3:1

The commonest cause of pancytopenia in our study is megaloblastic anaemia. Most of studies we compared which had same findings.Incidence of megaloblastic anaemia was 47% in our study as compared to 72% reported in Khunger JM et al, 22.2% in Kumar R et al, 68% in Tilak V et al, 44% in Khodke K et al, 12.3% in S Pudasaini et. al, 27.7% in Soma Yadav et al and18% in Phurailatpam Madhubala Devi et al [4-10] study. In our study we saw in 35 cases of megaloblastic anaemia, LDH (lactate dehydrogenase) was raised. All cases of megaloblastic anaemia patients improved with vit B 12 and folic acid therapy. In Eivazi-Ziaei J et al [11] study also observed increased LDH in megaloblastic anaemia . The expected increased LDH activity is the result of an an accelerated turnover of bone marrow cells implying the release of this enzyme from dividing and/or decaying cells [11]. In 35 cases Vit B12 were also reduced. Our study had 9 cases (9%),

as compared to 1% in Khunger JM et al ,3% in Kumar R et al and 3.9% in Tilak V et al.

We have observed in 2 cases (2%) of acute myeloid leukemia .This diagnosis was based on bone marrow aspiration . Khodke et al [7] reported a single case of AML –M2 out of 50 cases of pancytopenia. Kumar R et al reported 5 cases of all, 13 cases of of AML , 2 cases of hairy cell leukemia out 166 cases of pancytopenia over a 6 year study [5].S Pudasaini et al [8] reported 10.5% AML and 1.8% of AML. Phurailatpam Madhubala Devi et al [10] saw 14% of acute leukaemia and Soma Yadav et al [9] had 13.3% of acute leukaemia cases. The patho physiology of pancyopenia in acute leukemia is unclear but is probably related to a combination of suppression of normal haematopoesis and replacement of bone marrow by leukemic cells resulting in pancytopenia and immunosuppression [9]. 5 cases (5%) of Iron deficiency anaemia were reported in our study who

presented with pancytopenia. Phurailatapam Madubala Devi et al study [10] also 8% and S Pudasaini et al [8] study had 7% who presented with Pancytopenia as a cause of Iron deficiency disease.

Incidence of Aplastic anaemia in present study was 9 cases (9%) and it was 4% in Khodke et al and Khugner et al [6,7] but it was more that is 29.5% in Kumar et al study [5] and 38.3% in Soma Yadav et al [9] study .

HIV was one of the important cause of pancytopenia in our study having 17cases (17%) , it was 1.6% Soma Yadav et al [9] study in 2% in Khodke et al study [7] and 6% in Phurailatpam Madhubala Devi et al study [10]. Virtually all patients with advanced AIDS have pancytopenia as a rule, the causes are production of the antibodies which might be triggered by exposure of crypt antigens as a consequence of infection related damage of blood cells especially platelets and granulocytes. The haematopoietic cells especially platelets and granulocytes are antigenically similar to agents like HIV and other microorganisms infecting the patients. These antibodies could interact with tissue antigens. Third possibility is that HIV act as direct inducer of autoimmunity [9].

Present study revealed 2 cases (2%) having Idiopahic Thrombocytopenic Purpura as compared to 10.5% observed in S Pudasaini et al study [8].

Conclusion

In our study we have encountered, other than common reasons like megaloblastic anaemia, HIV infection etc. Presenting as Pancytopenia , even, Iron deficiency anaemia, subleukemic leukemia, Dengue and Malaria also had presented with pancytopenia. Bone marrow aspiration supported with biochemical profile is very important for confirmation of cause of pancytopenia. Proper diagnostic work up is essential before use of hematinics and blood transfusion in all patients presenting as pancytopenia.

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