Original Article

Bone marrow examination of pancytopenic children

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Abstract

Objective: To assess the clinical profiles and determine the frequency of different aetiologies of pancytopenia based on bone marrow examination.

Methods: This is a retrospective study conducted over a 15 month period and included 279 pancytopenic children of both sexes from 1 month to 16 years of age, who underwent bone marrow biopsy. Patients on cancer therapy or on immunosuppressive treatment and already diagnosed cases of aplastic anaemia were not included in the study. Clinical profiles and bone marrow morphology findings of the patients were reviewed.

Results: Acute leukaemia was the commonest aetiology 32.2% followed by Aplastic anaemia 30.8%, Megaloblastic anaemia 13.2% and miscellaneous aetiologies. Clinical presentation being pallor (81%), fever (68%), petechial haemorrhages (51%) bleeding manifestations (21.5%) and other features included hepatomegaly (44.8%), splenomegaly (37.2%) and lymphadenopathy (22.5%).

Conclusion: Attempts should be made to establish the aetiology of pancytopenia without delay. Easily treatable causes if identified early can have a positive impact on mortality and morbidity of pancytopenic children.

Keywords: Pancytopenia, Children, Bone marrow and aetiology (JPMA 62: 660; 2012)

Introduction

Pancytopenia is not a diseased entity but a triad of findings that may result from a number of diseased processes.[1] In pancytopenia there is reduction of all the three formed elements of blood below the normal reference range.[2] Incidence of various disorders causing pancytopenia varies according to geographical distribution and genetic differences.[3] A wide range of aetiologist have been linked to pancytopenia and bone marrow failure in childhood, however causality is frequently difficult to demonstrate.[4] Bone marrow biopsy plays a significant role in understanding the aaetiology of pancytopenia,[5] early recognition of the underlying condition will have an impact on the mortality and morbidity of the vulnerable paediatric patients.[6] This study was undertaken to identify the different aetiologies and clinical features of pancytopenia in paediatric patients.

Methods

This was a retrospective study, conducted in a tertiary care children's hospital and included all pancytopenic children aged 1 month to 16 years of both sexes referred for bone marrow examination over a fifteen month period from January 2010 to March 2011. Patients on cancer and immunosuppressive treatments and previously diagnosed cases of aplastic anaemia were excluded from the study. Clinical profiles of all patients and their complete blood counts including haemoglobin, total and differential leukocyte counts, platelet counts, reticulocyte counts and findings of bone marrow morphology were reviewed. The criteria for pancytopenia[7] were haemoglobin (Hb)<10g/dl, Total leukocyte count (TLC) <4000/cumm and platelets <100,000/cumm. These counts were done on haematology auto analyzer .sysmex -kx 21.

Descriptive statistics were used to calculate the percentage.

Results

A total of 1261 ,diagnostic bone marrow biopsies were done over a period of fifteen months , and 279 (22%) children that underwent bone marrow biopsy were pancytopenic. These were included in the present study . There were 183 (65.6) males and 96 (34.5) females, with male: female of 1.9:1, their ages ranged from one month to 16 years. Maximum number of patients 117 (42%) were in the 0-5 years age group ,followed by 112 (40%) in the 5-10 year group and the least number 50 (18%) in those above 10 years, all age groups had a predominance of males, Most common clinical feature (Table-1) was pallor present in 225 (81%), fever in 189 (68%) followed by petechial haemorrhages in 143 (51%) and bleeding from various sites like nose, gums and gastro intestinal tract in 60 (21.5%). Other features were hepatomegaly in 125 (44.8%), splenomegaly in 104 (37.2%) and lymphadenopathy in 62 (22.2%) cases. Bone marrow examination was helpful in identifying the aetiology in majority of patients (Table-2), among malignant conditions acute leukaemia's were the leading cause in 90 (32.2%) while in non malignant conditions maximum cases were of Aplastic anaemia 86 (30.8%) followed by megaloblastic anaemia 37 (13.2%) and miscellaneous aetiologies. Normal bone marrow morphology was seen in 16 (5.7%) cases.

Table-1: Clinical features of pancytopenic patients.

Feature	Number	Percentage (%)
Pallor	225	81%
Fever	189	68%
Petechial Haemorrhages	143	51%
Hepatomegaly	125	44.8%
Splenomegaly	104	37.2%
Lympadenopathy	62	22.2%
Bleeding Manifestations	60	21.5%

Table-2: Etiological Profile of Pancytopenic Children.

Disease	Number	Percentage (%)
Acute leukemia	90	32.2%
Aplastic anaemia	86	30.8%
Megaloblastic anaemia	37	13.2%
Normal bone marrow	16	5.7%
Mixed deficiency anaemia	15	5.3%
Reactive bone marrow	10	3.5%
Hodgkin's disease	6	2.1%
Gaucher's disease	5	1.8%
Hemophagocytic lymphohistiocytosis	3	1%
Marrow granulomas	3	1%
Marrow fibrosis	3	1%
Metastatic deposits	2	0.7%
Histiocytosis x	2	0.7%
Non-Hodgkin's lymphoma	1	0.3%

Discussion

There are varying reports on the underlying aetiology of pancytopenia from various parts of the world. The frequency of pattern of disease causing them varies in different population groups and this has been attributed to differences in methodology and stringency of diagnostic criteria, geographical area, period of observation, genetic differences, nutritional status, prevalence of infection and varying exposure to myelotoxic drugs among others.[3] A limited number of studies have been done on pancytopenic paediatric patients in Pakistan. A five year review study by Pine,[8] identified infections to be the leading cause of

pancytopenia in 64% hospitalized children without cancer followed by haematological causes in 28% and miscellaneous causes in 8%. Study by Gupta et al[9] comprising of 105 pancytopenic children reported Aplastic anaemia as the commonest aetiology in 43%, followed by acute leukaemia in 25%, Clinical features being fever and progressive pallor being present in 81.4% followed by bleeding manifestations in 72.9%, Naseem et al[7] reported aplastic anaemia as the most common non-malignant condition 33.8% and acute leukaemia in 26.6% pancytopenic children. In contrast to these are the results of several studies done in India in which megaloblastic anaemia stands out as the commonest aetiological factor. Bhatnagar[10] included 109 children in his study and found megaloblastic anaemia as the single most common aetiological factor in 28.4%, followed by acute leukaemia and infections in 21% patients each, and aplastic anaemia in 20% cases. Study of 200 cases by Khunger[11] reported megaloblastic anaemia in 72% cases followed by aplastic anaemia in 14%. Savage[12] from Zimbabwe included 134 patients identifying megaloblastic anaemia to be the leading cause followed by aplastic anaemia and acute leukaemias. Memon et al[13] from Pakistan reported aplastic anaemia (23.9%) to be the leading cause of pancytopenia in children followed by megaloblastic anaemia (13%), leukemias and infections. Clinical presentations being pallor, fever, petechial haemorrhages, visceromegaly and bleeding from nose and gastrointestinal tract to be the common clinical features. The clinical presentation depends on the primary cause and the severity of pancytopenia, In the present study 81% had pallor which was followed by fever, varying bleeding manifestations and visceromegalies The commonest aetiologies were acute leukemias 9 cases (32.2%), and among the non-malignant aetiologies the commonest were aplastic anaemia 86 cases (30.8%) megaloblastic anaemia 37cases (13.2%), mixed deficiency anaemia in 15 (5.3%) and miscellaneous aetiologies in remaining cases. Presence of megaloblastic anaemia can usually be suspected from examination of peripheral blood with oval macrocytes being characteristic but examination of bone marrow aspirate is crucial in the diagnoses. Marrow is hypercellular, erythropoesis is hyperplastic and characterized by the presence of megaloblasts.[14] Aplastic anaemia is characterized by pancytopenia and hypocellular marrow without any underlying neoplastic process.[14] While acute leukaemia is defined as the presence of more than over 20% blasts in peripheral blood or bone marrow at presentation it can be diagnosed with even less than 20% blasts if specific leukaemia associated cytogenetic or molecular genetic abnormalities are present.[15] Lysosomal storage disorders and haemophagocytic syndromes have been reported to be often diagnosed mainly by bone marrow examination[16] in this study Gaucher's disease was found in five cases and haemophagocytic syndrome in three cases. Out of six cases of diagnosed Hodgkin's disease with pancytopenia five had marrow infiltration detected only on trephine, as has been reported in previous studies[17] there was only one case of Non Hodgkin's lymphoma with pancytopenia, and marrow infiltration was not detected. Hypercellular or normocellular marrow in cases of pancytopenia can also be seen with ineffective haematopoiesis with cell death within the marrow,[18] 16 (5.7%) bone marrows in the present study showed no specific abnormality. Naseem et al[7] reported no specific changes in marrows in 12 (8.6%) pancytopenic children. Granulomas were seen in three patients on marrow trephines in this study, none of them showed necrosis, Langhan type giant cells were seen in two cases, marrow aspirates of these cases showed no specific features, a wide range of aetiological agents are associated with marrow granulomas.[19] Infections and malignancy account for more than 50% of all diseases associated with bone marrow granulomas.[20] Processes that either infiltrate or replace the bone marrow can also present as or result in an acquired pancytopenia.

Marrow fibrosis was seen in three cases, two cases had hepatosplenomegaly and extensive fibrosis in the third case was accompanied by infiltrates of lymphocytes and histiocytes. Myelofibrosis occurs in a variety of bony diseases , metastatic carcinoma ,inflammatory disorders and haemopoietic diseases.[21,22] Metastatic deposits were found on marrow trephines in two cases in this study , Bone marrow biopsy is a useful technique not only in the diagnosis of different blood disorders but also for detecting metastatic involvement with tumors.[23]

Conclusion

This study concludes that bone marrow examination is a very useful tool in diagnosing the various aetiologies of pancytopenia and in this study the commonest cause of pancytopenia was acute leukaemias followed by non malignant causes like aplastic anaemia and megaloblastic anaemia. Other causes included mixed deficiency anaemias, marrow infiltration with lymphomas and Gaucher's disease, haemophagocytic syndromes, granulomatous infections, histiocytosis x and fibrosis. Attempt should be made to establish the underlying aetiology so that treatable causes are identified without delay and prognosis improved.

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