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Solid Tumour Section

Mini Review

Soft tissue tumors: Synovial sarcoma

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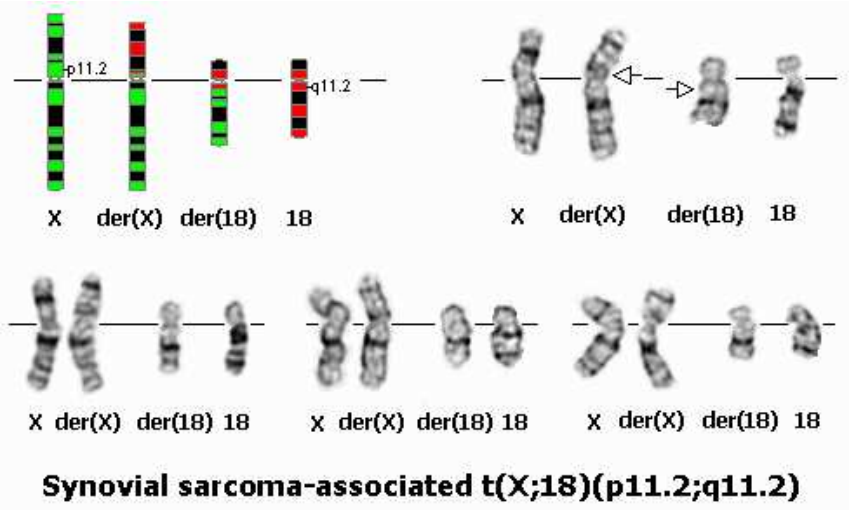
Identity

Phylum: Soft Tissue Tumors: Uncertain differentiation: Synovial sarcoma.

Alias : t(X;18)(p11.2;q11.2) in synovial sarcoma



t(X;18)(p11.2;q11.2) in synovial sarcoma G-banding - Courtesy Charles Bangs.

Clinics and pathology

Epidemiology

Rare soft tissue tumor, it accounts for up to 5 to 8% of soft tissue sarcomas, the fourth most common type of sarcoma after malignant fibrous histyocytoma, liposarcoma and rhabdomyosarcoma; the most common pediatric non rhabdomyosarcomatous soft tissue cancer; average incidence: 2,75 per 100000 population based on a canandian study.

Clinics

Most prevalent in adolescents and young adults, it occurs primarily in the para-articular regions of the extremities, especially the lower ones; rarely, it is encountered in various areas such as parapharyngeal region, abdominal wall, lung or cardiac tissue, ….

Pathology

Well-defined, apparently unrelated to synovium (cf various rare localisations), it displays characteristics of concurrent epithelial and spindle cell proliferation; several types are recognized: two major ones:
Biphasic, with epithelial and spindle cell components in various proportions and
Monophasic fibrous type;
Monophasic epithelial type is much less common;
May also present as a poorly differentiated small cell neoplasm; diagnosis may be difficult especially for the two later.

In general, very few problems in diagnosis in the biphasic type, may be not ascertained in some instances even after immunohistochemical examination.

Treatment

Complete surgical excision of the primary tumor is actually the basis of the treatment; the optimal treatment approach is to be determined as post operative radiotherapy and adjuvant chemotherapy may permit limb preserving surgery and limit local recurrence and (micro) metastasis disease (lung+++).

Prognosis

Traditionnally has had a bad prognosis what either the biphasic or monophasic type, poorer in the poorly differentiated small cell neoplasm.
EFS at 5 years: 45-60%; improved in a recent german study to 74% for children and adolescents; improvements in adults too.
Recents prognostic studies to identify risk groups and adequate treatment strategies indicate that synovialosarcomas might not be uniformely high grade tumors.

Cytogenetics

Cytogenetics Morphological

A t(X;18)(p11.2;q11.2) is found in almost all synovial sarcomas (80%) whatsoever the histologic type may be; t(X;18)(p11.2;q11.2) seems to be specific: it is not found in other spindle cell sarcomas, and very rarely detected in other tumors as malignant fibrous histyocytoma or fibrosarcomas.

Cytogenetics Molecular

Detectable by metaphasic and/or interphasic dual colour fluorescent in situ cytogenetics; hybridization combining centomere X or 18 probes with respectively 18 or X whole chromosome painting or YAC probes.

Additional anomalies

Both numerical and structural anomalies are found in 50% of cases, numerical anomalies only in 20% (+7,+8,+12,+21,-3, -11, -14, -22) and structural.anomalies only in 20% (involving chromosomes 1, 3, 11, 12, 15, 17 and 21: tumors may be hypodiploid, pseudodiploid, hyperdiploid or near tetraploid without a common pattern; DNA flow cytometry study revealed poorer prognosis for aneuploid tumors.

Variants

A few variants have been described, involving chromosomes 1, 3, 15 or 21,...; masked translocations were identified as t(5 ;18), t(X ;7) without chromosome X or 18 apparent involvement respectively.

Genes involved and proteins

SYT (Synovial tumor)

Location
18q11.2

DNA / RNA
3,7 kb mRNA.

Protein
387 amino acids; glutamin, prolin and glycin rich; three potential SH2 binding domains and one SH3; widely expressed, limited to cartlagenous and nervous tissues in early embryonal development; biological properties still unknown.

SSX1, SSX2, SSX4 (one case) (Synovial Sarcoma X)

Location
Xp11.2

DNA / RNA
1,6 kb mRNA.

Protein
188 amino acids; 81% homologie for SSX1 and SSX2; Kruppel associated box (KRAB) homology; restricted expression to testis and thyroid; biological properties still unknown.

Result of the chromosomal anomaly

Hybrid Gene

Description
5 prime SYT- 3 prime SSX1/2.

Fusion Protein

Description
Substitution of the 8 last amino acids of SYT by 78 amino acids of SSX, with exclusion of KRAB and one SH2 domain.

Oncogenesis
The important role is that of the transcript situated on the der(X).
RT-PCR diagnosis: there is a correlation between biphasic type and SYT/SSX1 variant (where SSX2 involvement is never detected), SYT/SSX2 is more common than SYT/SSX1 in monophasic one.
SYT/SSX1 variant might be less favorable, associated with higher tumor proliferating rate and reduced overall survival (metastasis free survival 42% vs 80%).

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