Leukaemia Section
Short Communication

t(2;9)(p23;q33) TRAF1/ALK

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Abstract
Review on t(2;9)(p23;q33) TRAF1/ALK, with data on clinics, and the genes implicated.

Clinics and pathology

Disease
Anaplastic large cell lymphoma, ALK-positive

Phenotype/cell stem origin
Mature (peripheral) T cell.

Etiology
No etiologic factors are known.

Epidemiology
The single reported case occurred in an adult male (Feldman et al., 2013).

Clinics
Presentation in the single reported case was with lymphadenopathy and rash.

Pathology
The pathologic findings in the single reported case were typical for the so-called “lymphohistiocytic pattern” previously reported in ALK-positive ALCLs.

Treatment
The patient in the reported case was treated with anthracycline-based multi-agent chemotherapy.

Prognosis
Among peripheral T-cell lymphomas, ALK-positive ALCLs tend to have favorable outcomes. The patient in the reported case had a recurrence requiring additional therapy, but was alive without evidence of disease at last follow-up, 28 years after diagnosis.

Cytogenetics

Note
Deep RNA sequencing of tumor tissue identified a chimeric transcript fusing the end of exon 6 of TRAF1 to the start of exon 20 of ALK. The TRAF1-ALK fusion transcript was confirmed at the mRNA level by Sanger sequencing and the encoded fusion protein was visualized by Western blot.

Cytogenetics morphological
Karyotypic findings have not been reported.

Additional anomalies
Unknown.

Variants
Unknown.
ALCL, ALK-positive, with t(2;9)(p23;q33) TRAF1/ALK. H&E stain of paraffin embedded tumor tissue shows large atypical cells with cytologic features of “hallmark” cells characteristic of ALCL. Immunohistochemical staining for CD30 shows strong positivity in the tumor cells, with a membranous and Golgi zone distribution. Staining for ALK shows strong cytoplasmic positivity without nuclear staining. The absence of nuclear staining is characteristic for an alternate (non-NPM1) ALK fusion partner. TRAF1 was identified as the partner gene by RNA sequencing.
Genes involved and proteins

**TRAF1**
Location 9q33.2
Protein TRAF1 encodes the TRAF1 protein, a member of the tumor necrosis factor receptor-associated factor family of signaling proteins. TRAF1 associates with, and mediates signal transduction from, various receptors of the TNFR superfamily. TRAF1 and TRAF2 form a heterodimeric complex, which is required for TNF-alpha-mediated activation of MAPK8/JNK and NF-kappaB.

**ALK**
Location 2p23.2
Protein ALK encodes a receptor tyrosine kinase, the anaplastic lymphoma kinase (ALK), which belongs to the insulin receptor superfamily and is critical in the development of the brain. ALK fusion proteins are critical in the pathogenesis of ALK-positive ALCs and a variety of other hematopoietic and non-hematopoietic neoplasms, in which they serve both as a diagnostic biomarker and potential therapeutic target.

Result of the chromosomal anomaly

**Hybrid gene**
Description Expressed, as demonstrated by next-generation and Sanger sequencing.

**Fusion protein**
Note The TRAF1-ALK fusion transcript and TRAF1-ALK fusion protein both were expressed in the reported case.
The function of the fusion has not been reported.

Description Expressed, as demonstrated by Western blot and immunohistochemistry.

References

This article should be referenced as such: