t(2;22)(q34;q12) in angiomatoid fibrous histiocytoma

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Disease
Angiomatoid fibrous histiocytoma is a rare soft-tissue tumour of low metastatic potential (local recurrence below 15% of cases, and metastases occur in less than 2% of patients), often located in the extremities; it is mostly found in children and young adults. Surgical excision is the treatment of choice.

Epidemiology
Twenty two cases of angiomatoid fibrous histiocytoma with a (2;22)(q34;q12) have so far been described; there were 13 male and 9 female patients, aged 16 years (median, range 3-38) (Antonescu et al., 2007; Rossi et al., 2007; Shao et al., 2009).

Pathology
Cases presented either a spindle or a mixed spindle and small cell morphology; there was no case of pure small cell morphology; one case showed pleomorphism; however, the prognosis in this later case has been as good as that of other cases.

Cytogenetics
Cytogenetics Morphological
The t(2;22)(q34;q12) appears to be the most frequent anomaly in angiomatoid fibrous histiocytoma, while the t(12;22)(q13;q12) (5’ EWSR1 - 3’ ATF1), and the t(12;16)(q13;p11) (5’ FUS- 3’ ATF1) are rarer.

Genes involved and proteins

**CREB1**
Location 2q33
Protein Contains a KID domain (kinase inductible domain), a basic motif (DNA binding) and a leucine-zipper for dimerization, like ATF1. Stimulates transcription by binding the cAMP response element TGACGTCA (CRE). Transcription factor.

**EWSR1**
Location 22q12
Protein From N-term to C-term: a transactivation domain (TAD) containing multiple degenerate hexapeptide repeats, 3 arginine/glycine rich domains (RGG regions), a RNA recognition motif, and a RanBP2 type Zinc finger. Role in transcriptional regulation for specific genes and in mRNA splicing.

Result of the chromosomal anomaly

**Hybrid Gene**
Description 5’ EWSR1 - 3’ CREB1. EWSR1 exon 7 is fused in frame to CREB1 exon 7 in all cases so far studied.
**Fusion Protein**

**Description**

Fusion of the N terminal transactivation domain of EWSR1 to the DNA binding domain of CREB1.

**References**


Shao L, Singh V, Cooley L. Angiomatoid fibrous histiocytoma with t(2;22)(q33;q12.2) and EWSR1 gene rearrangement. Pediatr Dev Pathol. 2009 Mar-Apr;12(2):143-6

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