Original Article

Significance of Bone Marrow Biopsy in Diagnosis of Pediatric Diseases; One Year Experience at a Single Pediatric Hematology/Oncology Center

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ABSTRACT

Background: Despite the recent advances in the field of hematology in the form of molecular studies and immunophenotyphing, morphological study of bone marrow remains a corner stone in the diagnosis of pediatric hematological diseases. It is also helpful in the diagnosis of many non-hematological diseases. This study is unique in a sense that bone marrow biopsy procedure and morphology reporting were done by a pediatrician trained in clinical hematology.

Objective: To describe the indications of bone marrow biopsy and frequency of pediatric hematological and non-hematological diseases on morphological basis.

Study Design: Descriptive Case Series

Place & Duration of the Study: This study was conducted at the Pediatric Hematology/Oncology Department, The Children Hospital & the Institute of Child Health Multan from January 2010 to December 2010.

Materials and Methods: This study was conducted on children whether admitted in hematology / oncology ward or referred from various departments of this hospital. A Performa was filled for each patient including detailed history, clinical examination, base line investigation reports and provisional diagnosis. All bone marrow biopsies were performed from posterior iliac spines according to standard protocol for this procedure. Biopsy samples were stained with Leishman stain for morphological study. Bone marrow biopsy report was issued with detailed morphology, morphological diagnosis and suggestion for further investigations e.g. immunophenotyping.

Results: Patients age range was 3 months to 13 years with Male: Female = 1:1. Out of 100 bone marrow biopsy reports , disease distribution was acute lymphoblast leukemia (ALL) 30%, acute myeloid leukemia (AML) 7%, lymphoma infiltration 3%, aplastic anemia 18%, idiopathic thrombocytopenic purpra (ITP) 7%, storage disorders 11%, hemolytic anemia 5%, congenital dyserythropoitic anemia (CDA) 2%, red cell aplasia (RCA) 2%, refractory anemia with excessive blasts (RAEB) 2%, nutritional anemia 3%, malaria 3%, reactive changes 5% and normal morphology 2%.

Conclusion: In children, acute leukemia is a leading hematological disease on bone marrow morphology followed by aplastic anemia and various non-hematological diseases. Despite availability of advanced diagnostic facilities, bone marrow biopsy is still a useful diagnostic test in many childhood diseases.

Key Words: Bone Marrow Biopsy, hematological diseases, Leukemia.

INTRODUCTION

Bone marrow examination is a very important investigation for the diagnosis of various hematological and non hematological diseases. Bone marrow sampling is the process of obtaining marrow tissue smear for analysis and diagnosis. First bone marrow examination was performed by Ghedini of Genoal[1] Initially bone marrow examination was based on smear histology but in 1927, examination of curetted tibia marrow section was introduced[2]. In 1933, an account of sternal marrow biopsy and touch preparation had been demonstrated[3]. During the late 1950, bone marrow core biopsies were introduced to overcome the difficulties of dry tap or when insufficient material was obtained during aspiration.[4] Absolute indications for bone marrow biopsy include evaluation of Leucopenia, anemia, Leucoerthroblastic picture, leukemia, storage disorders and post chemotherapy monitoring.[5,6] Relative indication include pyrexia of unknown origin, splenomegaly, iron metabolism and sampling for immunophenotyping or culture. The preferred sites for bone marrow aspiration and biopsy in both adults & children are posterior iliac Spine, sternum and vertebral spinous process. Tibia is proffered site for infants under 18 months of age.[5,6,8] Contraindications are Hemophilia and other coagulation disorders[9] Complications include vessel laceration, marrow embolization, perforation of bone , retroperitoneal hemorrhage , local infection and pain at biopsy site. Premedications and sedation are helpful measures before performing biopsy especially in children. It is a safe and simple procedure if performed by an expert and can be repeated many times if needed.[9] However, It should be performed with clear clinical indication[10].

This study shows experience of a pediatrician trained in clinical hematology and ascertaining the role of bone marrow examination in diagnosis of hematological and

non hematological diseases. It will also be helpful in deciding the appropriate indications of this invasive procedure.

MATERIALS AND METHODS

We carried out bone marrow biopsy in 100 Children with clear indications for this procedure. Patients whether admitted in hematology ward or referred from other departments were included. Patients with inadequate marrow material, inconclusive reports and incomplete History were excluded from the study. A Performa was filled for each patient containing history, examination and provisional diagnosis.

Standard protocol for bone marrow biopsy procedure was followed .Hemogram along with finger prick morphology and retics slide was evaluated at first. Hemogram was obtained from a hematology analyzer, Sysmex. Procedures were carried out under aseptic measures. Children were sedated with midazolam or diazepam in calculated doses. Medication was given intravenously. Lumbar puncture needle of gauge 16-18 were used to get the aspirate from posterior iliac spine. After infiltration of local anesthesia like lignocain ,concentrated marrow particles were Obtained and Smear Prepared . Air dried smear were stained with leishman .Marrow histochemical stains were used when needed.

Trephine biopsy was performed in selected cases like lymphoma, aplastic anemia or dry tap. Trephine was processed for decalcification, printing and staining at histopathology / hematology department, Combined Military Hospital Multan. Immunophenotyping was sent to tertiary research center on bone marrow Aspirate or Peripheral blood containing blast cells more than 30% in cases of leukemia.

Bone marrow biopsy report was issued Containing morphological findings, diagnosis and Suggestion for further investigations.

RESULTS

Out of 100 patients selected for bone marrow biopsies, Male Female = 1:1. Age of children ranged from 3 months to 13 years. In 45% children, age was less than 2 years while in 55% children were more than 2 years. Indications for bone marrow biopsy in descending order of frequency were 1) fever , pallor and evidence of bleeding (Petechiae , bruises, epistaxis) in 27 patients, fever in 19, Hepatosplenomegaly in 18, Anemia in 17, bleeding in 07 Hepatosplenomegaly with Lympha-denopathy in 07 and Splenomegly in 05 (Table – 1). On morphological study malignant diseases were found in 40 % cases with ALL being most common (30%) followed by AML(7%) and lymphoma infiltration(3%). Among non – malignant diseases, aplastic anemia was most common (18%) followed by storage disorders(11%), ITP(7%) hemolytic anemia(5%), malaria (3%), nutritional anemia(3%), red cell aplasia(2%), congenital dyserythropoitic anemia(2%) and RAEB(2%).Reactive changes were noted in 5% cases and normal bone marrow morphology in 2% (Table 2).

Table No.1: Indications of bone marrow biopsy

Clinical features	No of cases
Fever Pallor,Bleeding	27
Fever	19
Hepatoslenomegaly	18
Pallor	17
Bleeding	07
Hepatoslenomegaly,lymphadeopathy	07
Slenomegaly	05

Table No.2: Disease distribution on bone marrow morphology study

Diseases	No. of cases	Age < 2years	Age > 2 year
ALL	30	7	23
AML	07	4	3
Lymphoma	03	0	3
Aplastic anemia	18	6	12
Storage diseases	11	11	0
ITP	07	3	4
Malaria	03	0	3
Hemolytic anemia	05	3	2
Redcell aplasia	02	1	1
Congenital dyserythro-poietic Anemia	02	1	1
RAEB	02	1	1
Nutritional anemia	03	3	0
Reactive changes	05	3	2
Normal	02	2	0
Total number	100	45	55

DISCUSSION

Bone marrow biopsy is helpful test in approaching the final diagnosis of many pediatric diseases both malignant and non-malignant. It is one of the most common & safe procedure done in children, but its role and contribution has been questioned in recent years.[11] Rarely infection or embolism has been reported after bone marrow biopsy[12].

This study shows that ALL is the most common disorder (30%) in children among malignant and non-malignant diseases on bone marrow morphology and results are comparable to a study conducted by Layla A. and Bashawri which showed 33 % children having ALL on bone marrow biopsy.[13] collectively malignant disease including ALL, AML & Lymphoma account for 40 % cases which is comparable to a study conducted by Nina S and Kadan L, which showed incidence of malignant Neoplasm 40 % too.[14] Another study conducted by Fazlur Rahim, showed 24 % cases having malignant disease on bone marrow morphology.[15] Aplastic anemia was the 2nd most common and lethal non- malignant disease in our

patients (18 %) which is comparable to 14 . 6 %[15]. in a study conducted by Fazlur Rahim.

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[16,17]. Although not a common disease worldwide, aplastic anemia has a social impact disproportionate to its incidence[18]. Large prospective studies indicate an annual incidence of two new cases per million populations in Europe and Israel[19]. Its exact incidence in Pakistan is unknown due to lack of reliable population based studies. The rate is much higher in the developing world. This has been shown from the studies in Thailand[12] and China[13], where the incidence has been determined to be about threefold that in the West.

Storage disorders being 11% is the third most common non-hematological disorder found on bone marrow examination. All children of storage disorder were less than two years of age. Gaucher and Neiman pick disease were found among them. Naveen Naz study[22] was showing 11% of storage disorder and it is accurately comparable with our study. Nutritional anemia was at the lowest number in this study, the possible explanation being that majority of the cases of iron deficiency anemia and mixed anemia are diagnosed on smear examination on blood test. Hence bone marrow biopsy is usually not performed in these patients. Idiopathic thrombocytopenic purpra was also found on bone marrow examination in 7% cases, although its frequency in literature varies between 32 % to 48%. Fever with bleeding and anemia was the most common indication for bone marrow biopsy. hepatosplenomegaly was also an indication particularly in children having storage disorders, leukemia and malaria later on bone marrow morphology.

CONCLUSION

This study is in favor that bone marrow biopsy is an important investigation for the diagnosis of common hematological and various non-hematological diseases in children. Fever, pallor, hepatosplenomegaly and bleeding are the common indications of bone marrow biopsy.

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