t(1;1)(q24;q25) RCSD1/ABL2, inv(1)(q24q25) RCSD1/ABL2

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Abstract
Review on t(1;1)(q24q25)/inv(1)(q24q25), with data on clinics, and the genes involved

Keywords
RCSD1, ABL2, B-cell acute lymphoblastic leukemia

Clinics and pathology

Disease

Epidemiology
Only 2 cases described: a 20-years-old man (Roberts et al., 2014; Raca et al., 2015; Roberts et al., 2017) and a second patient without further data (case A530 in Boer et al., 2017). These cases were first classified as B-ALL, and reclassified later as "B-ALL, BCR-ABL1-like" after characterization of the RCSD1/ABL2 fusion. The RCSD1/ABL2 case described by Roberts et al, 2014 was part of a study of 1665 B-ALL cases, three of which with ABL2 fusions. In the case described in Boer et al., 2017, the RCDS1/ABL2 fusion case was identified in a series of 77 BCR-ABL1-like B-ALL cases.

Treatment
The 20-year-old case received induction therapy with vincristine/peg-asparaginase/daunorubicin/prednisone with intrathecal cytarabine and methotrexate; there was no response post induction at days 15 and 29). Additional therapy included Cytosan, cytarabine, 6-mercaptopurine, decadron, vincristine, peg-asparaginase and intrathecal therapy with methotrexate (8-week cycle) and produced a morphologic remission but high-level minimal residual disease (MRD) was detected by flow cytometry. The patient received a hematopoietic stem cell transplant (total body irradiation and etoposide based preparative regimen) from an unrelated donor (Raca et al., 2015). The other case was treated according to the ALL10-HR protocol. There was a good response to prednisone, and high MRD (Boer et al., 2017).

Evolution
The 20-year-old case was in complete remission 8 month post-transplant and with no evidence of MRD (Raca et al., 2015). The other patient has been followed up for 3-4 years (Boer et al., 2017).

Prognosis
The two cases showed a IKZF1 deletion. Roberts et al. showed a tyrosine kinase inhibitors sensitivity when the RCSD1/ABL2 fusion was tested in Ba/F3 cells and in vivo mice models, and dasatinib was proposed to be evaluated in the future treatment of BCR-ABL1-like B-ALL with ABL-class fusions, especially for RCSD1/ABL2 fusion)(Roberts et al, 2017)

Cytogenetics

Cytogenetics morphological
This abnormality was not detected by conventional cytogenetic in any of the two cases. A complex rearrangement necessarily occurs because the two genes are in opposite directions of transcription.
**Cytogenetics molecular**

The rearrangement can be detected by molecular cytogenetics or other molecular technics.

**Genes involved and proteins**

**RCSD1**

**Location** 1q24.2

**Protein**

416 amino acids. RCSD1 is also called CAPZIP. CapZ-interacting protein, implication in cytoskeleton regulation and cell migration. RCSD1 is a mediator of non-canonical Wnt/JNK signalling. It interacts with the actin capping protein CapZ (CAPZ A1, CAPZ A2, CAPZ B: capping actin protein of muscle Z-line subunits alpha 1, alpha 2 and beta). RCSD1 binds CapZ to prevent CapZ from binding to the actin cytoskeleton. The T-cell costimulatory receptor CD28 phosphorylation regulates RCSD1 (Hempel et al. 2017: Tian et al. 2015).

**ABL2**

**Location** 1q25.2

**Protein**

1182 amino acids. ABL2 is also called ARG. ABL2 is a member of the ABL family of tyrosine kinases. ABL kinases have been found to play essential roles for the downstream signaling of the T- and B-cell receptors. ABL1 and ABL2 have both overlapping and distinct functions. The two proteins diverge in their C-terminal halves: ABL2 contains two F-actin binding domains and a microtubule-binding domain and is a key regulator of actin cytoskeletal remodeling. ABL2 acts as a negative regulator of signaling downstream of the kinase activity of the transmembrane receptor protein tyrosine kinase FLT3; it partially blocks FLT3-induced AKT phosphorylation (Jacobsen et al., 2018; Kazi et al., 2017). ABL2 gene is often implicated in solid tumors.

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**

5'RCSD1 (exon 3) - 3'ABL2 (exon 5).
**Fusion protein**

**Description**

The transcript retains the tyrosine kinase domain of ABL2 and a portion of the SH2 domain, but not the NH2-terminal SH3 domain (Raca et al., 2015).

**References**


This article should be referenced as such: