EVALUATION OF BIPHENOTYPIC ACUTE LEUKEMIA WITH GENERALIZED LYMPHADENOPATHY: A CASE REPORT

Subhash Chandra Jha

Assistant Professor, Department of Pathology, Government Medical College, Bettiah
E-mail: jhapatho25@gmail.com

ABSTRACT

It's a rare case of acute biphenotypic leukemia which initially presented in an elderly lady with generalized lymphadenopathy and mild hepatosplenomegaly. Biopsy of cervical lymph node was done and diagnosed as Non-Hodgkin's Lymphoma. Bone marrow smears showed 40% lymphoma cells, a few showing single large nucleolus. Peripheral blood smear showed moderate anemia and leucopenia but normal platelet count. On the basis of cervical biopsy and bone marrow findings, patient was given two cycles of Cyclophosphamide Hydroxydaurorubicin Oncoverin Prednisolone (CHOP) but she did not respond. In view of non responsiveness to CHOP, Immunophenotyping of bone marrow aspirate was done and result showed co-expression of both T-lymphoid and myeloid markers in 90% of atypical cells along with marker of immaturity (CD34) in 72% cells. Analysis showed expression of CyCD3 in 90% cells, CD33 in 95% cells and 60% cells were cytochemically positive for Myeloperoxidase (MPO); thus it was a case of Biphenotypic Acute Leukemia (T-ALL+AML) as per WHO criteria for diagnosis of BAL. So it was an initial presentation of BAL with generalized lymphadenopathy and aleukemic peripheral picture.

Key Words: *Biphenotypic acute leukemia, Immunophenotyping, Aleukemic leukemia, Acute lymphoblastic leukemia (ALL), Acute myeloid leukemia (AML)*

INTRODUCTION

Biphenotypic acute leukemia (BAL) is an entity of acute leukemia which does not exist in FAB classification of acute leukemia but this has been described in recent classification of WHO under heading of acute leukemia of ambiguous origin [1]. The European group for the Immunological classification of leukemia proposed scoring system for various markers [2].

As some hematopoietic markers are predominantly restricted to particular lineage: CD3 (membrane or cytoplasmic) for T-lymphoid, CyCD22 for B-lymphoid and MPO (cytochemical or immunological) for myeloid lineages, thus they are called lineage restricted or specific markers. Other markers are called lineage associated markers because they are expressed on normal cells in particular lineage only but their expression on neoplastic cells of other lineages is common, thus they are called lineage-associated markers. CD117 is not considered specific for myeloid lineage but its expression is rare in T-lymphoid and B-lymphoid lineages of cells [3].

Markers are given different scores from 0.5 to 2 on the basis of their degree of specificity. Presence of one specific marker for two different lineages at almost equal score is essential for diagnosis of BAL. BAL could be T-Lymphoid + Myeloid, B-lymphoid + Myeloid, T-Lymphoid + B-Lymphoid or very rarely possibility of three lineages is also. BALs are rare, generally less than 4% of all acute leukemia's [4, 5].

CASE REPORT

A female patient of 65 years presented to the department of medical oncology, Tertiary Cancer Centre, Patna. At the time of first evaluation, she had complaints of multiple lymphadenopathies, low grade fever, swelling of both legs and foots. She was evaluated and advised to have Hemogram, Blood Chemistry, Ultrasonography (USG) of whole abdomen, bone marrow aspiration, Fine Needle Aspiration Cytology (FNAC) and Biopsy of cervical lymph node. Her blood chemistry was within normal limits, except increased LDH and hemogram showed moderate anemia and leucopenia (TLC: 2.9X103/µl hemoglobin: 9.5gm/dl) but no immature cells were found. Platelet count was within normal limit. USG showed mild hepatosplenomegaly.

FNAC favored NHL that was also confirmed by biopsy of lymph node. Bone marrow aspiration examination showed 40% atypical lymphoid cells, a few showing single large nucleolus; suggesting infiltration by high grade NHL cells. Thus final diagnosis of NHL with bone marrow infiltration was made in this case and patient was put on CHOP regimen. She was given two cycles of CHOP but no response was seen but her TLC and hemoglobin further decreased. Because after two cycles of chemotherapy, patient did not show any response, case was re-evaluated and discussed with hemato-pathologist.

She was advised to have immunophenotyping of bone marrow aspirate sample. Immunophenotypic findings of this patient showed very ambiguous results. Specific markers of both myeloid and T-lymphoid lineages were present (table 2). 90% atypical cells were positive for cyCD3. Cytochemically, 60% atypical cells were positive MPO (table2, figure 1). 72% atypical lymphoid cells were CD34 positive. Thus on the basis of immunophenotyping and cytochemical findings, diagnosis was revised

and final diagnosis of Biphenotypic acute leukemia (Myeloid +T-lymphoid) was made and patient treated as AML but patient succumbed to death due to severe septicemia.

Table 1: Scoring system for markers proposed by European Group for the immunological classification of Leukemia

SCORE	B-LYMPHOID	T-LYMPHOID	®MYELOID
2	CyCD79a,CyIgm, CyCD22	CD3(m/cy),anti-TCR	MPO
1	CD19,CD20,CD10	CD2, CD5,CD8,CD10	CD117,CD13, CD33, CD65
0.5	TdT, CD24	TdT, CD7, CD1a	CD14,CD15, CD64

®MPO demonstrated by cyto-chemical or immunological method

Table 2: Immuno-phenotypic Profile of Patient

Sr. No	Marker	% Positivity
1.	CD45	99
2.	CyCD3	90
3	CD5	48
4	CD7	99
5	CD10	00
6.	CD19	00
7.	CD22	00
8.	CD13	38
9.	CD33	95
10.	CD117	30
11	CD34	72
12	HLA-DR	06
13	MPO-cyto-chemistry	60

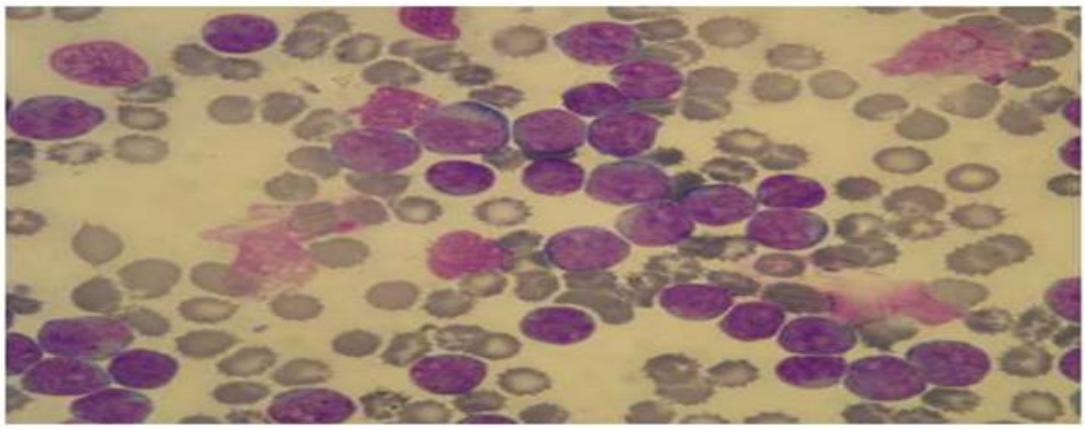

Fig. 1: Bone marrow aspirate showing undifferentiated blasts.

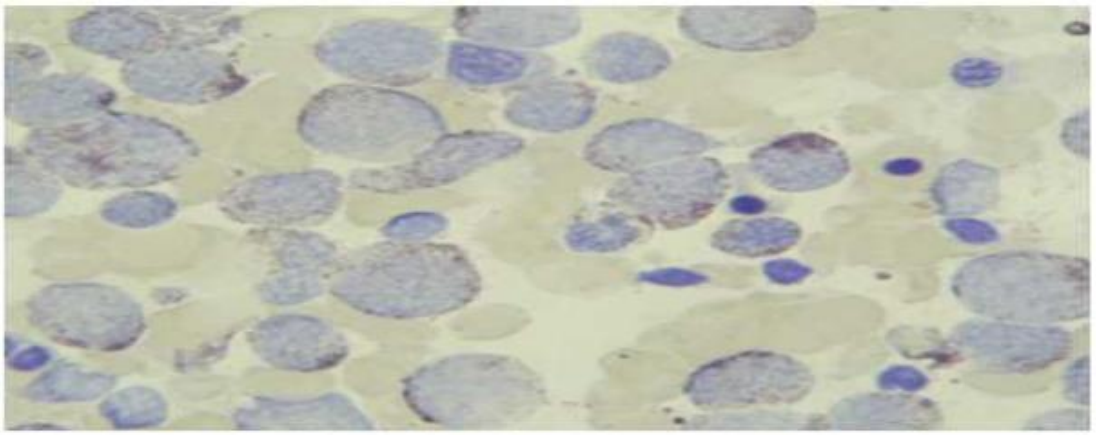

Fig. 2: Microphotograph showing strong positivity of cytochemical MPO positivity in 60% blasts

DISCUSSION

BAL occurs when neoplastic changes take place at the level of undifferentiated stem cells having potential to differentiate along two or more lineages [6]. Biphenotypic acute leukemia is different from aberrant expression of non-specific markers of other lineages. BAL is a rare variant of acute leukemia but diagnosis of more and more BAL is possible due to availability of immunophenotyping and scoring system for acute leukemia (Table:1). Thus incidence of BAL has increased because we have well defined scoring system and specific markers for acute leukemia [2]. It is very rare to have presentation of AML with generalized lymphadenopathy and without thrombocytopenia, although Non-Hodgkin' Lymphoma (NHL) commonly presents in this manner and few cases of ALL could have such type of presentation [1]. In AML, most common presentation is with bone marrow failure i.e. severe anemia and thrombocytopenia [1]. In this case, patient had presented with generalized lymphadenopathy, normal platelet count, anemia and leucopenia, so suspicion of AML or BAL was most unlikely. Infiltration of bone marrow with NHL is very common that could be of lymphoblastic lymphoma or other low grade lymphoma. As bone marrow showed 40 % atypical lymphoid cells with single large nucleolus mimicking lymphoblasts, diagnosis of lymphoblastic lymphoma with infiltration of bone marrow was better diagnosis. Still suspicion of BAL was out of question. Before starting the therapy, immno-pheno-tytping of bone marrow sample could have been done. In developing country like India flowcytometric studies of every case is not possible.

Thus morphological studies like bone marrow examination, FNAC and biopsy are still considered final diagnostic modalities. Ideally, knowing the diagnostic and prognostic significance of immunophenotyping, every case of suspected acute leukemia and high grade NHL must have flowcytometric studies, especially when presentation is atypical so that such rare diagnosis could be made to explain the prognosis [4]. BAL has worse prognosis than other acute leukemia. Co-expression or aberrant expression has not got clinical significance but expression of expression of one specific marker from two different lineages or having more than 2 score of each lineage have got clinical significance [7]. Therapy is planned considering effects of drugs on more malignant lineage, in a patient of BAL (Myeloid + Lymphoid); treatment is planned according to AML [4]. Treatment protocol of BAL is still not well defined prognosis is even worse than AML.

CONCLUSION

Diagnosis of BAL requires very high degree of suspicion for diagnosis. Immunophenotyping is the best method of diagnosis in the case of BAL.

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