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Case Report Section

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

Robert K McCall, Paula Moore, Nancy S Rosenthal, Angela G Niehaus, Bayard Powell, Mark J Pettenati

Cytogenetics and Molecular Cytogenetics, Wake Forest University Medical Center, Winston-Salem, North Carolina. pettenat@wakehealth.edu

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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 hepatomegal, 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: 1months

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 promotor 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

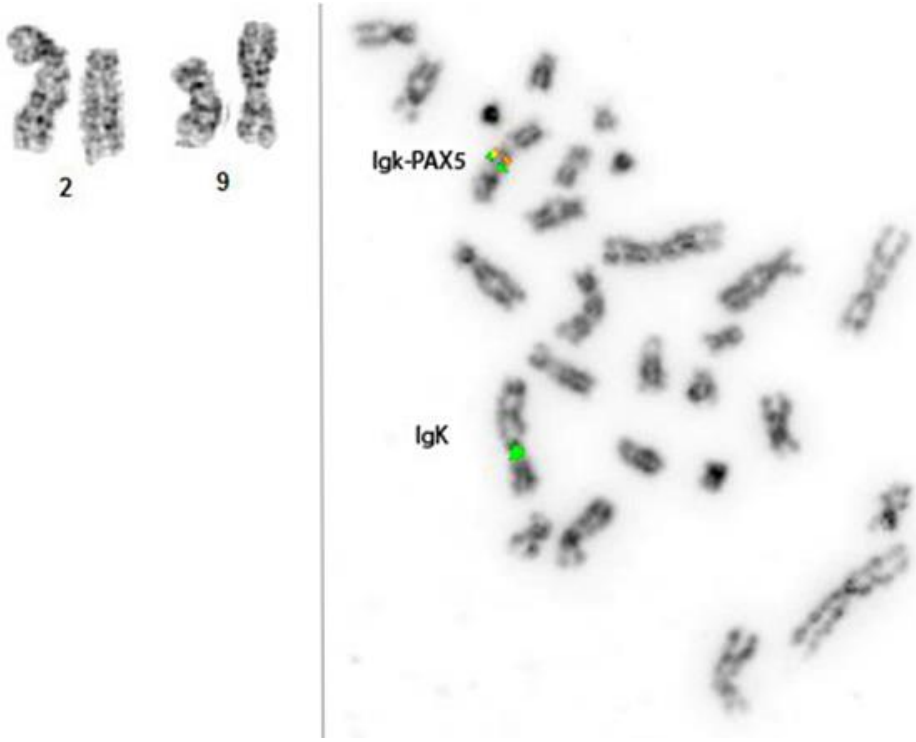
Chromosomal translocations involving PAX5 are known to occur in cases of B-lymphoblastic leukemia (B-ALL), often involving a range of possible fusion gene partners (1). In addition to these rearrangements, many cases of B-ALL demonstrate copy number variations involving PAX5 (2).

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

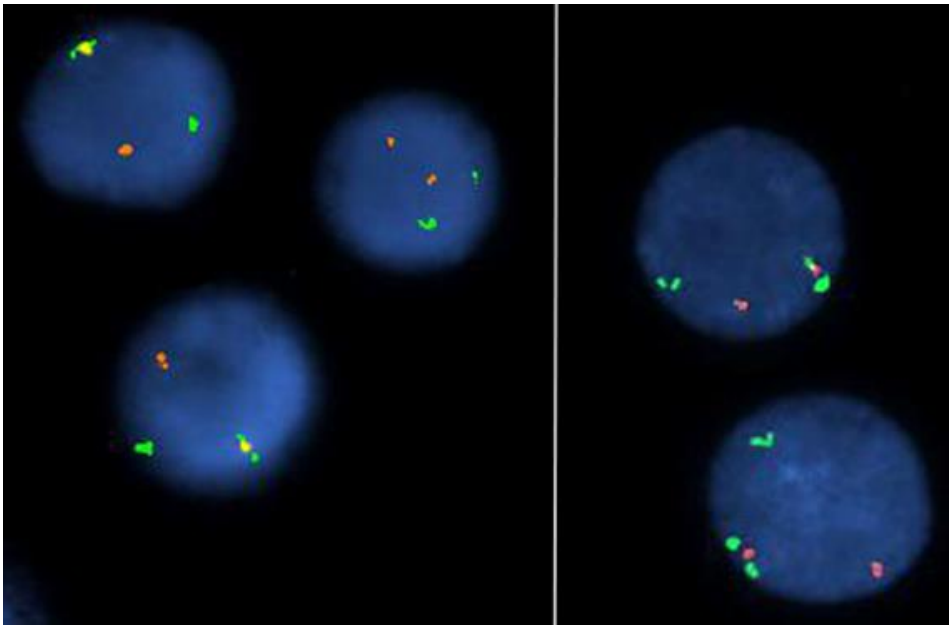
Neither of these reports confirmed the involvement of the immunoglobulin kappa locus as demonstrated in the present case.

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.

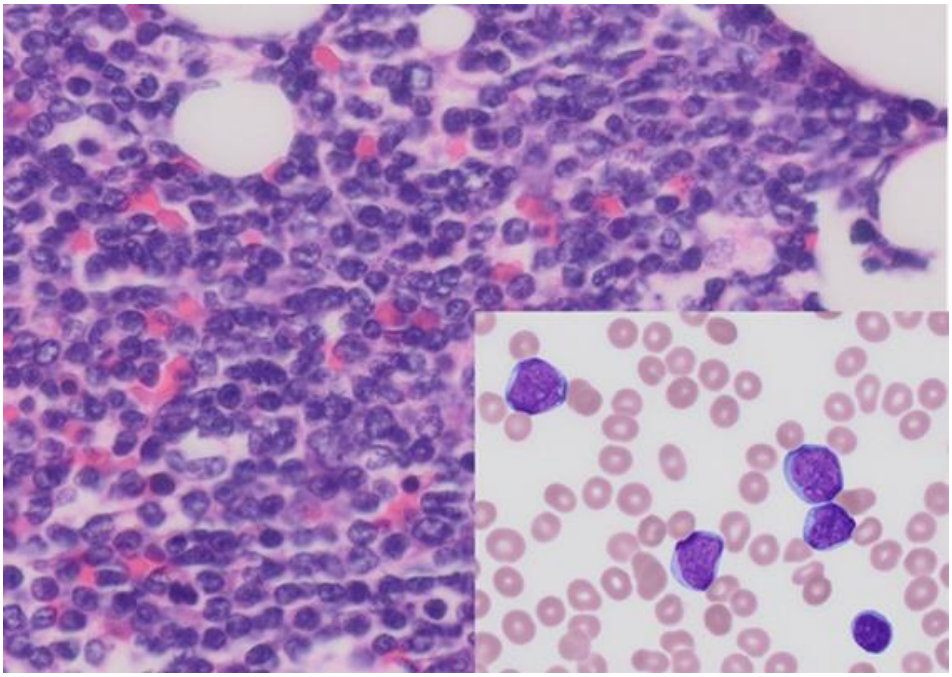
Note from the Editor: this translocation is a variant of the rare t(9;14)(p13;q32) PAX5/IGH, although the t(9;14) has so far only been described in lymphomas.



Example of chromosome 2;9 translocation. Note: A potential dicentric 9;20 was ruled out with centromeric probes of chromosome 9 and 20. FISH showing fusion (yellow) of IgK (green) [Cyto Cell] and PAX5 (red) [Empire Genomics] on the derived chromosome 9. Note: Negative for BCR/ABL1 fusion by FISH.



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



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

References

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