Original Article

A retrospective study of clinical and laboratory parameter of acute leukaemia's

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Abstract

Aim: To evaluate clinical and heamatological profile of patients with leukemia admitted to Goverment. Rajaji Hospital, Madurai. **Materials and Methods:** The present study is a retrospective study carried out in the Department of Pathology, Madurai Medical College for the period of 2 years. All patients with acute leukemia who were admitted in the departments of Pediatrics, Medicine and Medical Oncology at Govt. Rajaji Hospital were included in the study. The clinical and lab profiles were evaluated and were classified into AML / ALL using FAB classification. The results of 121 patients are presented in the study. A thorough history concentrating on specific epidemiologic pattern, family history, environmental and previous chemotherapy were noted, physical examination, lab investigation results such as HB,TC, Ultrasound abdomen, Peripheral Smear and Bone marrow aspiration were analyzed. Result and **Discussion:** In the present study the incidence of leukemia in Madurai 0.45 % which is comparable with Indian studies, quoting an incidents of 0.34 % to 1 %. The most common type of acute leukemia is ALL 62.8 % followed by AML 36.4 %. In the present study AML-M2 is most common 59.1 % of AML cases followed M4 18.2 %. ALL L1 and L2 have equal incident among ALL cases. The most common type of childwood leukemia is ALL 79.6 % followed by AML 16.6 %. The most common presenting symptom is fever. Generalized lymphadenopathy is present in 36 % of cases of ALL, hyperleukocysis was present in 8.3 % of cases. 78.4 % of cases were associated with thromphocytopenia, Subleukemic presentation was present in 14.2 % cases. 64.2 % of cases showed more than 90 % of blast in bone marrow. The percentage of blast in bonemarrow was higher in ALL cases.

Keywords: acute leukaemia's.

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Received Date: 28/03/2016 Revised Date: 20/04/2016 Accepted Date: 13/05/2016

Access this article online

Quick Response Code:

Website: www.medpulse.in

DOI: 18 May 2016

INTRODUCTION

Leukemia is the term used for hematopoietic neoplasm, presenting with wide spread involvement of bone marrow and peripheral blood by blasts and is the most common cancerous disorder in children[1].Virchow recognized leukemia as a distinct disease in 1845 when he used the term weissesblut to describe the findings in an autopsy in which the ratio of red corpuscles to "colorless (in mass white) "was reversed[2]. He used the term leukemia for the first time in 1847 and subsequently. Described lymphatic and splenic forms[3]. Friedriech recognized acute and chronic types in 1857. Neumann, in 1868, identified the bone marrow as origin of leukemia and used myelogenous as provisional term that has been validated over time. The first case of Acute Myeloid Leukemia (AML) was originally termed acute non lymphocystic leukemia in 1900. During the first half of the century most of the subcategories of myeloid leukemia were identified by light microscopy with the aid of cytohistochemical stains and were described based on the resemblance to normal hematopoietic precursors. The recognition of the Philadelphia chromosome in chronic myeloid leukemia (CML) bynor well and Hungerford in 1960 was the first demonstration of recurring chromosomal abnormality in leukemia. In 1976 FAB classification was proposed, with several subsequent modifications. The FAB group defines seven subsets of

How to site this article: M Sintha, M Muthuraman. A retrospective study of clinical and laboratory parameter of acute leukaemia's. *MedPulse – International Medical Journal.* May 2016; 3(5): 542-546. http://www.medpulse.in (accessed 20 May 2016).

AML. Four based on the percentage of maturing cells and three based on lineage. FAB classifies acute lymphoblastic leukemia (ALL) into three based on morphology as L1, L2 and L3. In the later half of the last century, numerous cytogenetic abnormalities, including specific translocations, were identified in subtypes of AML and led to changes in classifications, as proposed in 1997 by the WHO[4]. Cytogenetics has profound effect on prognosis and treatment. The Who subdivided AML into true denovo AML occurring predominantly in young to middle-aged adults, with recurring cytogenetic translocations or inversions and MDS related AML occurring in elderly adults often with complex chromosomal abnormality. The WHO recognizes therapy related AML and retains the morphologic subcategories of the FAB in cases not otherwise classified. The category of acute leukemia of ambiguous lineage is also added. As per WHO classifications (2001) the ALLs separated under three broader categories, precursor T-cell, precursor B-cell, and mature B-cell neoplasm based on their Immunophenotye[5]. The high cost of cytogenetics and Immunophenotypic studied stands in way of routine application in all patients. The present study is taken up to assess the incidence and haematological profile and the need to upgrade diagnostic and treatment modalities.

MATERIAL AND METHODS

The present study was carried out in the department of pathology, Madurai medical college, Maduraifor a period of 2 years. All patients with acute leukemia who were admitted in the departments of pediatrics, medicine andmedical oncology at Government Rajaji Hospital, Madurai were included in this study. The clinical and lab profiles were evaluated and were classified into AML/ ALL using FAB classification. The results of 121 patients are presented in the study. A thorough history concentrating on specific epidemiological pattern, family history, environmental and previous chemotherapy were taken into account. This was followed by detailed physical examination. On suspicion of leukemia the following investigations were performed. HB, TC,DC, ultrasound abdomen, peripheral smear, bone marrow aspiration, and special studies like PAS/ MPO for all cases. Immunophenotyping and karyotyping were done in selected cases.

Sample collectionand processing

For all patients smear were prepared and air dried and stained by leishman stain. The blasts were categorized into myeloblast depending on morphology, cytochemical staining were done within 24 hours and they were classified into AML or ALL depending on the staining pattern. Cases that were PAS and MPO negative were analyzed by flow cytometry using panel of markers.

Data Analysis

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with help of computer using epidemiological information package (EPI 2002).Using this software, frequencies, percentage, mean, standard deviation, *2 and ‘p’ values were calculated. A ‘p’ value less than 0.05 is taken to denote significant relationship.

OBSERVATION AND RESULTS

Table 1

Diagnosis	No. of cases					
	Children		Adults		Total	
	No	%	No	%	No	%
ALL						
L1	22	50	8	25	30	39.5
L2	22	50	24	75	46	60.5
L3	-	-	-	-	-	-
Total	44	100	32	100	76	100
AML						
M1	-	-	4	11.4	4	9.1
M2	6	66.5	20	57.2	26	59.1
M3	-	-	1	2.9	1	2.3
M4	2	22.3	6	17.1	8	18.2
M5	1	11.2	4	11.4	5	11.3
Total	9	100	35	100	44	100
By phenotypic leukemia	1	1.9	-	-	1	0.8
Grand Total	**54**	**100**	**67**	**100**	**121**	**100**

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Table 2: Age and diagnosis

Age Groups (in yrs)	No.	%
Children		
<1	6	11.1
1-5	17	31.5
6-12	31	57.4
Total	54	100
Adults		
13-20	30	44.8
21-30	17	25.4
31-40	11	16.4
41-50	2	3
51-60	4	6
➢ 60	3	4.5
Total	**67**	**100**

Table 3: Sex

SEX	ALL	AML	OTHER	TOTAL
MALE	55	28	-	83
FEMALE	21	16	1	38
TOTAL	**76**	**44**	**1**	**121**

Table 4: Present symptoms and diagnosis

PRESENT SYMPTOMS	NO. OF CASES PRESENT							
	CHILDREN		ADULTS			TOTAL		
	ALL	AML	ALL	AML	OTHERS	ALL	AML	OTHERS
Fever	33	7	32	26	1	65	33	1
Bleeding	6	1	11	7	-	17	8	-
Fatigue	12	1	5	8	1	17	9	1
Bony Pain	1	1	2	1	-	3	2	-
Others	1	-	2	2	-	3	2	-

Table 5: Clinical Features

Clinical features	No. of cases present						
	Children		Adults		Total		
	ALL	AML	ALL	AML	ALL	AML	OTHERS
Anaemia	32	5	19	28	51	33	1
GLP	12	1	16	6	28	7	-
Hepatomegaly	25	4	18	12	43	16	-
spleenomegaly	21	3	15	5	36	8	-
Testes	1	-	-	-	1	-	-
Fundus hemorrhage	-	-	1	3	1	3	-
Gingival hyperplasia	1	-	-	5	1	5	-
proptosis	-	2	-	5	1	2	-

Table 6: Hemoglobin (Hb)

HB in gm/dl	No. of Cases							
	AML		ALL		OTHER		TOTAL	
	NO	%	NO	%	NO	%	NO	%
<5gm/dl	13	29.5	28	36.8	-	-	41	34
5.1-10gm/dl	26	59	41	54	1	100	68	56
>10 gm/dl	5	11.5	7	9.2	-	-	12	10
Total	**44**	**100**	**76**	**100**	**1**	**100**	**121**	**100**

DISCUSSION

In the present study the incidence of leukemia in Madurai is 0.45% which is comparable with Indian studies quoting an incidence of 0.34%to 1%[7]. The most common type of acute leukemia in the present study is ALL (62.8%) followed by AML (36.4%). Which is comparable with the observations of kapoore. G in whose study ALL composed 62.03% of cases and AML 37.9% of cases [8]. In the present study 56.6% of cases of ALL is seen in children and 80 % of cases of AML are seen adults. In children the incidence of ALL L1 and L2 is equal. In adults L2 morphology is more common accounting for 75% of ALL cases. This is similar to the study conducted by Loffler H *et al*[12] in which L2 was common (68%). The comparative study of morphological distribution of ALL in children and adults is given in the table 16 and 17 respectively. In the present study AML M2 is most common,accounting for 59.1% of AML cases followed by M4 which accounts for 18.2% of cases. The incidence of M5 is 11.3% [13].This is comparable with those quoted by David H in his study on acute myelogenous leukemia in which the most common leukemia was AML M2 followed by M4 and M5. AML M0 was not encountered in this study.

In the present study the most common type of childhood acute leukemia is ALL (79.6%) followed by AML (16.6%). In the present study incidence of infantile leukemia is 11.1%. ALL constituted 66% and AML 44% of infantile leukemia cases. This is similar to the study conducted by somgee etal at the department of medical oncology TATA memorial hospital Mumbai [15].Western literature quotes AML M5 M4 to be more common[14]. In adults, the most common type of leukemia is AML constituting 52.3 % of cases. the AML: ALL ratios is 2.57:1 while other reviews quote a ratio of 4:1.

In the present study both types of leukemia is more common in males. The male female ratio is 2.5:1.1.This ratio is higher than quoted by singh *et al* (1.5:1) in his study[7].

There is no identifiable risk factor for ALL in this study. 7%of cases of AML had a definite etiology. 2 cases were associated with congenital disorder and 1 case was therapy related AML. As per literature in patients with downs syndrome, AML is more common in children less than 3 years of age and in neonatal period it may present as congenital leukemia or as Transient myeloproliferative disorder (TMD). Both cases have similar clinical feature and similar blast percentage and are differentiated only by follow up. TMD cases resolves spontaneously while congenital leukemia has a fatal outcome [20]. In our study, we encountered a 25 days old child with downs syndrome with 35% blast in PS and 50% blast in BM. The blast was of myeloid morphology. Unfortunately we lost follow up of the case. A 13 years old boy with AML M4 morphology presented with multiple congenital anomalies, dysmorphic feature, absent radius and growth retardation. In literature there are studies which relate syndromes such as TAR syndrome with AML[18]. These syndromes are associated with increased risk of mutations. A 40 year female operated for liposarcoma and on chemotherapy with methotrexate for the past 4 years developed therapy related AML. As per literature, leukemia onset after alkylating agent exposure ranged from 1 to 28 years and is most common in 5-9 years range [22].they have worse prognosis.

The most common complaint in 80% of cases in present study is fever followed by bleeding. This is comparable to that of singhetal study. There is no statistically significant difference in presenting symptoms between AML and ALL (p value.42)

Generalized lymphadenopathy is present in 28 cases of ALL and only 7 cases of AML. This is comparable with studies conducted by poplack DG in which he concluded that GLP is more commonly associated with ALL than with AML [29].

In the present study 4.9% of cases hasgingival hypertrophy of which 83.6% are AML. It is more commonly encountered in AML M4/AML M5. It is due to infiltration of gingival tissue by leukemiac blasts. As per literature 3-5% of acute leukemia patients develop gingival hyperplasia of which 88.9% are AML[30]. The various clinical features in different types of leukemia is statistically in significant p value 0.32.

In the present study subleukemic presentation % to refers, in which abnormal cells are present in peripheral blood, but the total leukocyte count is not elevated is seen in cases of acute leukemia. boggs DR in a 10 year study found 53 of 322 cases to have a subleukemic presentation[24]. In the present study hyperleucocytosis was present in 8.3% of cases. Patient's with hyperleucocytosis can present with leucostasis with studging of leukemic cells in capillaries of lungs and brain In the present study a normal platelet count is seen in 22.3 % of cases. Rest of them is associated with thrombocytopenia, with 11.7% of cases having a platelet count below 25,000. Marrow infiltration and chemotherapy are the most common causes of thrombocytopenia in acute leukemia cases[24]. In the present study a blast count of less than 20 % in PS is seen in 14. 2% of cases of acute leukemia. Of these 88 % are ALL and only 11.8 % are AML. In all these cases bone marrow is required for confirmation and typing of leukemia. This is in concordance with the observation made by Bennetetal who concluded that 1st in the

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sequence of diagnosis of acute leukemia is the distinction from other meoplastic and reactive diseases and confirmation of acute leukemia by morphological and cytochemical studies[36].

SUMMARY

The incidence of acute leukemia in and around Madurai is about 0.45 %. The most common type of acute leukemia is acute lymphoblastic leukemia. The most common type of leukemia in children and infants is acute lymphoblastic leukemia. The most common leukemia in adults is acute myelogenous leukemia. Leukemias are more common in males. Downs syndrome and post chemotherapy leukemias were associated with acute myelogenous leukemia. The most common presenting symptom is fever. The most common clinical feature is anemia.Generalized lymphadenopathy is most commonly associated with ALL than AML. Gingival hyperplasia is more commonly associate with AML than ALL. 90% of cases of acute leukemia is associated with Hb<10gms%. 8.3% of cases were associated with hyperleukocytosis. 14.2% of cases showed <20% blasts in peripheral smear for which marrow is essential for diagnosing acute leukemia. 64.2% of cases had blast count >90% in bonemarrow.

CONCLUSION

In a 2 years study period conducted at government rajajihospital, 121 cases of acute leukemia were identified. Our hospital cadres patients in and around Madurai as well as patients from southern districts of tamilnadu. The volume of cases necessitates toupgrade our diagnostic and treatment modalities for acute leukemia as well as rehabilitation facilities for these patients.

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Source of Support: None Declared
Conflict of Interest: None Declared