FREQUENCY OF DIFFERENT CAUSES OF PANCYTOPENIA IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine the frequency of different causes of pancytopenia on bone marrow examination.

Study Design: Descriptive study.

Place and Duration of Study: The study was carried out at Haematology (pathology) department of Army Medical College, National University of Sciences and Technology (NUST) and Military Hospital Rawalpindi from Jan 2012 – Dec 2012.

Patients and Methods: Total 67 cases of pancytopenia were included in the study. Bone marrow aspiration was done using 16 G LP needle and biopsy was done by using 11 G Trephine biopsy needle.

Results: Out of 67 patients, (15%) were children and (52%) were adults. Among children leishmaniasis and hypersplenism were the most common causes (20%) of pancytopenia followed by acute leukemia (3.8%), aplastic anaemia (6.7%) and megaloblastic anaemia (6.7%). Among adults megaloblastic anaemia was the most common cause (40.4%) followed by lymphoproliferative disorder (15.4%), hypersplenism (7.7%), aplastic anaemia, megaloblastic anaemia, acute leukemia and myelodysplasia.

Conclusion: Major causes of pancytopenia in children were leishmaniasis and hypersplenism whereas in adults they were megaloblastic anaemia and lymphoproliferative disorders.

Keywords: Hypersplenism, Leishmaniasis, Megaloblastic anaemia, Pancytopenia.

INTRODUCTION

Pancytopenia is a common clinico-pathological finding noticed routinely during clinical practice. It is a common finding on complete blood count in which all the three cell lines are depressed. Patients present with features of anaemia, thrombocytopenia and leukopenia whether the bone marrow is involved primarily or secondarily.

Causes of pancytopenia vary widely ranging from minor nutritional deficiencies like megaloblastic anaemia to complete bone marrow failure as in cases of aplastic anaemia and myelofibrosis. No matter what the underlying pathology, pancytopenia is a strong indication for bone marrow aspiration and trephine biopsy.

In haematology lab, we encounter a number of patients with pancytopenia, yet unable to define the definitive cause for this condition.

ABSTRACT

INTRODUCTION

Causes of pancytopenia vary worldwide among different geographical locations and ethnic groups. This study can help us to find the most common causes of pancytopenia both in adults and in children in our set up.

PATIENTS AND METHODS

It was a cross-sectional study carried out at Haematology department, Army Medical College, National University of Sciences and Technology (NUST) over a period of one year (Jan 2012-Dec 2012). Patients of all age groups fulfilling the criteria for diagnosis of pancytopenia that is haemoglobin less than 10 gms/dl, TLC less than 3500/mm³ and platelet count less than 100,000/mm³ were included. There were no exclusion criteria in this study. Out of 408 bone marrows aspirations performed during this period, 67 were indicated to diagnose the cause of pancytopenia. Bone marrow aspiration was done using 16 G LP needle from posterior iliac spine in adults and from tibial tuberosity in children less than one year of age. Trephine biopsy was done with 11 G Trephine biopsy needle. Data were collected from the
records saved in the official departmental registers, entered on a specifically designed proforma and analysed using SPSS version 15. Descriptive statistics were used to describe the results. Frequency and percentages were calculated for qualitative variables like symptoms, signs and causes of pancytopenia. Mean and standard deviation (SD) were calculated for quantitative variables like age. Chi-square test was applied to compare the frequencies of various causes in children and adults. p < 0.05 was considered significant.

**RESULTS**

Age range of patients included in the study was 8 months to 87 years. Out of 67 patients, 45 were males and 22 were females with male to female ratio of 2.4:1.

Fever was the most common complaint observed in 38 (56.7%) patients. Bleeding was the second most common presentation in 23 (34.3%) patients followed by dyspnea in 12 (17.9%) patients. On clinical examination splenomegaly was present in 20 (29.9%) patients followed by hepatomegaly in 12 (17.9%), petechial rash in 6 (9%) and lymphadenopathy in 3 (4.5%) patients. Forty one (61.2%) patients had no positive finding on clinical examination.

Peripheral blood examination revealed dimorphism as the most common finding observed in 25 (37.3%) patients. Seventeen (25.4%) had normocytic normochromic picture, microcytosis was observed in 15 (22.4%) and macrocytosis in 9 (13.4%) cases. Leucoerythroblastic picture was present in 15 (22.4%) patients. Among these, 7 (46.7%) cases were of megaloblastic anaemia, 3 (20%) of marked haemophagocytosis due to hypersplenism, 2 (13.3%) of lymphoproliferative disorder and 1 (6.7%) each of aplastic anaemia, acute myeloid leukemia and leishmaniasis.

Causes of pancytopenia were determined separately for children (< 15 years) and adults (> 15 years), 15 were children and 52 adults.

Among children the most common causes were leishmaniasis in 3 (20%) and hypersplenism in 3 (20%). Same frequency of pancytopenia was observed for marrows showing reactive changes. (Table-1)

In case of adults megaloblastic anaemia was the commonest cause affecting 20 (40.4%) patients. Eight (15.4%) patients were advised immunohistochemistry in view of atypical lymphoid infiltrate seen both on aspiration and

<table>
<thead>
<tr>
<th>Disease</th>
<th>Children (n=15)</th>
<th>Adults (n=52)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leishmaniasis</td>
<td>3 (20%)</td>
<td>0 (0%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Megaloblastic anemia</td>
<td>1 (6.7%)</td>
<td>21 (40.4%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Red cell aplasia</td>
<td>1 (6.7%)</td>
<td>0 (0%)</td>
<td>0.061</td>
</tr>
<tr>
<td>Marrow showing reactive changes</td>
<td>3 (20%)</td>
<td>3 (5.8%)</td>
<td>0.089</td>
</tr>
<tr>
<td>Lymphoproliferative disorder</td>
<td>0 (0%)</td>
<td>8 (15.4%)</td>
<td>0.105</td>
</tr>
<tr>
<td>Hypersplenism</td>
<td>3 (20%)</td>
<td>4 (7.7%)</td>
<td>0.170</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>2 (13.3%)</td>
<td>2 (3.8%)</td>
<td>0.172</td>
</tr>
<tr>
<td>Mixed deficiency anemia</td>
<td>0 (0%)</td>
<td>3 (5.8%)</td>
<td>0.341</td>
</tr>
<tr>
<td>Idiopathic thrombocytopenic purpura</td>
<td>1 (6.7%)</td>
<td>1 (1.9%)</td>
<td>0.342</td>
</tr>
<tr>
<td>Myelodysplasia</td>
<td>0 (0%)</td>
<td>2 (3.8%)</td>
<td>0.441</td>
</tr>
<tr>
<td>Erythroid hyperplasia</td>
<td>0 (0%)</td>
<td>1 (1.9%)</td>
<td>0.588</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>0 (0%)</td>
<td>1 (1.9%)</td>
<td>0.588</td>
</tr>
<tr>
<td>Essential thrombocytopenic purpura</td>
<td>0 (0%)</td>
<td>1 (1.9%)</td>
<td>0.588</td>
</tr>
<tr>
<td>Paroxysmal nocturnal hemoglobinuria</td>
<td>0 (0%)</td>
<td>1 (1.9%)</td>
<td>0.588</td>
</tr>
<tr>
<td>Aplastic anaemia</td>
<td>1 (6.7%)</td>
<td>4 (7.7%)</td>
<td>0.894</td>
</tr>
</tbody>
</table>
Infiltrate was suggestive of lymphoproliferative disorders in all these cases. Four (7.7%) patients revealed marked haemophagocytosis due to hypersplenism and aplastic anaemia. Mixed deficiency anaemia and reactive changes were observed in 3 (5.8%) patients. (Table-1)

In this study although difference lies in the frequency of various causes of pancytopenia among children and adults but statistically significant variation is seen only in cases of leishmaniasis (p = 0.001) and megaloblastic anaemia (p = 0.014) (Table-1).

Bone marrow aspiration and trephine biopsy was performed in all the patients as an obligation for diagnosing the cause of pancytopenia. Maximum patients 45 (67.2%) were diagnosed on bone marrow aspiration alone. Rest of 22 (32.8%) required trephine biopsy for final diagnosis. (Table-2)

**DISCUSSION**

Pancytopenia is the depression of all the three cell lines and is not an uncommon finding we come across in haematology department. It has a number of causes and is broadly classified as: decreased bone marrow function or increased peripheral destruction.

To investigate the cause of primary or secondary pancytopenia, bone marrow examination is required. In our setup bone marrow trephine biopsy is done in all the patients of pancytopenia except for children less than 1 year of age and those having no evidence of hepatosplenomegaly and lymphadenopathy. In this study, although all the patients underwent bone marrow biopsy but only in 22 (32.8%) patients it proved helpful in further diagnosis. Even this small number of positive patients cannot label this procedure as unnecessary because aplastic anaemia and lymphoproliferative disorders can never be diagnosed by just examining the aspiration slides.

Among children leishmaniasis is the most common cause of pancytopenia along with hypersplenism. Fever and splenomegaly was present in all the cases of leishmaniasis, supported by the study carried out in PIMS Islamabad. As Rawalpindi is one of the endemic area for this disease along with other surrounding regions like Chitral, Azad Kashmir, Dir, Swat, Quetta and Hazara division, this finding is not unusual. Most of the children from the above mentioned areas report to our hospital for bone marrow examination hence percentage is seen to be a little more than was expected. Once diagnosed, children show very good response to treatment with Aminosidine.

Hypersplenism was also present in the same frequency as leishmaniasis. This result is contrary to a study carried out in Karachi showing hypersplenism as one of the rare cause. Other studies give no evidence of hypersplenism as the cause of pancytopenia.

A cute leukemia is the second most common cause of pancytopenia. Frequency of acute leukemia matches the results of study carried out at Jamshuru, Sindh. Both acute lymphoblastic leukemia (ALL-L2) and acute myeloid leukemia (AML-M4) are reported in children but the age at which it presented was different. Children with acute lymphoblastic leukemia presented at 3 years of age, and at 11 years of age in case of acute myeloid leukemia. Supporting the study which states that M4 occurs more frequently in children with mean age 8.5 ± 4.5 years.

Acute leukemia is found as the most common cause of pancytopenia in Punjab.
followed by megaloblastic anaemia and aplastic anaemia\textsuperscript{13}. It is striking that we found only a single case of magaloblastic anaemia in this age group, contrary to different studies carried out in Pakistan\textsuperscript{12,13}.

Megaloblastic anaemia has shown the highest percentage (40.4\%) among all the causes, as all other developing countries of Asia\textsuperscript{14} and Africa\textsuperscript{15}. Such high frequency attributes to poor diet, hook worm infestations and medications especially methotrexate, administered during chemotherapy. During this study, we came across a case of psoriasis taking methotrexate that led to pancytopenia\textsuperscript{15} on peripheral blood and megaloblastic anaemia on bone marrow examination. Megaloblastic anaemia is prevalent in all the provinces of Pakistan\textsuperscript{17-19}, except Balochistan where the diet is rich in red meat\textsuperscript{20}.

Lymphoproliferative disorders are the second most common cause (15.4\%) of pancytopenia. This result coincides with only one study carried out in Larkana which shows a percentage of 10\%\textsuperscript{21}.

Hypersplenism was seen in a frequency of 7.7\% patients. In adults this is a common finding in cases of pancytopenia and is supported by other studies\textsuperscript{22}.

Aplastic anaemia is not present in a high frequency in adults in this study. In contrast aplastic anaemia has been found to be the commonest cause of pancytopenia among different areas of Pakistan\textsuperscript{17-19}. Whenever aplastic anaemia is suspected trephine biopsy becomes an obligation because diagnosis is not possible unless the degree of fibrosis is determined. One case of aplastic anaemia in this study was associated with Plasmodium falciparum infection. The patient was a female of 25 years within pancytopenia and was having persistant malaria which was non-responsive to antimalarials.

Leukemia and myelodysplasia were found to be the less frequent causes, as leukaemias usually present with leucocytosis due to presence of blasts and myelodysplasia has an overall decreased incidence in our setup\textsuperscript{24,25}.

**CONCLUSION**

Pancytopenia is not an uncommon hematological finding encountered in clinical practice. The present study concludes that underlying cause of pancytopenia can be diagnosed on bone marrow examination and the causes of pancytopenia are different in adults and children. Among children leishmaniasis and hypersplenism whereas in adults megaloblastic anaemia and lymphoproliferative disorders are more frequent.

**REFERENCES**

Causes of Pancytopenia


