Case study

Trisomy 5; an unusual occurrence in B-lymphoblastic leukemia

Abstract

Background:

B-lymphoblastic leukemia (B-ALL) is characterized by clonal cytogenetic abnormalities with numerical chromosomal aberrations being more common. Trisomy 5 as a sole abnormality is reported in a few cases only. Its prognostic and therapeutic implications are yet to be explored.

Case report: We report a case of a 14-year boy diagnosed as B-ALL. Cytogenetic analysis on his bone marrow aspirate revealed trisomy 5 as a sole abnormality with no evidence of any other clonal cytogenetic or molecular genetic abnormality.

Discussion: Cytogenetic studies still play a pivotal role in the sub- classification of B-ALL. In acuteleukemia, all diagnostic criteria and treatment protocols are based on cytogenetic findings. An extra copy of chromosome 5 is common to see in cases with hyper diploidy. However,again of chromosome 5 as a sole anomaly is exceptionally rare in B-ALL.

Conclusion: Trisomy 5 is more common in older children and showed dismal outcome in children and adults. The increasing number of reported cases raise thepossibility of a distinct cytogenetic entity.

Keywords: Cytogenetics, trisomy 5, acute leukemia, hyper diploidy

Introduction

Acute lymphoblastic leukemia (ALL) is the most commonly occurring cancer in children. [1] It has an impact on immune system, mainly B-cells and T-cells. ALL usually affects B cells in children. High doses of X-rays and other types of radiation exposure as well as chemotherapy for cancer treatment are amongthe factors that increase the risk of developing this condition. Children having Down syndrome or other genetic disorders are also more prone to develop ALL. B-ALL is the most frequent subtype of acute leukemia in children. With ~~the~~ recent advances, all major diagnostic criteria, risk stratification, and treatment protocols are based on cytogenetics and molecular genetics. [2]

The diagnosis of hematological malignancies is greatly influenced by cytogenetic analysis. [3] A huge number of chromosomal defects that are not random are connected to particular forms of leukemia. The conclusive diagnosis is frequently provided by the cytogenetic findings. With the use of traditional cytogenetic analysis and current advancements in molecular cytogenetic technologies, the accuracy of the findings has increased and new chromosomal abnormalities in leukemia have been discovered. [4]

We present here a case of B-ALL in which trisomy 5, a rarely occurring chromosomal abnormality was identified. In order to shed light on the clinical characteristics and prognosis of this clonal aberration, we compared it to cases already reported in the literature. The case is being reported to increase awareness of cytogenetic findings and to document the disease course of patients with these unusual chromosomal aberrations.

Case Presentation

A 14-year-old boy presented with a history of fever, lethargy, and episodes of nasal ~~bleed~~ for last two weeks.On physical examination, there was no ~~visceromegaly~~however~~sub centimeter~~cervical lymph nodes were palpable. X-ray chest was normal. Initial CBC results showed a high WBC count of 75.48x10^9/L, platelet 9X10^9/L, and hemoglobin of 5.1gm/dl. Peripheral blood film revealed small to medium-sized blasts characterized by a high

Comment [Ma1]: Change to 'bleeding'

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nuclear to cytoplasmic ratio, fine nuclear chromatin, ~~and~~ indistinct nucleoli, and scant to moderate pale basophilic non-vacuolated agranular cytoplasm.**(Figure 1).** Cytochemical myeloperoxidase was negative in blasts.

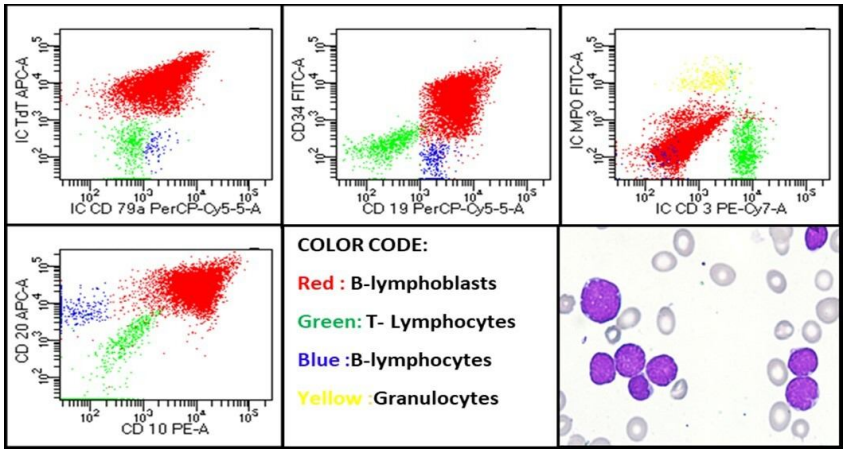

Figure 1: Immunophenotypic analysis performed on peripheral blood showing blasts and bright expression of Tdt, CD34, CD19,CD10 and CD20.

The immunophenotype analysis was performed on peripheral blood by 8-color flowcytometry which shows 77% small to medium sized blasts (forward light scatter properties) exhibiting following phenotype; TdT (+), CD34 (+), CD45 (Dim+), CD19 (+), CD79a (+), CD20 (+), CD10 (+), CD38 (+), CD58 (+), CD9 (+), CD123 (+), CD73 (+), Intracytoplasmic Myeloperoxidase (-), and ICCD3 (-). **(Figure 1)**In addition, it shows 3.3% benign B-lymphocytes, 7.3% benign T - lymphocytes and 7.6% granulocytes. The diagnosis of B-Lymphoblastic Leukemia was thus made. Cerebrospinal fluid examination at the time of diagnosis was consistent with CNS1 status.

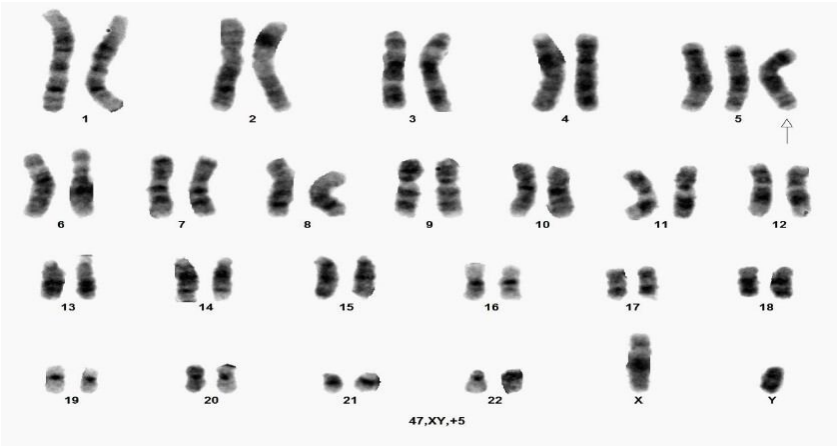

Figure 2: Karyotype performed by GTG banding

In addition, bone marrow specimen was received for conventional cytogenetics and fluorescence in situ hybridization (FISH) analysis. It was cultured in RPMI. Cells were harvested after 24hours, treated with Colcimidfor mitotic arrest, KCL and Carnoy's fixative. Chromosomes were G-banded using trypsin and Giemsa stain. The case was analyzed and subsequently karyotyped showing a gain of chromosome 5 as a sole anomaly. Furthermore, FISH test for *BCR::ABL1*, *ETV6::RUNX1*, and *KMT2A* gene showed normal results. The case was labelled as NCI high risk (HR)based onage and WBC. Hence, HRinduction chemotherapy was started as per protocol.

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Discussion

In childhood ALL, trisomy 5 is usually seen in cases with hyper diploidy and with other structural cytogenetic aberrations. Trisomy 5 is thought to contribute to leukemogenesis; however, the exact mechanism is yet unclear. The acquisition of an entire chromosome is thought to have the ability to cause a dosage effect or the duplication of a mutation with ~~a~~ carcinogenic potential.Although onlyafew cases of trisomy 5 are reported to date,~~but~~however, it is linked to a worse clinical outcome. [4] According to the literature, three reported ALL cases with trisomy 5 as the sole finding, two (one case each of adult and pediatric ALL) demonstrated short survival while one adult ALL case demonstrated event-free survival of four years. [6]Trisomy 5 as a sole abnormality has also been reported in T-lymphoblastic leukemia. [7]

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We can stratify our patients and choose the best course of treatment with the aid of a better understanding of the genetics of B-ALL. It can also help us in the development of new, ~~tailored~~ targetedtreatments. Our information on trisomy 5 as the only chromosomal aberration in B-ALL is currently insufficient to draw any firm conclusions about prognostic and therapeutic implications. [8,9] However,~~on the basis of our~~based on our case and thereported literature, we can state that trisomy 5 as the sole numerical abnormality occurs predominantly in older children, may be associated with an inferior outcome, and may represent a distinct, albeit rare, cytogenetic subgroup in ALL. [10]

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Conclusion

Cytogenetic findings play an important role in determining the treatment choice as well as predicting disease course. Since, there is limited literature available regarding this abnormality, this report would add some significant knowledge to existing data. Lastly, the significance of this unique cytogenetic entity would come to light as more cases of this sort are reported.

Consent

The parents of thepatient provided written informed consent to the publication of the case details.

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Ethical approval

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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