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Solid Tumour Section

Short Communication

Soft tissue tumors: Desmoplastic small round cell tumor

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Identity

Alias

t(11;22)(p13;q11) in desmoplastic small round cell tumor

Clinics and pathology

Phenotype / cell stem origin

Thought to be of peritoneal blastomatous cell origin.

Epidemiology

Rare; mostly in childhood and adolescent males (mean age: 22 years; sex ratio: 4.7 M/1F).

Clinics

Very aggressive tumor, located almost exclusively to the peritoneal surfaces of the abdomen with involvement of many abdominal organs; very rare localisations outside the abdominal cavity (thoracic, cranial or skeletal localisations).

Pathology

Characterized by nested pattern of small poorly differenciated tumor cell growth surrounded by dense desmoplastic stroma and immunohistochemistrical trilineage coexpression: epithelial (cytokeratin, EMA), mesenchymatous (desmin, vimentin) and neural (NSE).

Treatment

Surgery may be performed before intensive chemo and radiotherapy.

Prognosis

Very poor; 35% overall progression-free survival at 5 years; median survival of about 17 months, although tumors are responsive to aggressive therapy in some cases.

Cytogenetics

Note

Besides the specific t(11;22)(p13;q12), 2 variant translocations have been described.

Additional anomalies

Frequent additionnal abnormalities, sometimes complex.

Variants

The variant translocations are:
(t(2;21;22)(p23;q22;q13) and t(11;17)(p13;q11.2).

Genes involved and proteins

EWSR1

Location

22q12

DNA / RNA

Spans over 40 kb, 17 exons ; 2,4 kb mRNA.

Protein

656 amino acids; N-term gln-thr-pro-rich region; C-terminal proline rich region; wide expression; RNA binding protein.

WT1

Location

11p13

DNA / RNA

Spans over 50 kb, 10 exons; alternative splicings (in particular, the second site adds or remove 3 amino-acids (KTS) between the second and third zinc fingers and generates 2 isoforms); mRNA 3,5 kb.

Protein
52-54 Kda; 4 Cys2-His2 zinc fingers, glutamine-proline-glycine-rich transcriptional regulation domain, interacting with p53; nuclear localisation; transcriptional repressor.

Result of the chromosomal anomaly

Hybrid Gene

Description
5' EWS - 3' WT1

Transcript
mRNA detectable by RT-PCR (99% of DSRCT).

Fusion Protein

Description
The N-term trans activation domain of EWS (exon 7) is fused to the C-term zinc fingers domain of WT1(exon 8); molecular variants have been described (exons 9 or 10 of EWS); transcritional activator ; the 2 isoforms EWS-WT1 without KTS and EWS-WT1 with KTS having different properties.

Expression / Localisation
Nuclear.

Oncogenesis
Early: in the embryonal mesenchyme of the coelomic cavities; due to inapopriate transcriptional activition of WT1- responsive genes; the EWS-WT1 without KTS isoform would be dominantly acting as an oncogene.

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