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Study of Hand-mirror cell leukemia among 215 cases of Acute Myeloblastic and Lymphoblastic Leukemia

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ABSTRACT

Hand mirror cells (HMC) were first described in 1939 by Rich et al in normal lymph nodes. The HMC lymphoblast is characterized by asymmetric foot like cytoplasmic process that extends from the oval nuclear portion of the cell, resulting in a light microscopic appearance resembling a "hand mirror." . HMC blasts also occur irrespective of the cell line of origin having been identified in both lymphoblastic and myeloblastic leukemias. . HMCs have been previously reported in conditions such as infectious mononucleosis, multiple myeloma, lymphosarcoma, and T-cell lymphoma in adults, acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) . These studies have identified the prevalence of HMC in acute leukemia cases HMC are more commonly identified in ALL (20%) in comparison to AML (6.25%).

Aims and objectives: To diagnosed prevalence of cases acute leukemia with hand mirror cell variant.

Materials and methods: It is a prospective study done over a period of 2 years (July 2017 – June 2019) in M.Y. Hospital. Total 215 cases of all age group presented with clinical complain of fever ,pallor, weakness, fatigue, infections petechiae , bruising and bleeding manifestation, organomegaly (lymph nodes ,spleen ,liver ,others), bone pain ,tenderness, gum hypertrophy, CNS symptoms and CBC with peripheral smear examination show anaemia, granulocytopenia with thrombocytopenia . Bone marrow aspiration was done in all cases for the final diagnosis.

Result: Among 215 cases which were studied retrospectively. There were 115 paediatric and 100 adult cases. Out of 215 cases, 135 cases are of ALL & 80 cases are of AML. Out of 135 cases of ALL, 03 were hand mirror variant and out of 80 cases of AML, 01 were hand mirror variant . HMC were found in 3.2 %(N=215). Though HMC were more common in lymphoblastic cases 03 out of 135 ALL cases ie 2.2 % *and in acute myeloblastic cases 01 out of 80 AML cases i.e 1.25%.*

Conclusion: With this study, we calculate the prevalence of HMC in acute leukemia .We have found that HMC are more in ALL than in AML .Also we have found that HMC has prognostic significance .

Keywords: Acute myeloblastic Leukemia (AML), Acute lymphoblastic Leukemia (AML), Hand-mirror cells (HMC), French American british (FAB)

INTRODUCTION

Hematopoietic cells at rest maintain a spherical shape; however, unusual forms have been seen during motion, including the so-called hand-mirror cell (HMC) form [1,2] which is present in both bone marrow and lymph nodes[3] Among lymphocytes, both T and B cells are capable of being HMC.[4,5]" In addition, HMC blasts also occur irrespective of the cell line of origin having been identified in both lymphoblastic and myeloblastic leukemias. [1,2,6,7]. Some of the earlier reports seem to emphasize the relationship of HMC blast morphology and lymphoblastic origin [7,8] The importance of determining whether HMC morphology has prognostic significance in leukemia also has been stressed. We wish also to report the findings of our retrospective study of HMC in 215 adult and pediatric cases of leukemia. Hand mirror cells (HMC) were first described in 1939 by Rich et al [9] in normal lymph nodes. HMCs previously reported in conditions such as infectious mononucleosis, multiple myeloma, lymphosarcoma, and T-cell lymphoma in adults, acute myeloid leukemia (AML)

and acute lymphoblastic leukemia (ALL) [10,11.] In HMC there is asymmetric foot like cytoplasmic process that are extending from the oval nuclear portion of the cell, resulting in a light microscopic appearance resembling a "hand mirror.[12]" In this study we identified the prevalence of HMC in acute leukemia cases [13,14] HMC are more commonly identified in ALL in comparison to AML .[13,14]

Materials and methods: It was a prospective study conducted in department of Pathology, Mahatma Gandhi memorial Medical College and MY Hospital Indore done over a period of 2 years (July 2017 – June 2019) .Total 215 cases of all age group presented with clinical complain of fever ,pallor, weakness, fatigue, infections petechiae , bruising and bleeding manifestation, Physical examination may reveal organomegaly (lymph nodes ,spleen ,liver ,others), bone pain ,tenderness, gum hypertrophy, CNS symptoms. Laboratory investigation included show raised serum LDH normal range 100-200 U/L . Bone marrow aspiration was done in all cases for the diagnosis. Those investigation that are done in our department of Pathology including complete blood count with peripheral smear examination show anaemia, granulocytopenia with thrombocytopenia. Bone marrow examination was done after written consent to rule out other causes of bicytopenias and confirmation of diagnosis , to exclude other differential diseases including other malignancies and before starting therapy . Other investigations were collected from patients record.

RESULTS AND OBSERVATION

The patients' of all ages were included in this study, total 215 cases which were studied retrospectively. There were 115 paediatric (age <13 yrs) and 100 adult cases (age >13 yrs). Among 215 total cases, 135 cases are of ALL & 80 cases are of AML. Out of 135 cases of ALL, 03 were hand mirror variant and out of 80 cases of AML, 01 were hand mirror variant. So total HMC were found in 3.2 %(N=215). Though HMC were more common in lymphoblastic cases 03 out of 135 ALL cases ie 2.2 % *and in acute myeloblastic cases 01 out of 80 AML cases i.e 1.25%.* Peripheral smear examination show HMC in 03 cases of 135 ALL cases and 01 case in 80 AML cases. Which later confirmed by Bone marrow aspiration and flow cytometry . Bone marrow aspiration done in all cases from posterior iliac crest .Total 04 cases show HMC, in all cases showed hyper cellular marrow. Flow cytometric analysis show simultaneous expression of lymphoid antigen CD 19+ ,Tdt +,CD 7 +, CD3+,CD2+ and also express myeloid antigen CD13+,CD33+, CD34+ which shows poorly differentiated precursor cells with mixed lineage in these cases with HMC.

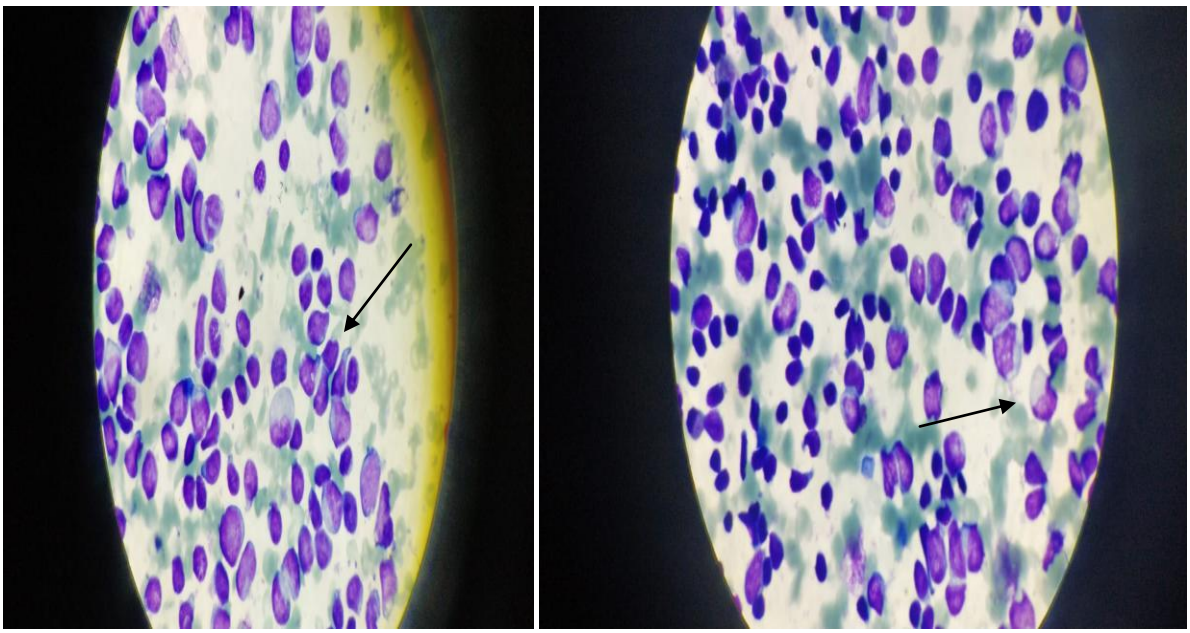

Figure 1a &1b –Case of ALL showing lymphoblast and mature lymphocytes with hand mirror cells (marked by black arrow)

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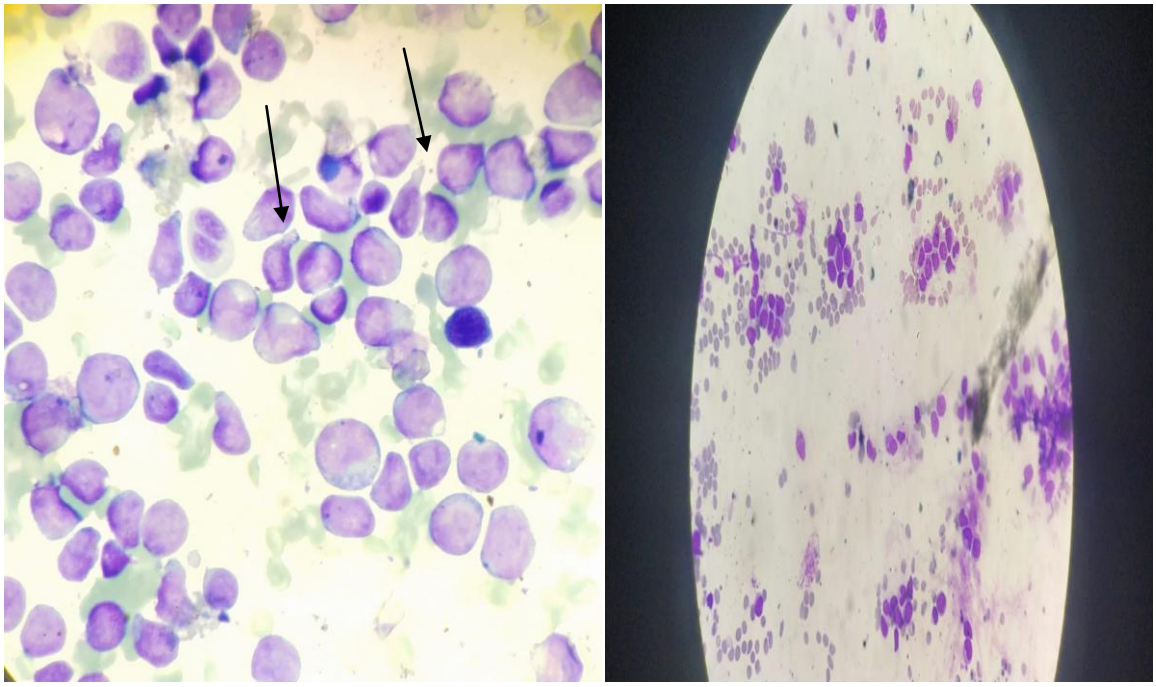

Figure 2a &2b –Case of ALL showing lymphoblast and mature lymphocytes with hand mirror cells (marked by black arrow)

Table 1: SEX WISE DISTRIBUTION OF CASES

SEX	Total Number of cases N=215	percentage
Male	126	58.6%
Female	89	41.3%
Total	215	100%

Table 2: AGE WISE DISTRIBUTION OF CASES.

AGE IN YEARS	Total number of cases N =215	percentage
0-13 years	115	53.4%
>13 years	100	46.5%
Total	215	100%

Table 3: HMC>10% IN BONE MARROW ASPIRATION CASES

AML with HMC	1/80	1.25%
ALL with HMC	3/135	2.2%
All cases with HMC	4/215	3.2%

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Table 4: FAB DIAGNOSIS OF CASES

FAB CLASSIFICATION OF ALL & AML	ADULT CASES N=100	PEDEATRIC CASES N=115
L1	9	86
L2	18	13
L3	7	2
M1	15	3
M2	7	8
M3	6	0
M4	29	2
M5	5	1
M6	4	0
Total	100	115

DISCUSSION

The material selected for this study constitutes a representative spectrum of pathologic types of acute leukemia. The number of myeloblasts and lymphoblastic cases is comparable. The majority of adult cases were myeloblasts, and M4 was the most common FAB subtype.

The majority of pediatric cases were lymphoblastic, and L1 was the most common FAB diagnosis. In general, hand-mirror cell forms were rare among the bone marrow blasts of most of these cases and significant difference was noted in myeloblasts *versus* lymphoblastic leukemia.

Using various techniques many investigators have tried to characterize the leukemic cells with HMC morphologic features [15,16] In contrast to these studies, Guyotat and co-workers[17] studied 41 cases of adult acute lymphoblastic leukemia in which 19 cases reacted with at least one myeloid antibody (CD 13, CD 15, or CD33) and 14 of these demonstrated surface expression of CD34. They suggested that these leukemias may originate in a poorly differentiated precursor cell with mixed differentiation capabilities. Our study support a similar hypothesis, as flow cytometric report give simultaneous expression of lymphoid antigen CD 19+ ,Tdt +,CD 7 +, CD3+,CD2+ and myeloid antigen CD13+,CD33+, CD34+ which shows poorly differentiated precursor cells with mixed lineage in these cases

Studies of acute lymphoblastic leukemia have suggested that the expression of myeloid surface markers may be associated with poor prognosis.[17,18] Our case of hand mirror cell acute lymphoblastic leukemia that expresses myeloid surface antigens probably belongs to the group described in 1986 by Mazur and co-workers.[19] Those patients demonstrated an indolent clinical course not responding to usual chemotherapeutic measures, with some showing disease stability despite lack of treatment Recent cases of acute mixed leukemia reported by Pui and co-workers[20] showed a high number of both acute lymphoid and myeloid leukemias with HMC. Therefore, the presence of hand mirror morphologic features should alert the hematologist to a possible underlying mixed lineage.

CONCLUSION– With this study we calculate the prevalence of HMC in acute leukemia .We have found that HMC are more in ALL than in AML .Also we have found that HMC has prognostic significance in acute leukemia cases.

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