A Novel Chromosomal Aberration in the Pathogenesis of Transient Leukemia of Down Syndrome

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To the Editor: The index case was a term girl with a smooth perinatal transition with Down phenotypic features. Examination revealed hepatosplenomegaly (liver span-7 cm and spleen 2 cm below the left costal margin). Blood investigations done on day 3 of life revealed hemoglobin of 12.8 g/dL, total leukocyte count 32,450 cells/ μ L and platelets 1,83,000 cells/ μ L. The peripheral smear showed a left-shift with 34% myeloid blasts which were positive for CD41, CD61 on flow cytometry. Since there was leucocytosis with nonerythroid blasts $\geq 10\%$ consistently in a background of Down phenotype, GATA1 mutation was not looked for and a diagnosis of transient leukemia of Down syndrome (TL-DS) was made based on Children Oncology Group (COG) and World Health Organisation (WHO) guidelines [1, 2]. The karyotyping was later confirmed to be 47,XX,t(1;13)(q31;q21),+21c[25]. The infant developed rapidly progressing liver dysfunction and succumbed over the next 3 d.

The molecular pathogenesis of TL-DS is complex and is believed to be driven by mutations in the *GATA1* gene. Karyotyping of our index case revealed a novel abnormality, balanced translocation (1;13) (q31;q21). This translocation has not been described in the literature so far in infants with TL-DS. The locus 13q21 is suspected to be a candidate region for familial chronic lymphocytic leukemia. Five genes from 13q21.33-q22.2, have putative function related to cell growth

[3]. Some of these genes are deregulated in breast and prostate cancer. Additionally, chromosome 1q contains the *ELK4* gene, a member of the E26 transformation specific (ETS) transcription factor family. It has been postulated that alterations and the consequent imbalance of chromosome 1 may be causative for certain types of cancer. AML-M2 has been previously associated with t(1;13) translocations with different breakpoints, but (q31;q21) has not been implicated in the causation of TL-DS till now [4]. The unusual rapid deterioration/disease progression in a case of TL-DS depends on the third hit. The role of this translocation as a third hit in the pathogenesis of TL-DS/ML-DS needs to be studied.

Declarations

Conflict of Interest None.

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