

SPECTRUM OF HEMATOLOGICAL DISORDERS IN CHILDREN OBSERVED IN 424 CONSECUTIVE BONE MARROW ASPIRATIONS/BIOPSIES

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ABSTRACT:

Objectives: To study the spectrum of hematological disorders in children at a tertiary care centre in Peshawar NWFP.

Settings: This study was conducted at the department of Child health and the department of Pathology of Khyber Teaching Hospital Peshawar. The study period was from January 2001 to December, 2003.

Design: This was a retrospective study.

Methods: A retrospective analysis of charts of those patients who underwent bone marrow examination (aspiration/trephine) was made. Charts were analyzed in detail regarding history, examination and investigations. All findings were entered on a standard proforma.

Results: A total of 424 patient's case histories including bone marrow examination results were analyzed. Nutritional anemias contributed 138 (32.55%) cases amongst the non-hematological group. Out of nutritional anemias, megaloblastic anemia was the most common i.e. 103 (24.92%) cases and Iron deficiency anemia was the least common i.e. 15 (3.53%) cases amongst the non-malignant hematological disorder. Other non-malignant hematological disorders in descending order of frequency were aplastic anemia 60 (14.15%) cases, idiopathic thrombocytopenic purpura ITP 40(9.43%) cases, visceral Leishmaniasis 25 (5.98%) cases, hypersplenism 11, falciparum malaria 10 (2.35%) cases and hemolytic anemia 3 (0.70%) cases. Amongst the malignant hematological disorders, acute lymphoblastic leukemia accounted for 76 (17.92%) cases and was found to be the most common disorder, followed by acute myeloid leukemia 27 (6.36%), lymphomas 5 (1.17%), chronic myeloid leukemia and neuroblastoma (0.47%) each.

Conclusion: Nutritional anemias as a group was the most common hematological disorder found on bone marrow examination in our patients. Megaloblastic anemia was the most common while iron deficiency anemia was the least common in the nutritional anemia group. Acute lymphoblastic leukemia was the most common amongst the malignant hematological disorders followed by acute myeloid leukemia.

KEY WORDS: non-malignant hematological disorders, malignant hematological disorder, bone marrow aspiration/biopsy, anemia, leukemia and lymphoma.

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INTRODUCTION

Hematological disorders are quite frequent in pediatric population. Unlike adults the spectrum of hematological disorders in children is very wide, ranging from very common condition like iron deficiency anemia to relatively rare congenital disorders like Blackfan Diamond syndrome and Fanconi's anemias. Similarly the spectrum of hematological disorders is relatively different in the developing world than the developed countries¹. Most of the time the diagnosis can be arrived at by detail clinical examination and few simple investigations. However without bone marrow examination

the diagnosis is usually not a confirmatory one.

Bone marrow examination is one of the most frequent and relatively very safe invasive procedures done routinely in pediatric units. Though an invasive, procedure, it can be easily performed even in the presence of severe thrombocytopenia with little or no risk of bleeding. Commonly it is done for the evaluation of unexplained cytopenias and malignant conditions like leukemias. Bone marrow examination is also at times done for the diagnosis or staging of a neoplasm and storage disorders. Trephine biopsy is usually performed when there is hypoplasia or aplasia on aspiration. At time it is also done in cases of lymphomas, granulomatous conditions and osteoporosis. So there are wide variety of disorders in children where bone marrow examination provides diagnostically important information, which otherwise would not be possible in our hospital. This study was undertaken with the view to study the etiological spectrum of disorders as diagnosed on bone marrow examination.

PATIENTS AND METHOD

All children who underwent bone marrow aspiration or trephine biopsy during the study period between January, 2001 to December, 2003 were included in this study. Every patient history sheet was examined in detail and findings were recorded on a standard proforma including demographic data, symptoms

Table-I: Spectrum of Non-malignant hematological disorders

<i>Disease</i>	<i>No. of cases</i>	<i>Percentage</i>
Megaloblastic anemia	103	24.29%
Aplastic anemia	60	14.15%
Immune thrombocytopenic purpura	40	9.43%
Visceral Leishmaniasis	25	5.98%
Miscellaneous disorders	22	5.18%
Mixed deficiency (microcytic & macrocytic) anemia	20	4.71%
Iron deficiency anemia	15	3.53%
Hypersplenism	11	2.59%
Falciparum malaria	10	2.35%
Hemolytic anemia	3	0.70%
Total	309	72.91%

and signs and all the relevant investigations. Particular note was made up of any drugs taken in the past. Bone marrow aspiration or trephine biopsy results were also recorded. Data was analyzed to know the relative frequencies of different hematological disorders in our paediatric patients.

RESULTS

A total of 424 patient's case histories were studied. Ages of the patients ranged from 2 months to 15 years. Males were 281 (66.27%) and females were 143 (33.73%). Non-malignant hematological disorders were seen in 309 (72.88%) patients (Table-I) and malignant hematological disorders were seen in 115 (27.12%) patients (Table-II). Nutritional anemias i.e. megaloblastic, mixed deficiency (microcytic and macrocytic) and iron deficiency together accounted for 138 (32.55%) cases amongst the non-hematological group. Of the nutritional anemias, megaloblastic anemia was the most common non-malignant hematological disorder i.e. 103 (24.92%) followed by mixed deficiency anemia i.e. 20 (4.71%). Iron deficiency anemia was the least common i.e. 15 (3.53%) cases. Other non-malignant hematological disorders in descending order of frequency were aplastic anemia 60 (14.15%) cases, idiopathic thrombocytopenic purpura 40 (9.43%), visceral Leishmaniasis 25 (5.98%) cases, hypersplenism 11 (2.59%) cases, falciparum malaria 10 (2.35%) and hemolytic anemia 3 (0.70%) cases (Table-II). Amongst the

Table-II: Spectrum of Malignant hematological disorders

<i>Disease</i>	<i>No. of cases</i>	<i>Percentage</i>
Acute lymphoblastic leukemia	76	17.92%
Acute myeloid leukemia	27	6.36%
Lymphoma	5	1.17%
Chronic myeloid leukemia	2	0.47%
Neuroblastoma	2	0.47%
Round cell tumor	1	0.23%
Burkitt lymphoma	1	0.23%
Bone marrow secondaries with primary tumor in abdomen cavity	1	0.23%
Total	115	27.08%

malignant hematological disorders, acute lymphoblastic leukemia was the most common i.e. 76 (17.92%) cases, followed by acute myeloid leukemia 27 (6.36%) cases, lymphomas 5 (1.17%), chronic myeloid leukemia and neuroblastoma 2 (0.47%) each (Table-III).

DISCUSSION

The spectrum of hematological disorders in children is very wide. Bone marrow examination is a useful test in reaching the final diagnosis. It is one of the most common and safe procedures done on children in medical practice. Rarely infection, excessive bleeding or embolism has been reported after bone marrow biopsy².

This study shows that amongst the micronutrient deficiency anemias, megaloblastic anemia is the most common non-malignant disorder in our patients. In other similar studies (both national and international) its frequency ranges from as low as 24%³ to as higher as 68%⁴. In almost all these studies pancytopenia was the main presentation and so was the case in our study. Rarely megaloblastic anemia may present with thrombocytopenia only⁵. Though we were unable to determine the underlying cause of megaloblastic anemia, but folate deficiency is more common in children, while B12 deficiency is more common in adults⁶. The usual presenting feature of megaloblastic anemia in our patient was anemia and varying degree of skin and mucosal bleeding (which is usually alarming to the parents and the clinician but bone marrow examination settles the issue). It is a common problem in the developing countries. The usual presenting age in the developed world is infancy. But in developing countries like ours it can occur at any age which is an irony as Pakistan is an agricultural country and folate and B12 are abundant in the food especially green leafy vegetables. A possible explanation of folates deficiency in older children in our country could be the various chronic inflammatory disorders of the gut like chronic diarrheas and malabsorptive states apart from poor nutrition.

Amongst other micronutrient anemias, mixed deficiency anemia (microcytic & mac-

rocytic) was 15% and iron deficiency (microcytic) was 5% only. This percentage is much lower than expected as an estimated 60 to 80% of the world population is affected by iron deficiency anemia and is the most common preventable nutritional deficiency in the world⁷⁻⁹. The possible explanation is that majority of the cases of iron deficiency anemia and mixed anemias are diagnosed on smear examination and are treated as outpatients. Aplastic anemia was the second most common and most lethal non-malignant disorder found in our patients (14.6%). Epidemiologically, aplastic anemia has a pattern of geographic variation opposite to that of leukemias, with higher frequency in the developing world than in the industrialized West^{1, 9}. Although not a common disease worldwide, aplastic anemia has a social impact disproportionate to its incidence¹⁰. Large prospective studies indicate an annual incidence of two new cases per million populations in Europe and Israel¹¹. Its exact incidence in Pakistan is unknown due to lack of reliable population based studies. The rate is much higher in the developing world, where aplastic anemia may rival acute myelogenous leukemia in frequency of diagnosis in hematology clinics. This has been shown from the studies in Thailand¹² and China¹³, where the incidence has been determined to be about threefold that in the West.

European studies have confirmed and quantified medical drugs as risks for the development of marrow failure. Surprisingly, drug use accounts for only a small fraction of the disease in Thailand, where it is almost always idiopathic. Same was the case in our study. Symptoms of anemia and mucocutaneous hemorrhage usually prompt medical attention. Prognosis is directly related to the reduction in peripheral blood counts, particularly the neutrophil number: < 200 granulocytes/ μ L defines the category of super-severe disease¹. In the early twentieth century, patients often died within days or weeks of congestive heart failure, profuse hemorrhage, or overwhelming infection. Recurrent bacterial sepsis or fungal invasion of critical organs secondary to refractory neutropenia are the usual causes of death

in the modern era. Its exact etiology is still not known but an autoimmune mechanism has been inferred from positive responses to non-transplant therapies and laboratory data^{10, 14}.

Idiopathic thrombocytopenia was the third most common hematological disorder found on bone marrow examination in our patients. It is the most common cause of mucocutaneous bleeding in children. Its frequency on bone marrow examination varies between 32% to 48%^{4,5}.

In this study 105 cases (24.76%) of leukemias were noted with acute lymphoblastic leukemia as the commonest malignancy in our patients (17.92%). Approximately 2500 cases per annum are diagnosed in the United States, accounting for about One third of all the cases of childhood cancers. Eighty percent of these are acute lymphoblastic leukemia (ALL), 17% are acute myeloid leukemia (AML) and the rest are cases of chronic myeloid leukemias¹⁵. Little is known regarding the epidemiology, etiology and incidence of childhood cancer in developing countries. The incidence of ALL in our country is lower as compared to the developed countries, as is the case in India and China^{16,17}.

CONCLUSIONS

Amongst the non-malignant hematological disorders, nutritional anemias as a group was the most common disorder found on bone marrow examination in this study. Megaloblastic anemia was the most common and iron deficiency anemia was the least common in the nutritional anemia group. Aplastic anemia was the second common and most serious non-malignant disorder found in this study. Acute lymphoblastic leukemia was the most common amongst the malignant hematological disorders followed by acute myeloid leukemia.

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