ORIGINAL ARTICLE

Spectrum of Pancytopenia in Children Based upon Bone Marrow Study

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ABSTRACT

Aim: To identify the incidence of various underlying etiologies in children less than fifteen years, presenting with pancytopeniaat 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 findingwhich was common to all children was pancytopenia on initial CBC report.Bone marrow studies comprising both aspirations and biopsieswere performed.Children who had received previous blood transfusionsand 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[1].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 withsigns and symptoms related to anemia,leucopenia and thrombocytopenia[2].Pancytopenia is a common findingin our day to day clinical practice in pediatric patients[3].Diagnostic criteria for pancytopenia is when hemoglobin less than 10g/dL,total leucocyte countless than 3,500/cu.mm and platelet count less than 1,00,000/cu.mm[4,5].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[6]. 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[7,8].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[9].Careful examination of blood film followed by bone marrow aspiration /biopsymay 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

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three years. A total of 200 children under fifteen years of agewere 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 smearexamination. 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 was1.5:1.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, followedby 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).

Table 1: Signs and symptoms of pancytopenia

Clinical Features	Frequency	%age
Pallor	170	85
Generalized weakness	132	66
Fever	96	48
Bruises	102	51
Splenomegaly	60	30
Hepatomegaly	42	21
Epistaxis	48	24
Joint pain	86	43
Lymphadenopathy	36	18
Bleeding gums	40	20
Malena	30	15

Table 2: Etiological spectrum of pancytopenia (n=200)

Etiology	n	%age
Megaloblastic Anemia	63	31.5
Aplastic/Hypoplastic Anemia	45	22.5
Leukemias	36	18.0
Idiopathic thrombocytopenic purpura	13	6.5
Infections	11	5.5
Iron deficiency anemia	10	05
Mixed deficiency anemia	06	03
Myelodysplastic syndrome	04	02
Malaria	04	02
Lymphoma	04	02
Visceral Leishmaniasis	02	01
Gaucher disease	02	01

DISCUSSION

Pancytopenia is a serious pediatric hematological problem in which there is a decrease in erythrocytes, leucocytes and platelet counts in peripheral bloodleading 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[10].

In our study megaloblasticanemia was the commonest etiology63(31.5%), almost close to study conducted by Bhatanger[11], in which 28.4% pancytopenic childrenproved to be of megaloblastic etiology. Similarstudy comprising two hundred

children by Khunger[12]reportedmegaloblastic etiology in 36% children. Another study by Shazia et al[13]including 230 children concluded the incidence of megaloblastic anemia as 17.39%.Study done by Gomber et al[14] reported 11%,Mukiibi et al[15]47% andSarode et al[16] an Indian group declared the result as 80.5%.A research projectdone by Ayub and Khan[17](2009) at pediatric department,GomalMedical College D.I.Khan,Pakistan,showing megaloblastic maturation as the most common contributor of pancytopenia in children.

Hypoplastic/ aplastic anemia were next most common etiology of pancytopenia comprising of 45(22.5%) cases.Study conducted by Jan AZ et al[17] including 205 children reported aplastic anemia in58(28.3%) children. K.Afzalet al[18]reported frequency of aplastic anemia as 40(20.2%) cases out of total 198 cases. Another study by Shazia memon[13]from Hyderabad concluded the incidence in 55(23%) cases out of total 230 cases.

In this research study, hematological malignancies were reportedin 36(18%) children. Out of these, ALL 26(13%) was reported as the commonest malignant disorderpresenting 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%).AfzalK et al[18]also reported hematological malignancies incidence in 11.3% of cases.Idiopathic thrombo-cytopenicpurpura 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 alhave 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.

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