Acute Leukemia of Ambiguous Lineage with a Rare Abnormality Del17p by FISH Analysis

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Abstract: The World Health Organization (WHO) has categorized acute undifferentiated leukemia (AUL) as a rare subtype of acute leukemia of ambiguous lineage (ALAL). The prognosis of AUL is considered poor and it expresses no known lineage-specific markers. In majority of the cases, AUL has been associated with karyotypic abnormalities, most commonly deletion 5q and complex karyotype. Deletion 17p correlation with acute myeloid leukemia and myelodysplastic syndrome has been previously established and is associated with poorer outcomes. Herein we are reporting a case of forty years old male who was referred to National institute of blood diseases and bone marrow transplantation with complains of fever, multiple neck swellings, and early satiety and was diagnosed as Acute Undifferentiated Leukemia along with deletion 17p. This is a rare entity and can aid in further diagnostic and therapeutic approaches.

Keywords: Acute undifferentiated leukemia, Deletion 17p, F lourescnece in situ hybridization, Allogeneic haematopoetic stem cell transplantation, Flow cytometry.

INTRODUCTION

Diagnosis and classification of acute leukemia is based on morphology, immunophenotyping, chromosomal analysis and specific genetic tests [1]. In majority of cases diagnosis and lineage categorization in to myeloid, B-lymphoid or T-lymphoid can easily be established by multiparameter flowcytometry, but in few cases lineage attribution is problematic [2]. These cases which do not show lineage specific antigens are currently classified by WHO as acute undifferentiated leukemia which are the subtype of acute leukemia of ambiguous lineage [3].

Deletion of short arm of chromosome 17 (Del 17p) predicts shorter survival, resistance to available therapy in chronic lymphocytic leukemia, other non hodgkin's lymphoma and multiple myeloma cases [4, 5]. 3-4% of acute myeloid leukemia and myelodysplastic syndrome cases exhibit this chromosomal abnormality [6]. We are reporting here a case of acute undifferentiated leukemia with del 17p chromosomal aberration.

CASE PRESENTATION

40 years old male patient was referred to National Institute of Blood Disease and Bone Marrow Transplantation with complaints of multiple swellings in necks, intermittent fever and history of 5 kg weight loss in last 1 month. On examination both right and left cervical lymph nodes were palpable along with enlarge spleen that was palpable 2 fingers below the left costal margin. CBC showed Hemoglobin 10.7 G/dl Total Leukocyte Count 93.22x10^9/L and Platelets 60x10^9/L differential count showed 94% Abnormal lymphoid cells as showed in (Fig. 1). These abnormal cells were small to medium in size further characterized by high nuclear to cytoplasmic ratio, scant pale blue agranular cytoplasm, condensed chromatin pattern and inconspicuous nucleoli as represented in (Fig. 2). No any myelodysplasia related findings were observed. The morphology of these cells was not straightforward indicator of acute nature of disease, so Del17p by FISH was also sent along with other diagnostic workup. Myeloperoxidase stain on aspirate smear was negative illustrated in (Fig. 3). Trephine section exhibited interstitial to diffuse infiltration by these abnormal cells as shown in (Fig. 4). Immunohistochemistry was performed for further evaluation and lineage attribution. Initial panel showed CD45 and TdT diffuse positivity as seen in (Fig. 5). While these cells did not express CD34 and CD117 represented in (Fig. 6). For lineage specification B-lymphoid (CD19, CD 79a, CD20) demonstrated in (Figs. 7, 8) T-lymphoid (CD3) shown in (Fig. 9). Myeloid (CD13, CD33) as seen in (Figs. 10, 11) these all markers were negative. Before concluding it as acute undifferentiated leukemia CD38 and CD56 exhibited in (Figs. 12, 13) were also performed to see for if plasmacytoid or NK cell precursors were present, but these blast cells did not express any lineage specific antigen. Immunophenotyping by Flowcytometry was also performed and diagnosis turned out to be same. Conventional cyogenetic analysis showed 46 XY normal male karyotype, while del17p was detected by FISH analysis as illustrated in (Fig. 14).

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Acute undifferentiated leukemia with del 17p chromosomal abnormality [6]. We are reporting here a case of acute myeloid leukemia and myelodysplastic syndrome cases exhibit this chromosomal abnormality. 3-4% of acute myeloid leukemia, other non hodgkin's lymphoma and leukemia of ambiguous lineage [3]. Specific antigens are currently classified by WHO as acute leukemia rather than other markers of immaturity (CD34 and CD117). T-lymphoid can easily be established by multiparameter and specific genetic tests [1]. In majority of cases diagnosis is problematic [2]. These cases which do not show lineage specific pattern and inconspicuous nucleoli as seen in (Fig. 1). Myeloid (CD13, CD33) as seen in (Fig. 7). Blast Cells Population is CD19 Negative. (Fig. 5). Blast Population Showing Diffuse Positivity of TDT. (Fig. 6). Blast Population is CD117 Negative. (Fig. 8). Blast Cells Population is CD79a Negative. (Fig. 9). Blast Cells Population is CD 3 Negative. (Fig. 10). Blast Cells Population is CD 13 Negative. (Fig. 11). Blast Cells Population is CD 33 Negative. (Fig. 12). Blast Cells Population is CD 38 Negative. (Fig. 13). Blast Cells Population is CD56 Negative.

Myeloperoxidase stain on aspirate smear was Negative. Deletion 17p by FISH was also sent along with other diagnostic findings were observed. The morphology of these cells was condensed chromatin pattern and inconspicuous nucleoli as seen in (Fig. 2). Bone Marrow Aspirate Showing Large Number of Blast Cells and Suppressed Trilineage Hematopoiesis. (Fig. 14). Deletion 17p Analysis by FISH.

Myelodysplasia related complex karyotype in only one case, Heesch et al. reported and has been mostly associated with Acute Myeloid leukemia. Del 17p is associated with poor overall and disease free survival. A previous report described a patient with del17p but no myelodysplasia related complex karyotype as a major cytogenetic abnormality [2, 8]. The 2016 revision to the classification of acute leukemia [3] Arber DA, Orazi A, Hasserjian R, et al. Mutations in TP53 are most frequently associated with del (5q) and trisomy 13 [7] Cuneo A, Ferrant A, Michaux JL, et al. The 2016 revision to the classification of acute leukemia [3] Arber DA, Orazi A, Hasserjian R, et al. Most frequent are del (5q) and trisomy 13 [7] Cuneo A, Ferrant A, Michaux JL, et al. Cytogenetic and molecular cytogenetic analysis was performed in a case of acute lymphoblastic leukemia. Del 17p by FISH was also sent along with other diagnostic findings were observed. The morphology of these cells was condensed chromatin pattern and inconspicuous nucleoli as seen in (Fig. 1). Myeloid (CD13, CD33) as seen in (Fig. 7). Blast Cells Population is CD19 Negative. (Fig. 5). Blast Population Showing Diffuse Positivity of TDT. (Fig. 6). Blast Population is CD117 Negative. (Fig. 8). Blast Cells Population is CD79a Negative. (Fig. 9). Blast Cells Population is CD 3 Negative. (Fig. 10). Blast Cells Population is CD 13 Negative. (Fig. 11). Blast Cells Population is CD 33 Negative. (Fig. 12). Blast Cells Population is CD 38 Negative. (Fig. 13). Blast Cells Population is CD56 Negative.

Previously it has been reported in few studies that expression of specific antigens are currently classified by WHO as acute leukemia rather than other markers of immaturity (CD34 and CD117). T-lymphoid can easily be established by multiparameter and specific genetic tests [1]. In majority of cases diagnosis is problematic [2]. These cases which do not show lineage specific pattern and inconspicuous nucleoli as seen in (Fig. 1). Myeloid (CD13, CD33) as seen in (Fig. 7). Blast Cells Population is CD19 Negative. (Fig. 5). Blast Population Showing Diffuse Positivity of TDT. (Fig. 6). Blast Population is CD117 Negative. (Fig. 8). Blast Cells Population is CD79a Negative. (Fig. 9). Blast Cells Population is CD 3 Negative. (Fig. 10). Blast Cells Population is CD 13 Negative. (Fig. 11). Blast Cells Population is CD 33 Negative. (Fig. 12). Blast Cells Population is CD 38 Negative. (Fig. 13). Blast Cells Population is CD56 Negative.

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INTRODUCTION

1 del17p was detected by FISH analysis as illustrated in (Fig.

ic analysis showed 46 XY normal male karyotype, while

Immunophenotyping by Flowcytometry was also performed

these blast cells did not express any lineage specific antigen.

For lineage specification B-lymphoid (CD19, CD 79a, CD20) demonstrated in (Figs.

6). T-lymphoid [43x291]CT scan chest and abdomen with contrast showed extensive

lymphadenopathy and hepatosplenomegaly. Echocardiogra-

phy showed normal function of ventricles and viral markers

were negative. Cytoreduction therapy with Hydroxyurea was

started along with antiviral and antifungal prophylaxis, allopurinol was also started along with intravenous fluids to

prevent tumor lysis syndrome, when cytoreduction was

achieved by reduction of white blood cell count, he was

offered with (7+3) cytarabine and daunorubicin induction

protocol. However, patient did not complete the treatment

because of socioeconomic issues and was continued with low

dose cytarabine according to the patient’s will.

DISCUSSION

Acute Undifferentiated leukemia is more common in older

adults with cytogenetic abnormalities in 80-90% of cases. Most frequent are del (5q) and trisomy 13 [7]. Cuneo et al. reported that del(5q) was seen in 33% of acute undifferentiated leukemia cases, trisomy of chromosome 13 in 33%, and

complex karyotype in only one case, Heesch et al. reported complex karyotype as a major cytogenetic abnormality [2, 8].

Del 17p is associated with poor overall and disease free survival in Chronic Lymphoproliferative disease and multiple

myeloma and is resistant to conventional chemotheraphy regimens [5]. Its association in Acute Leukemia is sparsely reported and has been mostly associated with Acute Myeloid Leukemia and Myelodysplastic Syndrome. A large study of 2272 acute myeloid leukemia patients showed deletion 17 p in 105 patients (05%) [9]. The multivariate analysis exhibited del 17p (p53) aberrations as an independent negative prognos-
tic factor for overall survival, disease-free survival and increased relapse risk.

Previously it has been reported in few studies that expression

of Tdt is more frequently seen in acute undifferentiated leukemia rather than other markers of immaturity (CD34 and CD 117) mostly associated with Myeloid differentiation [10]. Our patient also had the same findings though no prognostic significance has yet been associated with this finding.

To the best of our knowledge and literature search, this is the

first case of Acute Undifferentiated Leukemia associated with
deletion 17p, this could aid in including deletion 17p testing in

Acute Leukemia especially those having aggressive or

resistant disease.

CONFLICT OF INTEREST

Declared none.

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AUTHORS’ CONTRIBUTION

All authors have been contributed equally.

REFERENCES


A 40-year-old male patient was referred to National Institute of Hematology and Blood Transfusion, Pakistan. On examination, he complained of multiple swellings in necks, intermittent fever, and fatigue. The patient had a history of 5 kg weight loss in the last month.

On examination, the Total Leukocyte Count was 93.22x10^9/L and Platelets were 60x10^9/L. The left costal margin was palpable. The CBC showed Hemoglobin 10.7 G/dl.

Cervical lymph nodes were palpable bilaterally. The patient was diagnosed with undifferentiated leukemia with del 17p chromosomal aberration. The diagnosis was supported by FISH analysis, which detected the del17p.

Immunophenotyping by Flowcytometry was performed, and these blast cells did not express any lineage specific antigen. Myeloid (CD13, CD33) as seen in most acute leukemia cases, trisomy of chromosome 13 in 33%, and del(5q) were also performed to see if plasmacytoid or NK cell precursors were present, but these findings were negative.

Myeloperoxidase stain on aspirate smear was not straightforward indicator of acute nature of disease, so Yohimbine test was performed, which showed diffuse positivity as seen in TdT.

Outcome of patients with del(17p) shows shorter survival, resistance to available therapy in chronic lymphoproliferative disease and multiple myeloma. The 2016 revision to WHO diagnostic criteria for acute undifferentiated leukemia (EUL) encompasses neoplastic blast cells with ambiguous phenotype; these cases are associated with del(17p) and TP53 mutation, increased relapse risk, and complex karyotype as a major cytogenetic abnormality.

The patient underwent apheresis for autologous peripheral blood stem cell transplantation. Leuk Lymphoma 2018; 59(12): 3006-9. DOI: 10.1080/10428194.2018.1441410

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