Soft tissue tumors: Alveolar soft part sarcoma

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Published in Atlas Database: Update -July 2007

Online updated version: http://AtlasGeneticsOncology.org/Tumors/AlveolSoftPartSID5125.html

DOI: 10.4267/2042/38534


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Identity

Other names: Malignant nonchromaffin paraganglioma; Malignant organoid granular cell myoblastoma

Clinics and pathology

Embryonic origin

The histogenesis of this tumour is still unknown, despite immunohistochemistry studies and electron microscopy. It may have a myogenic origin, and might be a variant of rhabdomyosarcoma.

Epidemiology

Rare tumour: represents less than 1% of soft tissue sarcomas of adults and 1-2% of soft tissues sarcomas in children.

Occurs most often in the young adult, less frequently in children.

Median age is 20 years in female patients, and 30 years in male patients. More frequently, patients are females (ratio M/F is 2/3).

Clinics

Involve the muscles and soft tissues, in particular those of the lower extremities (buttocks, thighs and legs). This represents more than half cases in the adults. It may also arise in the upper extremities, in the head and neck regions, especially in the child, but it can also have extra muscular localizations, such as the female genital tract, the trunk, the mediastinum, or the retroperitoneum.

Metastases are frequent. They occur mainly in lungs, bones, and brain.

Symptoms at diagnosis may be pain and/or swelling. Diagnosis is often retarded.

Pathology

Well circumscribed tumours with a multinodular pattern, haemorrhagic and necrotic. Microscopically, exhibits an alveolar structure, the center of the alveolar space being formed by detachment of necrotic cells, and with surrounding capillaries (there is a more solid pattern in children). Cells are large, with abundant cytoplasm. Mitoses are rare.

Secretory process with the formation of cytoplasmic membrane-bound crystals (PAS+, diastase resistant) can often be seen with electron microscopy, a feature of great diagnostic value (they are pathognomic). These granules contain monocarboxylate transporter 1 (MCT1) - CD147 complexes.

Immunohistochemistry: in general, alveolar soft part sarcomas are negative for neuroendocrin and epithelial markers, and often positive for vimentin, muscle-specific actin, and desmin. The strong nuclear staining of an anti C-term TFE3 can be used for diagnosis (although cytogenetics and/or molecular genetics are the most relevant tools for diagnosis). To be noted is that a subset of renal cell carcinomas, the primary renal ASPSCR1-TFE3 tumour, share some morphological features with the alveolar soft part sarcoma (it may be a differential diagnosis); they also share a common genetic substratum.

Treatment

Primary tumours: large surgical excision (a complete resection is of great importance) and radiation.

Metastases: chemotherapy, with or without radiation or surgery, depending on the number of metastases.

Evolution

Slow growing tumour, but highly angiogenic, which favours metastases dissemination.
Metastases appear in more than half of the patients who presented without metastases at diagnosis (up to 70% in one study); however, there is a long disease-free interval before appearance of metastases (median 6 years) in these patients.

**Prognosis**

Relatively indolent clinical course. In one study, overall survival of adult patients without metastases reached 87% at 5 years, but that of adult patients with metastases at diagnosis was only 20% at 5 years, with a median survival of 40 mths. Pediatric cases had a better prognosis, with a 5 years survival of 80% for all cases included, reaching 91% in cases without metastases. Median survival in patients without metastases at diagnosis was noted above 10 years in a large -but old (period 1923-1986)- study, and it may be expected that progress has been made. Due to the rarity of the disease and its long course, survival data are outdated.

**Cytogenetics**

**Cytogenetics morphological**

t(X;17)(p11;q25) is found in all alveolar soft part sarcomas so far studied, but also in primary renal ASPSCR1-TFE3 tumours. In the case of alveolar soft part sarcoma, the chromosome rearrangement is found in an unbalanced form, as a der(17)(X;17)(p11;q25), in 80% of cases; the unbalanced form implicates:

1- the formation of a hybrid gene at the breakpoint, but also,
2- gain in Xp11-pter sequences, and loss of heterozygocicty in 17q25-pter, with possible implications, although no clinical (including prognostic) nor pathological differences have so far been noted between balanced and unbalanced cases... but, again, the disease is rare, and cases with cytogenetic studies even rarer (about 25 cases).

**Note:** the t(X;17)(p11;q25) in primary renal ASPSCR1-TFE3 tumours is balanced in all known cases.

**Result of the chromosomal anomaly**

**Hybride Gene**

**Description**

5' ASPSCR1 - 3' TFE3; the reciprocal 5' TFE3 - 3' ASPSCR1 is most often absent. ASPSCR1 is fused in frame either to TFE3 exon 3 or to exon 4 (type 1 and type 2 fusions respectively).

**Fusion protein**

**Description**

234 NH2 term amino acids from ASPSCR1, fused to the 280 or 315 C term amino acids from TFE3, including the activation domain, the helix-loop-helix, and the leucine zipper from TFE3.

**Notes**

Retention of heterozygocicty in the tumours of female patients (i.e. a normal maternal X and a normal paternal X are present, in addition to the Xp11-pter involved in the translocation) has been noted in all (n=7) female cases studied, showing that the translocation occurred in G2 phase.

**References**


This article should be referenced as such: