ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 7, Issue, 10, pp.21824-21826, October, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

CLINICO-PATHOLOGICAL STUDY OF LEUKEMIAS

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ARTICLE INFO

Article History:
Received 11th July, 2015
Received in revised form
29th August, 2015
Accepted 08th September, 2015
Published online 31st October, 2015

Key words:

Leukemia,
Clinicopathological study,
Peripheral smear,
Bone marrow,
Cytochemistry.

ABSTRACT

Background and objectives: Leukemias represent one of the most important problems in the field of haematology. Early diagnosis of various subtypes of leukemia and intervention has improved the prognosis and disease free survival. This is a clinicopathological study of leukemia undertaken at KIMS, Hubli, with the following objectives,

- To study the pattern of leukemias in this part of North Karnataka.
- To study clinical and haematological presentations of acute leukemias.
- To ascertain the utility of cytochemistry in the diagnosis of acute leukemias.

Methods: Clinical history of eighty leukemia patients was recorded. Peripheral smear examination was done and various haematological parameters were noted. Cytochemistry was done in all 37 cases, of acute leukemia using MPO, SBB and PAS stains.

Interpretation and Conclusion: Leukemia is prevalent in this region of North Karnataka as in other parts of India. In almost all age groups and types of leukemias, males predominated. The commonest type of leukemia observed in this study was CML and CLL was less frequent. The presenting symptoms and clinical features of these patients were similar to those observed in other reported studies. While peripheral smear examination and bone marrow studies remain key to the diagnosis of leukemia, conventional cytochemical techniques need to be used for typing and subtyping of leukemias.

Citation: Arathi, S., Sujata.Giriyan and P. K. Rangappa, 2015. "Clinico-pathological study of Leukemias", *International Journal of Current Research*, 7, (10), 21824-21826.

INTRODUCTION

Lympho-haematopoietic malignancies constitute 9.5% of cancer in men and 5.5% in women. Leukemias are 10th most common cancer in men and 12th in women and constitute 3% of total global cancer burden (Manisha Bhutani and Vinod Kochupillai, 2003). The diagnosis of leukemia has moved from evaluation by morphology and cytochemistry to assessment by modern methods immuno-phenotyping, cytogenetics and molecular chemistry (Rajive Kumar, 2004).

Aims and Objectives

- To study the pattern of leukemias in this region of North Karnataka.
- To study clinical and haematological presentations of acute leukemias.
- To ascertain the utility of cytochemistry in the diagnosis of acute leukemias.

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MATERIALS AND METHODS

A prospective study, in the Department of Pathology, KIMS, Hubli. Clinical history of each patient was recorded. Various haematological parameters were noted. The peripheral smears were stained with Leishman's stain and examined. Cytochemical stains employed for the diagnosis were Myeloperoxidase (MPO) stain, Sudan black B (SBB) stain and Periodic Acid Schiff (PAS) stain.

Observation

The present study is a clinico-pathological profile of 80 cases of leukemia. Leukemia was seen in age groups ranging from 1.5 to 86 years. Sixteen (20%) patients were children less than 12 years and the rest 64 (80%) were adults. Out of 80 patients, 51 were males and 29 were females. Male to female ratio was 1.8: 1. Of the 80 cases, 37 (46.2%) cases were acute leukemias and 43 (53.8%) cases were chronic leukemias. In the present study, 17 cases were diagnosed as AML comprising 21.25 % of all cases and 45.94% of acute leukemia. AML cases were seen in the age range of 4 – 59 years with the mean age being 23. 29 years.

Out of 17 cases 9 were males and 8 females, with a male to female ratio of 1.1:1. AML was further sub typed using FAB criteria on morphological & cytochemical grounds. The distributions of various sub types of AML cases in this study are as follows, AML M1 -3 cases (17.65 %), AML M2 - 10cases (58.82%), AML M3 -2 cases (11.76%), AML M4-1 case (5.88%), AML M5 -1 case (5.88%). AML M6 and M7 were not encountered.

The presenting symptoms in patients with AML were fever in 13 (76.5%) cases, generalized weakness in 9 (53%), and loss of appetite in 8 (47%), cough in 7(41%) and mass per abdomen in 6 (35.3%) cases. One (5.9%) patient of AML M2 had bleeding tendency. Physical examination revealed pallor in 16(94.12%) cases, oedema in 5(29.4%) and signs of haemorrhage in one (5.9%) case. Lymphadenopathy was seen in 8 (47.6%) cases. Splenomegaly was seen in 12 (70.6%) cases. Hepatomegaly was seen in 14 (82.35%) cases.

In the present study haemoglobin level was less than 8 gm/dl in 15(88.23%) cases with microcytic hypochromic being the commonest morphologic type. Total leucocyte count (TLC) ranged from 5-100 $X10^9$ /L. Platelet count ranged from 50-100 X 10^9 /L. Peripheral smear examination showed myeloblasts ranging from 0 to 95 % with a mean blast count of 61.7%. Seven (41.2 %) cases showed *Auer* rods in myeloblasts. In 3(17.65%) cases peripheral smear showed no blasts and the diagnosis was made on the basis of bone marrow examination.

In this study 20 cases were diagnosed as ALL comprising 25 % of all leukemias and 54.06% of acute leukemias. ALL cases were seen in age range of 1.5 to 38 years with a mean age of 14.1 years. Out of 20 cases 13 were males and 7 females with male to female ratio of 1.86: 1.

The presenting symptoms were fever in 15(75%) cases, generalized weakness in 10(50%), bleeding tendencies in 7(35%), breathlessness 5(25%) and loss of appetite in 4(20%) cases. Mass per abdomen, neck swelling and bone pain were seen in 3 (15%) cases each. Physical examination showed pallor of varying degree in all cases. Oedema and signs of haemorrhage were seen in 4(20%) cases each. Lymphadenopathy was noted in 16(80%) patients. Splenomegaly was seen in 18 (90%) cases. Hepatomegaly was seen in 17 (85%) cases. In the present study, haemoglobin level was less than 8 gm/dl in 16(80%) cases with microcytic hypochromic being the commonest morphologic type. TLC ranging from 5-100 X 10^9 / L. Platelet count less than 50 X 10^9 /L was seen in 10(50%) cases of ALL. Four (20%) cases had platelet count more than 100 X 10^9 / L.

Table 1. Clinical features of AML and ALL

Presenting Symptoms	AML	ALL
Fever	13(76.5%)	15(75%)
Generalised Weakness	9(53%)	10(50%)
Loss of Appetite	8(47%)	4(20%)
Cough	7(41%)	-
Mass per abdomen	6(35.3%)	3(15%)
Oedema and signs of haemorrhage	1(5.9%)	4(20%)
Lymphadenopathy	8(47.6%)	16(80%)
Splenomegaly	12(70.6%)	18(90%)
Hepatomegaly	14(82.35%)	17(85%)
Total	17	20

Cytochemical stains used in all cases of acute leukemia. Out of 17 cases of AML, 14 showed MPO/SBB positivity (AML M1, AML M2). Two cases of AML M3 showed strong positivity. AML M5 case was negative for MPO/SBB. All 17 cases of AML did not show block positivity for PAS. All 20 cases of ALL were negative for MPO/SBB. Eleven (55%) cases of ALL showed block positivity for PAS. Nine (9%) cases of ALL were negative for PAS.

Table 2. Cytochemical staining for acute leukemias

	MPO/SBB		PAS (Block Positivity)	
Results	Positive N (%)	Negative N (%)	Positive N (%)	Negative N (%)
AML (17cases)	16(94%)	1 (6%)	0	17 (100%)
ALL (20 cases)	0	20 (100%)	11 (55%)	9 (45%)
TOTAL (37)	16	21	11	26

DISCUSSION

Leukemia was more common in males than females in the present study as has been reported by most authors in India and western countries. In the present study, AML constituted 21.25% (17 cases) of all cases of leukemias. The mean ages and M: F ratio are comparable with the study done by Tyagi *et al*. (1992). The presenting features of AML in this study were fever and generalized weakness as noted by other studies also. Bleeding as an initial manifestation was seen in 5.88%, which is much lower as compared to other studies. Pallor, lymphadenopathy and hepatosplenomegaly compare well with the findings of Mathur *et al*. (1985) and Tyagi *et al*. Anaemia (Hb <10 gm/dl) was seen in 16 (93%) cases of AML in the present study is same as Shome *et al* (Shome *et al.,* 1985) 88%. TLC more than 100 X 10^9 /L was seen in 35.3% cases as compared to Shome *et al* (12%). Thrombocytopenia (Platelet count < 100 X 10^9 /L) was present in 11(64.7%) cases as compared to the findings from other studies, which reported figures of 86% (Mathur *et al*., 1993). Applying the FAB classification, M2 was found to be the commonest subtype in this study that was comparable to the observations made in the studies done by Advani *et al*. (1979) and Shome *et al*. In 3 cases of AML, it was difficult to differentiate from ALL based on morphology alone. In these cases, cytochemistry (using MPO and PAS) helped to arrive at the diagnosis of AML.

In the present study, ALL L1 subtype was more common as noted in the study done by Shome *et al*. No cases of ALL L3 were found. Sex ratio showed male predominance in both subtypes of ALL, a finding comparable with other studies.

Main presenting symptoms of ALL in both subtypes, in this study were fever and generalized weakness. Similar findings were also noted in other studies. Bleeding manifestations were seen in 30% of the cases of ALL and more common in ALL L2whereas higher incidences were noted by Shome *et al*. (55%), and Mathur *et al*. (47%). Pallor was seen in all cases of ALL, which was alsonoted by Mathur *et al*. Lymphadenopathy was consistently seen in all studies. Hepatosplenomegaly was more frequent in the present study than compared to the studies done by Tyagi *et al*. Sternal tenderness was noted in 15% cases in the present study as compared to 12.1% in the study done by Tyagi *et al*. Anaemia (Hb <10 gm/dl) was seen in all cases of

ALL, comparable with the findings of Shome *et al*. (87%) and Mathur *et al*. (100%). Subleukemic counts were noted in 15% of the cases, a similar observation was made by Shome *et al*. TLC > 100 X 10^9 was seen in 25% of cases comparable to Shome *et al*. Thrombocytopenia (Platelet count < 100 X 10^9 /L) was present in 80% of the cases in this study which is in concordance with findings of Shome *et al*. (89%). Out of the 20 cases, 11(55%) cases showed block PAS positivity. In the study done by Shome *et al*. 20% cases showed PAS positivity.

Conclusion

The occurrence of leukemia appears to be worldwide. It is also prevalent in this region of North Karnataka as well as in other parts of India. In almost all age groups and types of leukemias, males predominated and presented with generalized weakness and fever. Pallor and hepatosplenomegaly were seen in majority of the patients. Although many cases could be diagnosed as leukemia based on clinical features, haematological evaluation plays an important role in typing and subtyping the leukemias. Peripheral smear examination and bone marrow studies remain key to the diagnosis of leukemia while cytochemistry, immunophenotyping and cytogenetics give valuable additional information.Since not all leukemias manifest specific genetic aberrations and not all institutions are equipped with required facilities; FAB criteria based on morphology and cytochemistry still holds good. Therefore conventional cytochemical techniques need to be used routinely.

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