Pseudomyogenic hemangioendothelioma: 
t(7;19)(q22;q13) SERPINE1/FOSB

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Abstract

Pseudomyogenic hemangioendothelioma (PHE) is an intermediate malignant vascular tumor primarily affecting soft tissues in children and young adults. The molecular basis of this neoplasm is unknown. Chromosome banding analysis, fluorescence in situ hybridization (FISH), mRNA sequencing, RT-PCR, and quantitative real-time PCR have shown that PHEs are characterized by a balanced translocation t(7;19)(q22;q13), resulting in the fusion of the SERPINE1 and FOSB genes. The role of SERPINE1, which is highly expressed in vascular cells, in this gene fusion is probably to provide a strong promoter for FOSB. FOSB encodes a transcription factor belonging to the FOS family of proteins, which together with members of the JUN family of transcription factors are major components of the Activating Protein 1 (AP-1) complex.

Keywords
Pseudomyogenic hemangioendothelioma; SERPINE1; FOSB; translocation

Clinics and pathology

Note
Newly recognised entity. Rare. Exact incidence not known.

Etiology
Not known.

Epidemiology
Often young adults. Predominantly male (4.6:1)

Clinics
Two thirds of the lesions seen in limbs followed by trunk and head and neck. Size 0.3-5.5 cm. Often multifocal and ill circumscribed. Situated subcutaneously but often in different tissue planes, including bone. Painful nodules in 50% of the cases. Locally aggressive and often recurring but rarely distant metastases. (Hornick et al., 2011)

Pathology
Spindle cells in fascicles and sheets. Vesicular nuclei. Distinct eosinophilic cytoplasm. Cells often show a rhabdomyoblast-like appearance.

Treatment
Surgical resection

Genetics
PHE consistently displays a SERPINE1-FOSB fusion gene, resulting from a translocation between chromosomes 7 and 19, presumably constituting the essential driver mutation in this neoplasm (Trombetta et al., 2011).
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SERPINE1/FOSB

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Interphase FISH with BAC probes showing normal red (SERPINE1) and green (FOSB) signals and yellow fusion (SERPINE1-FOSB) signal.

Chromatogram showing the fusion junction in a case of PHE. Sixty-one nucleotides from intron 1 of SERPINE1 were inserted at the fusion junction (blue double arrow). The translation start codon in FOSB is indicated (black arrow).

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**Cytogenetics**

*Cytogenetics Morphological*

A recurrent translocation t(7;19)(q22;q13) has been seen.

**Genes involved and proteins**

*Note*

SERPINE1 and FOSB

**SERPINE1**

Location

7q22.1; chr7:100,770,370-100,782,547

DNA / RNA

12,178 nt

**Protein**

SERPINE1 (aka PAI-1, plasminogen activator inhibitor type 1) encodes a protein that is a member of the serine protease inhibitor family, and that inhibits tissue- and urokinase-type plasminogen activators. These activators convert plasminogen to plasmin, which in turn mediates fibrinolysis and proteolytic degradation of extracellular matrix. It is highly expressed in many tumors, being implicated in invasion, angiogenesis and metastasis (Declerck et al., 2013).

**FOSB**

Location

19q13.32; chr19:45,971,253-45,978,437

DNA / RNA

7,185 nt
Protein
Member of FOS family of genes, which code for leucine zipper proteins that act as transcription factors. FOSB consists of 338 amino acids (aa), with a central basic leucine-zipper region and a carboxy-terminal transactivation domain (TAD) (Milde-Langosh, 2005).

Result of the chromosomal anomaly

Hybrid Gene
Transcript
RT-PCR and subsequent sequencing of amplified products from two cases identified an in-frame SERPINE1/FOSB fusion transcripts in both cases. In both tumors the breakpoints in SERPINE1 were located in the non-coding exon 1. The breakpoint in FOSB was located in the beginning of exon 2 in one case and in the non-coding exon 1 in the other. Both cases showed small insertions (61 bp in Case 1, 59 bp in Case 2) of material from intron 1 of SERPINE1 at the fusion junction (Walther et al., 2014).

Fusion Protein
Oncogenesis
The role of SERPINE1 in the SERPINE1-FOSB chimera is probably to provide a promoter allowing strong expression of FOSB.

References

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