CASE REPORT

A case of hypotriploid chromosome in a patient with acute lymphoblastic leukaemia

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Abstract

A 58-61, XXXX, hypotriploid chromosome was detected in the cytogenetics report of a 28 years old female patient, known case of B-cell Acute Lymphoblastic Leukaemia. On admission, the patient had normal physical examination findings and mental status, except history of fever spikes and generalized bone pains. The patient was admitted for induction of chemotherapy. Bone Marrow/Trephine biopsy report showed diffuse infiltration with blast cells with overall cellularity around 80-85% and suppressed normal haematopoiesis.

Hypotriploid chromosome number in patients with B-cell Acute Lymphoblastic Leukaemia is a unique finding which, according to WHO classification of ALL, is an important prognostic factor itself and these cases have a favourable prognosis. There are only a few medical reports published about cases with similar presentations in Pakistan. Therefore, this case is very unique and further work should be done for better understanding of similar presentations and to find out more about its epidemiology.

Keywords: Hypotriploid, Cytogenetics, Leukaemia, Karyotype.

Introduction

Acute Lymphoblastic Leukaemia is a malignant disease of white blood cells, characterized by clonal proliferation and accumulation of neoplastic cells. This accumulation of immature cells known as lymphoblasts result in suppression of normal haematopoiesis of the bone marrow.[1] Although these leukaemias are mainly regarded as childhood diseases, they have a bimodal age distribution with a peak at age 50 and a rise in incidence with increasing age.[2]

The World Health Organization classifies ALL into B-cell and T-cell precursor types[3] and according to multiple researches, B-cell phenotype is more commonly diagnosed. According to a retrospective analysis conducted in 2014 in Pakistan comprising of 166 acute lymphoblastic leukaemia diagnosed patients, majority (n=120, 72.3%) had a B-cell phenotype.[4]

In majority of cases of B-cell ALL there is an abnormal karyotype which is seen in the form of nonrandom numerical or structural changes that can be detected by cytogenetic analyses.[5] Cytogenetic study is now routinely done in acute leukaemia to not only help in diagnosis but it also plays a role in patient management and prognosis.

Amongst many cytogenetic abnormalities found in B-cell ALL, we are describing the coincidence of hypotriploid chromosome number in a patient admitted in Jinnah Postgraduate Medical Center in the department of Oncology.

Case Report

A 28 years old woman was admitted to Oncology department in Jinnah Postgraduate Medical Center on 10th August 2016, with a history of B-cell Acute Lymphoblastic Leukaemia for Induction of Chemotherapy. Patient reported having recurrent fever and bone pain since last four months and was diagnosed with B-cell ALL in June 2016. Physical examination of the woman showed no pathological signs. Laboratory work-up showed anaemia (Haemoglobin 8.7 g/dl), platelet count (22x10^9/L) and WBC (8.1x10^9) with 45% lymphocytes. Bone marrow trephine report showed 80% blast cells on peripheral blood with heterogenous population of blast cells and suppressed haematopoiesis. Results of cytochemical PAS stain showed 20% blast cells with block positivity. Flow cytometry was performed using a broad panel of antibodies including CD10, CD19, CD20, CD22, cCD79a and cCD3 (Figure-1).

This population showed reactivity with Pan-B-Cell markers i.e., CD10, CD19, CD22 and cCD79a. Diagnosis of B cell ALL was confirmed and this population also showed positivity to TdT with viability index of 97%. Cytogenetic analysis was performed using 5 Colour Cytomics FC500 flow cytometer and the banding method was GTG banding. Karyotypes were described according to the international system for human cytogenetics nomenclature (ISCN) criteria. In all 20 cells that were

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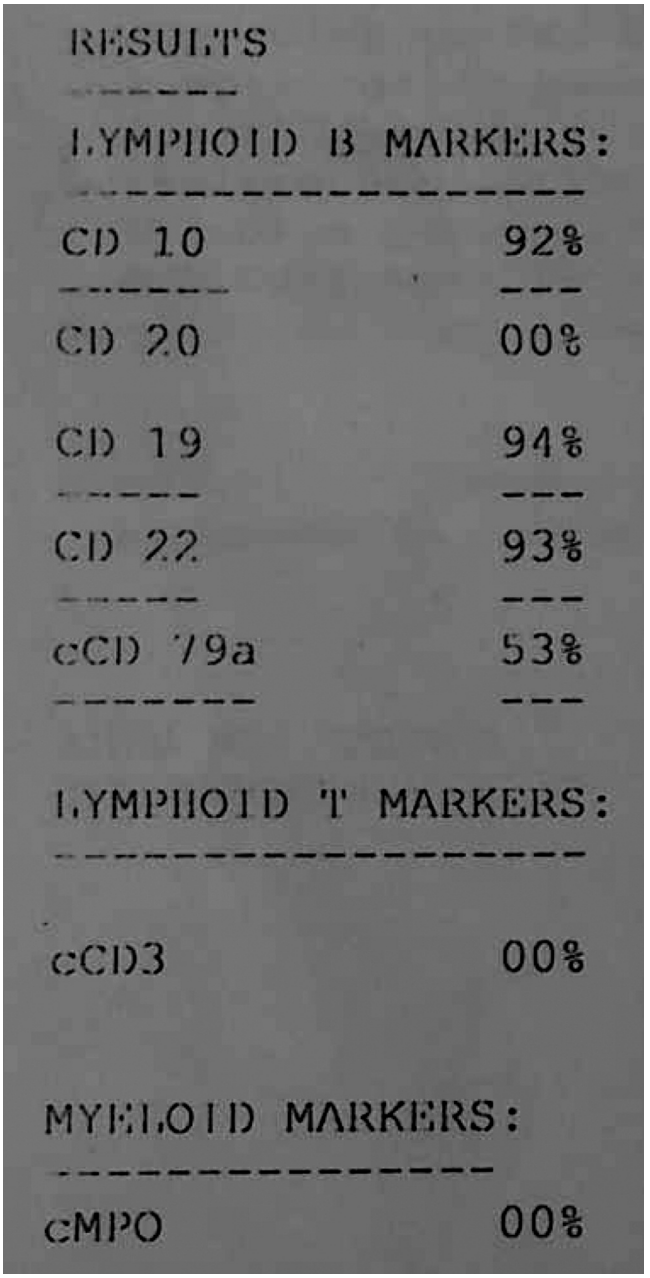

Figure-1: Flow cytometry.

counted and analyzed, the cytogenetic analysis showed chromosomes number amounting to be Hypotriploid; 58-61, XXXX (Figure-2). The patient showed chromosomal gains in X, 1, 2, 4, 5, 6, 8, 10, 11, 12, 21 and 22. This patient does follow the nonrandom chromosomal gain pattern shown in multiple researches on cytogenetics chromosomal gain pattern, gains of which occur more often in patients with 57 or more chromosomes.[6]

The patient received an induction chemotherapy

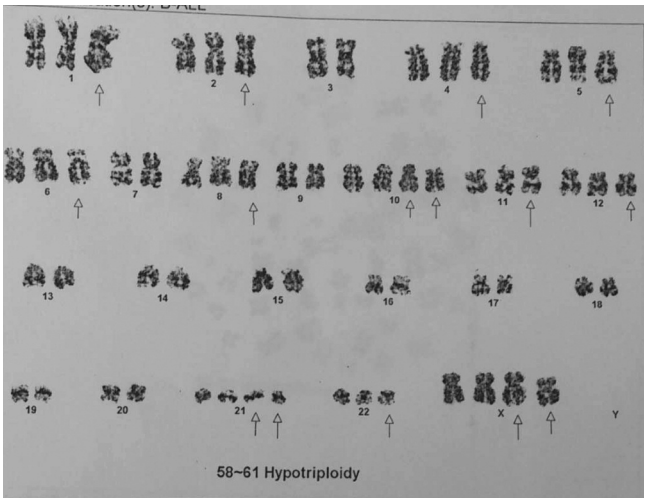

Figure-2: Cytogenetic analysis.

consisting of Daunorubicin (60 mg/m^2/day IV) and Vincristine (2 mg/m^2 IV) leading to complete remission. Other drugs included L-Asparaginase (IV), Ondansetron, Prednisone, Risek, and Loritin.

Our patient achieved complete remission without any signs and symptoms of disease after first induction chemotherapy.

Discussion

Majority of B cell ALL have cytogenetic abnormalities and cytogenetic analyses have revealed a great number of non-random chromosome abnormalities. According to a study in Pakistan, the cytogenetics of the disease such as presence of Philadelphia Chromosome is higher in adults and do affect the remission and survival rates.[7] There are only few case reports or articles published in Pakistan about a Hypotriploid or Hypertriploid chromosome number in patients with ALL and we think more data should be collected and studied to better understand the pattern and demographics of chromosomal abnormalities in B-cell ALL in Pakistan.

In case of hypotriploidy with chromosomal number of more than 50, there is a standard pattern around the world of being more common in adults and occurring in a lower frequency in children.[8] And according to a research, these cases of hypotriploid chromosome tend to have better outcome just like our case where the woman achieved complete remission.[8] The patient received induction chemotherapy with Daunorubicin and Vincristine without reporting any serious side effects. This favourable prognostic outcome and similar pattern in Pakistanis reassuring in terms of management and treatment protocols.

Although our patient showed complete remission, even after remission induction therapy, there are chances that the cancer might come back. To try to stop this, we have second phase of treatment called consolidation therapy. The consolidation therapy may include more chemotherapy or allogeneic hematopoietic stem cell transplantation (HSCT). However, HSCT is associated with increased treatment related mortality so it is not a favourable treatment for all patients.[9] Since our patient is young and has favorable prognosis, BMT can be considered in this case if she falls into the criteria of HSCT. So for this reason, further follow-up plan was discussed to help her understand the disease, its management and treatment options. However, the patient refused to go for HSCT because her family couldn't afford the treatment.

According to a research article published in June 2002,[10] recurrent chromosomal abnormalities in cells of patients with B-cell ALL are distinctive features of the disease as karyotype itself is an independent prognostic indicator and has an impact on the choice of the treatment. This shows the importance of cytogenetics in different cases of leukaemia in clinical oncology. Even though hypotriploid number has good prognostic outcome after treatment, some patients do relapse. Therefore, our patient needs to be followed timely so that any relapse can be detected as early as possible.

Conclusion

We conclude that cytogenetics play an important role in management and prognosis of B-cell Acute Lymphoblastic leukaemia with hypotriploid chromosome number. 58-61, XXXX hypotriploid chromosome number in our patient is a unique case and very few research articles have been written on this rare occurrence. To know more about its epidemiology in Pakistan, more research work and data collection should be done. This will not only help in better understanding of similar cases but also further help in improving clinical management and treatment.

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Conflict of Interest: There were no financial, professional or personal interest that could have influenced the work.

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