A Unique Translocation, t (5;8)(q21.1;q21.13) in Early Precursor T-ALL

Yenamandra A*, Gardner-Hollis A, Zhao K and Barba E
Department of Pathology, Immunology and Microbiology, Vanderbilt University Medical Center, USA

EDITORIAL

Over the past several years Cancer cytogenetics involving recurring chromosome abnormalities has evolved in the understanding of hematologic malignancies. Recurring non-random clonal cytogenetic changes have been identified in specific morphologic tumor types. In a multidisciplinary approach to patient care, Cytogenetics, Fluorescence in Situ Hybridization (FISH) and Chromosomal Microarray (CMA) play a crucial role in contributing to diagnosis, prognosis, and genotype-specific therapy decisions for clinicians in the management of hematological neoplasm.

Various deletions along the length of the long arm of chromosome 5 have been reported in 20-30% of Myelodysplastic Syndrome (MDS), Acute Non Lymphocytic Leukemia and (ANLL) and Acute Leukemia (AL) either as a sole abnormality or in combination with other abnormalities of monosomy or deletion of long arm of chromosome 7, trisomy of chromosome 8 and deletion of long arm of chromosome 20. Deletion of chromosome 5q has also been reported as an uncommon finding in a few cases of both adult and pediatric Acute Lymphoblastic Leukemia (ALL); however, significance of this finding in ALL is poorly understood [1-5].

We report an 11-Year old male who presented with Early T-precursor lymphoblastic leukemia (ETP-ALL) with spinal chloraoma and meningeal involvement. He had no significant past medical history and developmental milestones were appropriate for his age. His bone marrow biopsy (BM) sample collected on 10/04/2013 was hypercellular with 82% blasts. Bone marrow Morphology and immunophenotype demonstrated CD1-, CD2-, CD4-, CD5+, CD8-, CD10-, CD13-, CD19-, CD45+, CD33+, CD34+, CD117+, CD5+, CD7+, HLA-DR- and TdT partial.

Molecular genetic studies of the (BM sample dated 10/04/13) revealed a rearrangement of the T cell receptor gamma chain locus (chromosome 7p15) and negative for FLT3-ITD. Cytogenetics, FISH and microarray revealed abnormal results. FISH for ALL panel was normal with no rearrangement for t(1;19), 11q23, t(9;22) and t(12;21) and 9p21 but revealed an additional copy of TCF3 locus (19p13.3) in 45% of cells. Karyotype analysis revealed an apparent interstitial deletion of long arm of chromosome 5 and trisomy of chromosome 19. FISH with PDGFRB (platelet derived growth factor receptor B) probe specific for 5q32–q33 region confirmed the deletion of PDGFRB in 95% of cells analyzed. Although the karyotype was initially described as 47, XY, del(5)(q22q33),+19[19]/46,XY [1], the 5q- chromosome did not seem to have the appearance of a typical deleted 5q. SNP chromosomal microarray (Affymetrix) of the same sample was performed subsequently, to investigate the 5q- abnormality. Array revealed a large deletion in the long arm of one chromosome 5 extending from 5q21.1 to q35.3, partial trisomy of the long arm of chromosome 8 extending from 8q21.13 to q24.3. Additional abnormalities observed with the array were deletion of chromosome 4q with in the q31.23 band, Regions of Homozygosity (ROH) of chromosome 11 extending from p11.12

![Figure 1 Array pictures of Chromosome 5 with deletion and Chromosome 8 with duplication.](image-url)
Figure 2 Array-Detailed view of 5q deletion- copy number state, Log2 ratio, SNP tracks and the smooth signal.

Figure 3 Array- Detailed view of partial trisomy of 8q- copy number state, Log2 ratio, SNP tracks and the smooth signal.

Figure 4a G banded karyotype of the patient’s bone marrow sample.
to p15.5, deletion of chromosome 12p extending from p13.1 to p13.2. The deleted 5q included loss of 80MB with at least 11 known genes including PDGFRB, the partial gain of chromosome 8 included addition of 62MB with at least 30 known genes, deletion of 4q included 0.8MB with no known genes, ROH of 11p included 51 MB with at least 10 known genes including WT1 gene and the deletion of 12p included a deletion of 1MB with at least 10 known genes. Also, clinically relevant genes were not observed at the breakpoint junction of t(5;8) with the array. The above described abnormal finding of der(5) was not expected based on the clinical diagnosis. In an effort to correlate the array finding of the large deletion and duplications of chromosomes 5 and 8 respectively, with the cytogenetics result, sequential FISH (FISH on G banded slides) was performed with probes specific for 5p (EGR1), 5q (5q31) and 8q24 (MYC breakapart probe). FISH confirmed that the del (5q) in the karyotype was indeed a der (5) of a t (5;8), an unbalanced translocation product, with monosomy for 5q and trisomy for 8q (Figure 4, 5). Karyotype was updated as 47,XY,der(5)t(5;8)(q21.1;q21.13), +19[19]/ /46,XY[1]. Deletion of 12p did not include ETV6 gene and the deletion was not visible in the karyotype. Subsequent BM biopsy (dated 10/14/13, 11/04/13 and 12/09/13) revealed persistent T-ALL.

Although T-ALL in conjunction with an MDS/myeloproliferative disease specific genetic change of del(5q) has been previously reported, der [5] of t(5;8) with the above described breakpoints resulting in partial monosomy for 5 and partial trisomy for 8 has not been reported in T-ALL [1-6]. Early T cell Precursor acute lymphoblastic leukemia (ETP-ALL)
has been identified as high risk subgroup of T-ALL with a high rate of FLT3 mutations in adults [7]. This case was positive for T cell receptor rearrangement, negative for FLT3-ITD mutation and initial cytogenetic study revealed a del (5q), +19. However, subsequent array identified a large deletion of 5q and partial additional 8q and was confirmed by FISH. The relationship between der (5q), the ROH of chromosome 11p and deletion of 12p, +19 and T-ALL in this case is unclear. It is also not clear if these rearrangements occurred in a multi-potent progenitor cell that gave rise to both T –ALL and a der(5) rearrangement, or if the der(5) is a secondary change. There was no original lymph node biopsy available to investigate this aspect. This case is an example where multidisciplinary approach to Cytogenetics, FISH and array play a critical role in the identification of unanticipated genetic changes.

REFERENCES