Bone: Aneurysmal bone cysts

Paola Dal Cin

Department of Pathology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA (PD)

Published in Atlas Database: June 2004
Online updated version: http://AtlasGeneticsOncology.org/Tumors/AneurBoneCystID5133.html
DOI: 10.4267/2042/38115
This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2004 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Clinics and pathology

Etiology
The most widely accepted pathogenetic mechanism of aneurysmal bone cysts involves a local circulatory disturbance leading to markedly increased venous pressure and the development of a dilated and enlarged vascular bed within the affected bone area. However, the recent identification of recurrent chromosome abnormalities has challenged this historical perception.

Clinics
Aneurysmal bone cysts (ABC) are benign lesions that occur more frequently in the metaphyses of long bones, especially distal femur, the proximal tibia and vertebral posterior bodies. It can occur at any age but most patients are diagnosed in the first 2 decades of life. It can exist as primary bone lesion or as secondary lesions arising in association with other osseous conditions, namely giant cell tumor, chondroblastoma, chondromyxoid fibroma and fibrous dysplasia. Pain and swelling are the most common complaints.

Pathology
As the name implies, the lesion is histopa-thologically characterized by hemorrhagic cystic and cavernous spaces surrounded by fibrous septa composed of mildly to moderately mitotically active spindle cells intermixed with scattered osteoclast-like multinucleated giant cells. Approximately 95% of ABC have typical histology whereas the remaining 5% are "solid" variants in which the usual cavernous channels and spaces may not be identified. An extrasosseous counterpart of ABC has been described, sometimes referred to as ABC of soft tissues, and is histologically identical to ABC but diagnosed much less frequently.

Treatment
ABC is most frequently treated by curettage, but local recurrences can still occur in a substantial number of cases.

Cytogenetics

Cytogenetics Morphological
Chromosome bands 16q22 and/or 17p13 are non randomly rearranged in ABC, regardless of tumor type (classic, solid) and or location (osseous and extrasosseous). A recurrent t(16;17)(q22;p13) has been identified, but other chromosomal segments as translocation partner for each chromosome have been described: t(1;17)(p34;p13) THRAP3 -USP6, t(3;17)(q21;p13) ZNF9 -USP6, t(9;17)(q22;p13) OMD -USP6, t(17;17)(q12;p13) COL1A1 -USP6. Although additional cases should be studied, it appears that in combined giant cell tumor and secondary aneurysmal bone cyst, both lesions can retain their characteristic chromosomal aberrations.

Genes involved and proteins

USP6 (Ubiquitin Specific Protease 6).
Also known as TRE-2 or TRE17.

Location
17p13

DNA / RNA
7878 bp (major transcript).

Protein
786 amino acids; USP6 is a hominoid-specific gene that was initially cloned from an Ewing sarcoma cell line. It arose from an evolutionary chimeric gene fusion
between the TBC1D3 (also known as PRC17) and USP32 (NY-REN-60) genes, which are both located on the long arm of chromosome 17. Sequence comparisons indicate that the first 14 exons of USP6 are derived from TBC1D3 (PRC17) whereas exons 15 to 30 are derived from USP32 (10). TBC1D3 (PRC17) is located at chromosome band 17q12 and encodes a protein with a TBC/GAP domain involved in Rab/Ypt GTPase signaling. USP32 is located at chromosome band 17q23 and encodes a protein composed of two EF-hand calcium-binding motifs, a myristoylation site, and a UBP domain. Because USP6 is absent in non-hominoid primates and is primarily expressed in testicular tissue, it has been suggested that USP6 contributed to hominoid speciation. Until recently USP6 function was poorly know but recent data suggest that USP6 is a component of a novel effector pathway for Rho GTPases Cdc42 and Rac1 and stimulates actin remodeling.

**CDH11 (Cadherin 11 or Osteoblast Cadherin or OB-Cadherin)**

**Location**
16q21-q22.1

**DNA / RNA**
3.6 and 3.8 kb mRNA (two major transcripts).

**Protein**
693 and 796 amino acids; Membrane protein that mediate calcium-dependent cell-cell adhesion, member of the cadherin superfamily. CDH11 seems to be highly expressed during the development and differentiation of the osteoblastic lineage, indicating an important role in bone development. Two splice variants have been identified, one of which encodes an isoform with a shorter cytoplasmic domain.

**Result of the chromosomal anomaly**

**Hybrid Gene**

**Description**
5’ CDH11 - 3’ USP6.

**Oncogenesis**
The oncogenic mechanism of CDH11-USP6 is still unknown but very likely involves transcription upregulation of USP6 mediated by the highly active CDH11 promoter.

**References**


This article should be referenced as such: