Case Report Section

B-cell acute lymphoblastic leukemia with t(2;9)(p11;p13) involving the immunoglobulin kappa locus (IGK) and PAX-5

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Abstract
Case report on B-cell acute lymphoblastic leukemia with t(2;9)(p11;p13) involving the immunoglobulin kappa locus (IGK) and PAX-5.

Clinics
Age and sex: 30 years old male patient.
Previous history: no preleukemia, no previous malignancy, no inborn condition of note
Organomegaly: no hepatomegaly, no splenomegaly, enlarged lymph nodes (Tender right axillary, left posterior cervical, and left inguinal lymphadenopathy.), central nervous system involvement (Cytology revealed rare atypical mononuclear cells, favor reactive.)

Blood
WBC: 17.8X 10^9/l
HB: 11.3g/dl
Platelets: 38X 10^9/l
Blasts: 85%
Note Hypercellular marrow (>90%) with sheets of blasts on bone marrow core biopsy. Bone marrow aspirate smears contained 97% blasts with fine chromatin, single to multiple small nucleoli, and scant pale-blue cytoplasm.

Cyto-Pathology Classification

Immunophenotype Flow cytometric analysis of the peripheral blood identified a population of blasts (80% of all cells) expressing CD45, CD10, CD19, CD20, CD34, HLA-DR, CD33 (variable), CD11b (dim), cCD22, cCD79a, and nTdT. The blasts were negative for CD3, CD4, CD5, CD7, CD56, sIg kappa, sIg lambda, CD13, CD14, CD15, CD36, CD64, and cMPO.

Rearranged Ig Tcr: Not performed
Pathology: Acute lymphoblastic leukemia
Electron microscopy: Not performed
Diagnosis: B-lymphoblastic leukemia/lymphoma, not otherwise specified

Survival
Date of diagnosis: 04-2018
Treatment: ECOG 1910
Complete remission was obtained
Treatment related death: no
Relapse: No relapse in the context of a short follow-up period
Status: Alive
Last follow up: 05-2018
Survival: 1 months

Karyotype
Sample: Bone marrow
Culture time: 24h
Banding: GTG
Results: 45,XY,t(2;9)(p11;p13),-20[18]/46,XY[1]

Other Findings
Genes involved and Proteins
PAX5 (paired box gene 5) (9p13.2). The PAX5 coding region extends over a genomic interval of approximately 200kb and comprises 10 exons. Two alternative transcripts have been identified, originating from alternative promoter usage, containing exon 1A or 1B. Full length mRNA is 3650 bp. PAX5 belongs to the paired box family of transcription factors. It is involved in a multitude of developmental processes. PAX5 was originally identified as a B-cell specific transcription factor (B-cell-specific activator protein, BSAP). Recently, PAX5 expression has been shown not only continuously required for B cell lineage commitment during early B cell development but also for B lineage maintenance. PAX5 contains a paired box (DNA binding) domain, a truncated homeo domain homology region, a transactivation domain, and an inhibitory domain.

IGK (Immunoglobulin Kappa) (2p11.2). The human IGK locus at 2p12 spans 1820 kb. It consists of 76 IGKV genes belonging to 7 subgroups, 5 IGKJ segments, and a unique IGKC gene.

Comments
Chromosomal translocations involving PAX5 are known to occur in cases of B-lymphoblastic leukemia (B-ALL), often involving a range of possible fusion gene partners (1). In addition to these rearrangements, many cases of B-ALL demonstrate copy number variations involving PAX5 (2).

Despite these reports, only two other case of t(2;9) involving fusion of PAX5 and 2p11 have been reported to date (3,4).

Neither of these reports confirmed the involvement of the immunoglobulin kappa locus as demonstrated in the present case.

We report the first case of PAX5/IgK fusion confirmed by FISH, suggesting a possible mechanism in B-ALL that mirrors other lymphomas which overexpress gene products as a result of joining with immunoglobulin heavy or light chain loci.

Note from the Editor: this translocation is a variant of the rare t(9;14)(p13;q32) PAX5/IGH, although the t(9;14) has so far only been described in lymphomas.
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McCall RK et al.

Atlas Genet Cytogenet Oncol Haematol. 2020; 24(6) 261

Two interphases demonstrating consistent connection of IgK (green)-PAX5 (red)-IgK (green) suggesting rearrangement/fusion of PAX5/IgK.

Bone marrow core biopsy showing extensive blast proliferation and peripheral blood (inset) demonstrating atypical blast cytomorphology with occasional deep nuclear fissures.

References


This article should be referenced as such: