HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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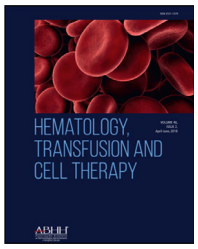

Case Report

TCRAD rearrangement in B-cell precursor leukemia: an unexpected finding

Wellington F. da Silva [a,*], *Maria Gabriella Cordeiro* [a,b], *Renata K. Kishimoto* [b], *Elvira Deolinda Rodrigues Pereira Velloso* [a,b]

[a] *Instituto do Cancer do Estado de São Paulo (ICESP), São Paulo, SP, Brazil*
[b] *Hospital Israelita Albert Einstein, São Paulo, SP, Brazil*

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Introduction

B-lymphoblastic leukemia (B-ALL) is a genetically heterogeneous disease, with several structural and numerical aberrations already described.[1] While some alterations are intrinsically associated with phenotypical and prognostic features, others are rarely seen, posing a challenge to the clinician. Rearrangements involving the T-cell receptor alpha-delta locus (*TCRAD*) at the 14q11.2 chromosome are found in around 17% of T-lymphoblastic leukemias.[2] Over the last decades, very few B-ALL cases with 14q11 translocation were reported – in most of these cases, the *CEBPE* (CCAAT enhancer binding protein epsilon) gene was the implicated.[3–8] Herein, we describe an intriguing case of B-ALL with a *TCRAD* translocation, followed by a brief literature review.

Case report

Informed consent was obtained from the patient. A 22-year-old male presented at our center with fatigue and pallor. Blood count revealed leukocytosis (37.2×10^9/L) with 80% blasts. The bone marrow was infiltrated by 90% agranular blasts with a B-common phenotype ($CD10^+$, $CD19^+$, $CD20^+$, $CD22^+$, $CD34^+$, $CD38^+$, $cyCD79a^+$, TdT^+) (Figure 1, panels A and B). There were no T-cell markers expressed. Screening for BCR-ABL, E2A-PBX1, KMT2A-AFF4 and ETV6-RUNX1 fusions were negative by reverse-transcriptase polymerase chain reaction (RT-PCR). These results led to a diagnosis of B-ALL. Cytogenetic analysis was described as: 45,XY,t(8;14)(q24;q11.2),−9,der(12)t(9;12)(q12;p13)[11]/46,XY[7] (Figure 1, panel C). Fluorescence in situ hybridization (FISH) analysis confirmed a *TCRAD* translocation in 50% of nuclei (Figure 1, panels D and E). Although we could not detect *MYC* rearrangement by FISH (Figure 1, panel F), it suggests a *TCRAD-MYC* fusion. The patient was treated with a pediatric protocol, and he is currently under the maintenance phase, with a negative measurable residual disease since the end of induction.

* **Corresponding Author at:** Ambulatório de Hematologia, Instituto do Cancer do Estado de Sao Paulo (ICESP) – Avenida Dr Arnaldo, 251, 1 andar, Cerqueira Cesar, São Paulo, SP CEP 01246000, Brazil.
E-mail address: wellington.fernandes@hc.fm.usp.br (W.F. da Silva).

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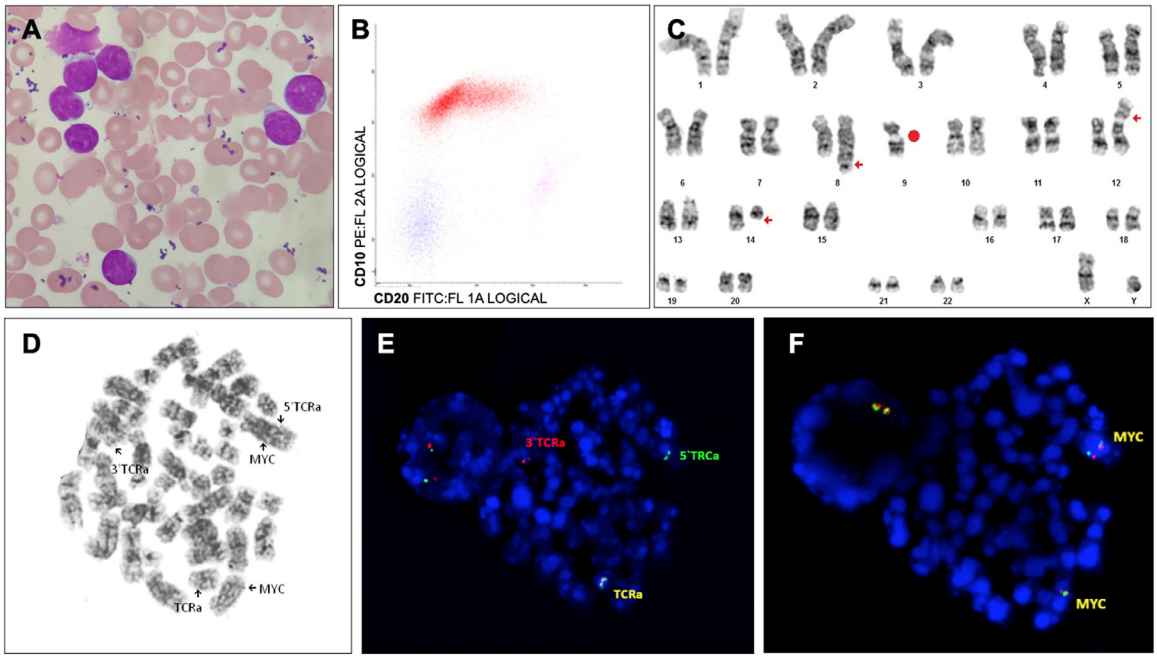

Figure 1 – A: peripheral smear (original × 1000; Leishman stain); B: blasts in red and T-lymphocytes in blue by flow cytometry; C: conventional karyotype, G-banding; D and E: metaphasic FISH with *TCRAD* dual-color break-apart probe; F: metaphasic FISH with *MYC* dual-color break-apart probe. Note that D, E and F represent the same metaphase and the 5′ signal of *TCRAD* (Figure 1E) is located near the position of *MYC* gene in Figure 1F, suggesting *TCRAD-MYC* translocation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Discussion

TCRAD rearrangements are usually seen in T-lymphoblastic leukemia, where they do not seem to add prognostic value individually.[9] Regarding B-ALL, *IGH-MYC* translocations are infrequently seen in patients with Burkitt-like presentation, and it is more common in adults.[10] FISH confirmation of *TCRAD* involvement was crucial as the CEBPE gene seems more implicated in B-cell cases.[5]

In this case, we encountered a *TCRAD* fusion, which resembles the previous finding of lineage crossover of somatic V(D)J rearrangements between B and T-cell leukemia subtypes.[11] The main question is whether this lineage promiscuity is an aberrant phenomenon of the malignancy itself or is a physiological process, usually developed during early stages of differentiation.[11] In a previous case, a chromosome 9 deletion, also seen in this case, led to CDKN2A and CDKN2B disruption.[4] Deletion of 9p is a recurring chromosomal aberration in B-ALL.[12] Numerous cancer-associated genes are contained in this chromosome, such as PAX5 and JAK2, with several of these being implicated in leukemogenesis.[12]

The t(9;12) seen in this case have been described in a subset of B-ALL cases, related to ETV6 disruption after translocation with a partner gene, more frequently ABL1 gene.[13] ETV6 has firmly been implicated in the pathogenesis of ETV6-RUNX1 - associated childhood leukemia as there is invariably bi-allelic loss of ETV6 due to deletions of the second (non-translocated) ETV6 allele.[14] This translocation was negative by RT-PCR in our case at the diagnosis.

In conclusion, the prognosis of this rare entity is currently unknown, and how this alteration leads to a B-cell phenotype deserves further studies. This case highlights the outstanding value of conventional karyotype and the further confirmation of striking findings in genetic evaluation of acute leukemia.

Conflicts of interest

The authors declare no conflicts of interest.

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