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Original Research Article

Bone marrow examination in cases of pancytopenia

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ABSTRACT

Background: Pancytopenia is a relatively common hematological entity. This study was undertaken to find out the various causes of pancytopenia by bone marrow examination of patients admitted to New civil hospital, Surat, Gujarat, India.
Methods: This was a prospective study carried out to identify the causes of pancytopenia based on bone marrow examination. Bone marrow examinations were performed in 144 cases for different indications over a period of one year 2015, out of which 40 cases have fulfilled the criteria of pancytopenia.
Results: Total 40 cases of pancytopenia were examined during period of one year. The commonest cause of pancytopenia was megaloblastic anemia (35%) followed by aplastic anemia (32.5%). other cause includes acute leukemia, myelodysplastic syndrome (MDS) and round cell tumor.
Conclusions: Bone marrow aspiration coupled with trephine biopsy can diagnosed majority cases of pancytopenia. Megaloblastic anemia and aplastic anemia are the commonest causes of pancytopenia. A comprehensive clinical and hematological study of patients with pancytopenia will help in the identification of underlying cause.

Keywords: Bone marrow, Megaloblastic anemia, Pancytopenia

INTRODUCTION

Pancytopenia is a relatively common hematological entity which is encountered routinely. Pancytopenia is a disorder in which all three formed elements of blood; red blood cells, white blood cells and platelets decreased than normal. Pancytopenia is not a disease entity but a triad of finding that may results from number of disease processes. Pancytopenia develops from variety of mechanism. It could be associated with decrease in hematopoietic cell production either due to destruction of marrow tissue by toxins or replacement by malignant or abnormal cells or suppression of normal growth and differentiation. Other mechanism including ineffective haematopoiesis with cell death in the marrow, formation of defective cells which are rapidly removed from circulation, sequestration and/or destruction of cells by the action of antibodies or, trapping of normal cells in a hypertrophied and over-reactive reticuloendothelial system.[1] Bone marrow cellularity varies depending upon the cause. Marrow is hypocellular in primary production defect while in case of ineffective erythropoiesis, increased peripheral utilization or destruction of cell and bone marrow with malignant infiltration are associated with hypercellular and normocellular marrow.[2]

The presenting symptoms are usually attributable to the anemia or the thrombocytopenia. Leucopenia is an uncommon cause of initial presentation of the patient, but can become the most serious threat to life during the subsequent course of the disorder.[2] The frequency of underlying pathology causing pancytopenia varies considerably depending upon various factors including geographic distribution.[3]

Marrow aspiration is assessed for cytology and trephine biopsy provides overall cellularity, detection of focal lesion and infiltration. The severity of pancytopenia and

underlying pathology determine the management and prognosis of patients. The aim of present study was to identify diagnostic reliability of bone marrow aspiration and biopsy in various cause of pancytopenia.

METHODS

This was a prospective study conducted over a period of one year (January 2015 to December 2015) in the department of Pathology, Government medical college, Surat. All the cases of pancytopenia with hemoglobin less than 10 gm/dl, total leucocyte count of less than 4000/mm3 and platelet count less than 150,000/mm3 were included in the study. Cases of chemotherapy induced pancytopenia were excluded. Relevant clinical findings of the patients were obtained. All the patients fulfilling the criteria were subjected to complete blood count, and peripheral blood smear examination. After taking informed consent bone marrow aspiration (BMA) was performed from posterior iliac crest of the patients. Then bone marrow trephine biopsy was performed. Bone marrow aspiration smears were stained with Giemsa stain for microscopy and when required special stains such as periodic acid-Schiff and myeloperoxidase stain were performed. Trephine biopsy specimens were processed and hematoxylin and eosin stained sections were examined.

RESULTS

During the study period of one year, 40 cases of pancytopenia fulfilling the inclusion criteria were included in the study. Age ranged from 8months to 68 years. Maximum number of cases were seen in age group of 15-35 years (29.4%). 21 cases were male and 19 cases were female, male to female ratio is 1.1:1 (Table 1).

The commonest presenting complaint was fever in 40% (16/40) of the cases. Pallor was present in all the patients, Splenomegaly was seen in 20% (08/40) and hepatomegaly in 12.5% of the cases (5/40). Petechial hemorrhages were present in 5% (2/40) (Table 2).

Table 1: Bone marrow aspiration and biopsy findings in 40 cases of pancytopenia.

Diagnosis	No. of cases	Percentage
Megaloblastic anaemia	14	35
Aplastic anaemia	13	32.5
Acute lymphoblastic leukemia	01	2.5
Acute myeloblastic leukemia	01	2.5
Aleukemic leukemia	01	2.5
Hairy cell leukemia	01	2.5
Myelodysplastic syndrome	01	2.5
Reactive marrow	01	2.5
Round cell tumor	01	2.5
Normocellular marrow	03	5
Erythroid hyperplasia	01	2.5
Undiagnosed	01	2.5
Inconclusive	01	2.5
Total	40	100

Table 2: Clinical findings in pancytopenic patients.

Diagnosis	Total No	Fever	Splenomegaly	Hepatomegaly	Petechiae	Lymphade nopathy	Sternal Tenderness
Megaloblastic anaemia	14	3	2	1	-	-	-
Aplastic anaemia	13	6	-	-	1	1	-
Acute leukemia	03	2	1	2	-	-	-
Hairy cell leukemia	01	-	1	-	-	-	-
Myelodysplastic syndrome	01	-	-	-	-	-	-
Reactive marrow	01	1	1	-	-	-	-
Round cell tumor	01	-	-	-	-	-	-
Normocellular marrow	03	3	2	1	1	-	-
Erythroid hyperplasia	01	-	-	-	-	-	-
Undiagnosed	01	1	1	1	-	-	-
Inconclusive	01	-	-	-	-	-	-
Total	40	16	8	5	2	1	-

Hypersegmented neutrophils were seen in 25% (10/40) and circulating erythroblasts in 7.5% (3/40) of cases. Peripheral blood film showed features dimorphic anemia in 30% (12/40) of cases. Reticulocytosis was seen in 15% (6/40) of the cases (Table 3). The commonest cause of pancytopenia was megaloblastic anemia and was seen in 14/40 (35%), and followed by aplastic anemia (32.5%). The other causes of pancytopenia were acute leukemia,

round cell tumor, myelodysplastic syndrome and erythroid hyperplasia.

DISCUSSION

Pancytopenia is a common hematological finding with variable clinical presentations. It often creates diagnostic challenge to physician and the knowledge of accurate etiologies of this condition is crucial in the management of the patient.[2]

In this study, most cases were seen in adults (15-35 years) and only 13 cases were seen in children. Male patients slightly outnumbered the female with male to female ratio 1.1:1 and this was similar to study of Makaju et al 1.5:1, Jha et al (1.3:1) However Aziz et al found more in females.[2,4,5]

The incidence of megaloblastic anemia varies from 0.8% to 32.26% of all panctytopenic patients.[3,6-8] In present study megaloblastic anemia is still the commonest cause of pancytopenia. This constituted 35% of total cases of pancytopenia. Findings are similar to other studies tilak and khodke et al in which megaloblastic anemia is a common cause of pancytopenia.[3,9] While this findings are sharp contrast with various studies from the world in which aplastic anemia is commonest cause this may be due to high prevalence of nutritional anemia in Indian subjects leads the increased frequency of megaloblastic anemia.[3] The cause of megaloblastic anemia was not studied in this study and evaluation of serum folate or vitamin B12 was not available in this study.

The second major cause of pancytopenia was aplastic/ hypoplastic anemia in present study (32.5%)which was correlated with Tilak et al and khodke et al.[3,9] Jha et al and Pathak et al have aplastic anemia as common cause of pancytopenia.[2,4] In a study by Keisu et al neoplastic disease was the commonest cause of pancytopenia.[7] Aplastic anemia may be due to environmental factors or exposure to pesticides/ drugs/ toxic chemicals. In study of 13 cases of aplastic anemia, 8 cases were diagnosed in bone marrow aspiration. And when correlated with bone marrow biopsy it increases to 13.

This study provides a very important message that in all the cases of pancytopenia both bone marrow aspiration and bone marrow biopsy must be performed. Although the incidence of aplastic anemia is higher our study than west which is reported to be between 10-25%.[5]

Table 3: Peripheral blood smear findings.

Diagnosis	Total No	Anisocytosis	Dimorphic picture	Circulating erythroblasts	Hyperseg. Neutrophils	Circulaying immature cells	Relative lymphocytosis	Reticulocytosis
Megaloblastic anaemia	14	6	7	2	10	-	-	3
Aplastic anaemia	13	6	2	-	-	-	1	1
Acute leukemia	03	1	-	1	-	-	-	-
Hairy cell leukemia	01	-	-	-	-	-	-	-
Myelodysplastic syndrome	01	1	1	-	-	-	-	1
Reactive marrow	01	-	1	-	-	-	-	-
Round cell tumor	02	1	-	-	-	-	-	-
Normocellular marrow	02	1	-	-	-	-	-	-
Erythroid hyperplasia	01	1	-	-	-	-	-	1
Undiagnosed	01	-	-	-	-	-	-	-
Total	40	20	12	3	10	-	1	6

Acute leukemia was found to be third most common in our study constituted 7.5% of total cases of pancytopenia in present study findings are similar to the study of Aziz et al acute leukemia constituted almost 10% of cases of pancytopenia and was third most common cause of pancytopenia.[5] However percentage very low as compared to study of Jha et al in which it constituted 19.59% of total cases of pancytopenia.[4] However, in study of Tilak et al only 1 case of acute leukemia was

detected as a cause pancytopenia.[3] Immature cells can be seen in peripheral smears or in smears made from buffy coat. Bone marrow aspiration establishes the diagnosis; however, if the tap is dry then bone biopsy becomes mandatory for diagnosis.

Only one case of myelodysplastic syndrome was diagnosed in our study. It was the second most common cause of pancytopenia in studies by International agranulocytosis and aplastic anemia group.[6] One case of eythroid hyperplasia was noted. Erythroid hyperplasia by itself is not the cause of pancytopenia. Relationship of erythroid hyperplasia to pancytopenia is uncertain. A possible hypersplenism needs to be ruled out in addition to different hemolytic anemias in cases of marrow showing erythroid hyperplasia. No splenomegaly was seen in case of erythroid hyperplasia in present study. In cases of erythroid hyperplasia, correlation with clinical parameters and other laboratory parameters are required.[2] Incidence of Kala azar was high as cause of pancytopenia in various studies however we did not get kala azar as cause of pancytopenia. This is due to different geographic distribution. Kala azar is most common in residence of Bihar.[10] Difference in the frequency of disorders causing pancytopenia has been due to variation in study design, diagnostic criteria, geographic area, duration of observation, genetic differences and varying exposure to cytotoxic/chemical agents.

Table 4: Common causes of pancytopenia in different studies.

Study	Country	Year	Number of cases	Commonest cause	2nd Most common cause
International agranulocytosis and aplastic anemia group	Israel & Europe	1987	319	Hypoplastic anemia (52.7%)	Myelodysplastic syndrome (4.5%)
Keisu M et al[7]	Israel & Europe	1990	100	Neoplastic disease, radiation (32%)	Hypoplastic anemia (19%)
Tilak et al[3]	India	1999	77	Megaloblastic (68%)	Hypoplastic anemia 7.70%
Khodke et al[9]	India	2000	50	Megaloblastic anemia (44%)	Aplastic anemia (14%)
Jha A et al[4]	Nepal	2008	148	Hypoplastic anemia (29.05%)	Megaloblastic anemia (23.64%)
Pathak R et al[2]	Nepal	2010	102	Hypoplastic anemia (42.15%)	Hematological malignancies (19.4%)
Present Study	Surat	2016	40	Megaloblastic anaemia (35%)	Aplastic anemia (32.5%)

CONCLUSION

The present study concludes that physical examination, primary hematological investigations along with bone marrow aspiration coupled with biopsy in pancytopenic patients are helpful for understanding disease process and to diagnose or to rule out the causes of pancytopenia. These are also helpful in planning further investigations and management.

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