Spectrum of Pancytopenia in Children Based upon Bone Marrow Study

SYED NADEEM MANSOOR¹, MUHAMMAD ALI², FATIMA MUEEZ³, SYED MAAZ NADEEM⁴, WAJEEHA NADEEM⁵, SYED MOIZ NADEEM⁶

ABSTRACT

Aim: To identify the incidence of various underlying etiologies in children less than fifteen years, presenting with pancytopenia at a tertiary care hospital of Lahore, Pakistan.

Settings: Clinical pathology laboratory at department of pediatrics, Mayo hospital / KEMU, Lahore, during the period of January 2011 to December, 2013.

Design: Retrospective study.

Methods: A retrospective analysis of children under 15 years of age over a period of three years, presenting with variable clinical features. One finding which was common to all children was pancytopenia on initial CBC report. Bone marrow studies comprising both aspirations and biopsies were performed. Children who had previous blood transfusions and were either on chemotherapy or radiotherapy were excluded from this study. Patients charts were studied in detail and a standard proforma was used to enter the findings.

Results: Among the 200 cases studied, 120 were male and 80 were female children. Most common symptom was generalized weakness (56%) followed by fever (48%) and pallor (85%) was the predominant sign. Megaloblastic anemia (32%), was the commonest etiology of pancytopenia, next in descending orders were aplastic anemia (22%) and acute leukemia (18%) cases.

Conclusion: In our study, megaloblastic anemia is the commonest etiology followed by hypoplastic/aplastic anemia and leukemias.

Keywords: Pancytopenia, bone marrow study, children, megaloblastic anemia, leukemia.

INTRODUCTION

Pancytopenia is a common pediatric hematological finding seen on routine CBC report. It is defined as a simultaneous decrease in number of cells of three cell lineages, in the peripheral blood resulting in anemia, thrombocytopenia and leucopenia. Patients presenting with anemia, thrombocytopenia and leucopenia on CBC report are labelled as having pancytopenia, so it is not a disease entity by itself, just a finding, may be the result of different underlying disorders. These children usually present with signs and symptoms related to anemia, leucopenia and thrombocytopenia. Pancytopenia is a common finding in our day to day clinical practice in pediatric patients. Diagnostic criteria for pancytopenia is when hemoglobin less than 10 g/dL, total leucocyte count less than 3,500/cu.mm and platelet count less than 1,00,000/cu.mm. Fatigue, exertional dyspnea, generalized weakness and cardiac symptoms are due to anemia whereas epistaxis, bruising and mucosal bleeding result from thrombocytopenia. Neutropenic child is always at high risk of increased susceptibility to serious infections. Pancytopenia is most often the result of diseases affecting bone marrow either primarily or secondarily or it may be the outcome of anti-cancer therapy, HIV infection and radiotherapy leading to bone marrow depression or complete failure. So the underlying pathogenesis in these disorders leading to pancytopenia is a decreased cells production by stem cells, abnormal cells infiltrating marrow cavity, growth and cellular differentiation in marrow is suppressed, non-productive hematopoiesis, defective cellular production and polling of these cells by hyperactive reticuloendothelial system. Careful examination of blood film followed by bone marrow aspiration/biopsy may be needed to conclude a confirmatory diagnosis and management of these children.

PATIENTS AND METHODS

This retrospective study was carried out in the clinical pathology laboratory at department of pediatric medicine, Mayo Hospital, Lahore, over a period of...
three years. A total of 200 children under fifteen years of age were included in this study. All children were selected after looking at their CBC and peripheral blood smear report. Bone marrow was aspirated in all children and trephine biopsy done where ever indicated.

**Inclusion criteria:**
1. All children were under fifteen years of age.
2. All children were having pancytopenia on CBC report.
3. Hemoglobin levels less than 10g/dL.
4. Total leucocyte count less than 3.5x10^9/L
5. Platelet count less than 1.0x10^9/L

**Exclusion criteria:**
1. Children over fifteen years of age.
2. Children with a history of recent blood transfusion.
3. Children receiving chemotherapy or radiotherapy.

Blood counts were done by semi-automated hematology analyzer, Sysmex Kx-21, and then results were re-checked by Giemsa’s stained blood smear examination. Marrow aspirations were performed from posterior superior iliac spine or posterior iliac crest in children above two years and from tibia in children under two years of age. In case of hypoplastic marrow, a bone marrow trephine biopsy was obtained from iliac crest or posterior superior iliac spine.

**RESULTS**

Out of 200 children selected for this study, 120(60%) were male and 80(40%) female children, male to female child ratio was 1.5:1. Average age of male children was 6.67 years and that of female 5.80 years. The youngest child in this study was of 04 months whereas the eldest one was of 15 years. Four months to 05 years age group contained maximum number of children 94(47%), then were 71(35.5%) in 06 to 10 years age group and lowest numbers 35(17.5%) in age group of 11 to 15 years. The most common symptoms were pallor 170(85%) followed by generalized weakness 132(66%) and fever 96(48%). Other symptoms included petechial hemorrhages, joint pain, epistaxis and bruises. Splenomegaly 60(30%), and hepatomegaly 42(21%) were observed on ultrasonography. Bleeding manifestations were observed in 64(32%) of the children (Table 1).

Considering the etiological spectrum of 200 cases included in our study, megaloblastic anemia 63(31.5%) was the commonest, followed by aplastic/hypoplastic anemia 45(22.5%) and leukemias 36(18.0%). Less common problems in descending orders were idiopathic thrombocytopenic purpura 13(6.5%), infections 11(5.5%), iron deficiency anemia 10(05%), mixed deficiency anemia 6(3%), myelodysplastic syndrome 4(2%) and malaria parasite in 4(2%) bone marrow aspirations (Table 2).

**DISCUSSION**

Pancytopenia is a serious pediatric hematological problem in which there is a decrease in erythrocytes, leucocytes and platelet counts in peripheral blood leading to symptoms of anemia, increased susceptibility to infections along with hemorrhagic manifestations. Pancytopenia must be highly suspected on clinical grounds whenever a child presents with pallor, prolonged unexplained fever, H/O repeated infections and hemorrhagic manifestations.

Bone marrow study (aspiration/biopsy), is an important diagnostic tool inconcluding the final diagnosis in children having pancytopenia. It is a simple and commonly performed procedure in pediatric medical practice for both hematological and non-hematological disorders. Excessive bleeding at puncture site, infections and embolic manifestations are rarely reported after these procedures.

In our study megaloblastic anemia was the commonest etiology 63(31.5%), almost close to study conducted by Bhatanger, in which 28.4% pancytopenic children proved to be of megaloblastic etiology. Similar study comprising two hundred
children by Khunger\textsuperscript{12} reported megaloblastic etiology in 36\% children. Another study by Shazia et al\textsuperscript{13} including 230 children concluded the incidence of megaloblastic anemia as 17.39\%. Study done by Gomber et al\textsuperscript{14} reported 11\%, Mukibi et al\textsuperscript{15} 47\% and Sarode et al\textsuperscript{16} an Indian group declared the result as 80.5\%. A research project done by Ayub and Khan\textsuperscript{17} (2009) at pediatric department, Gomal Medical College, D.I. Khan, Pakistan, showing megaloblastic maturation as the most common contributor of pancytopenia in children.

Hypoplastic/a aplastic anemia were next most common etiology of pancytopenia comprising of 45(22.5\%) cases. Study conducted by Jan AZ et al\textsuperscript{17} including 205 children reported aplastic anemia in 58(28.3\%) children. K. Afzalet al\textsuperscript{18} reported frequency of aplastic anemia as 40(20.2\%) cases out of total 198 cases. Another study by Shazia memon\textsuperscript{19} from Hyderabad concluded the incidence in 55(23\%) cases out of total 230 cases.

In this research study, hematological malignancies were reported in 36(18\%) children. Out of these, ALL 26(13\%) was reported as the commonest malignant disorder presenting on CBC report as pancytopenia, next was acute myeloid leukemia 06(03\%) and chronic myeloid leukemia was reported in 04(2\%) cases. This finding is close to the findings of a study carried out by Shazia et al, ALL (8.69\%), AML (2.17\%) and CML (0.89\%). Afzalet al\textsuperscript{18} also reported hematological malignancies incidence in 11.3\% of cases. Idiopathic thrombocytopenic purpura comprises 12(06\%) of cases. ITP is one of the common hematological problem in both children and adults and a commonest cause of purpura. Other studies, done by Ng Sc et al have concluded 32\% to 48\% frequency whereas Khan Aet al reported the incidence as 15.7\%.

CONCLUSION

Pancytopenia is not an uncommon finding in children. This study concludes that to diagnose the various etiologies of pancytopenia, bone marrow examination is an essential tool. Megaloblastic anemia and partial or complete failure of bone marrow are the commonest etiologies of pancytopenia, next and also frequently seen are acute leukemias and immune thrombocytopenic purpura. Megaloblastic anemia, leukemias and immune thrombocytopenic purpura are treatable and reversible causes whereas hypoplastic or aplastic etiology is reversible in some of the cases; so a prophylactic as well as therapeutic trial must be given. Every attempt should be made to confirm the etiology as early as possible so that prompt treatment may be initiated in treatable oncological and benign hematological disorders, to relieve the misery of these children.

REFERENCES