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Solid Tumour Section

Mini Review

Soft tissue tumors: Extraskeletal myxoid chondrosarcoma

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Couturier J. Extraskeletal myxoid chondrosarcoma. Atlas Genet Cytogenet Oncol Haematol 2000;4(3):145-146.

Clinics and pathology

Disease

Malignant tumour of soft tissue origin, distinct from the primary skeletal chondrosarcoma with myxoid alteration.

Epidemiology

It is a rare tumour: 2.3% of soft tissue sarcomas in a Japanese series; mean ages reported in various series range from 46 to 57 years, this tumour being exceptional in children and adolescents; males are affected about twice as often as females.

Clinics

Location: deep soft tissues of the lower extremities in about 75% of the cases, especially the thigh, the popliteal fossa, and the buttock; occasionally, a bone involvement may exist, as a minor component.

Pathology

Macroscopic findings: the tumour presents as lobulated or multinodular mass, generally well circumscribed by a distinct fibrous capsule.The size of the tumour at the time of diagnosis may vary from 1 to about 20 cm (mean size: about 7 cm).
Histology: typically, tumour nodules are composed of round or slightly elongated cells, with minimal features of chondroblasts, separated by mucoid substance; differentiated cartilage cells are rare; histological diagnosis may be very difficult, especially in highly cellular forms devoid of myxoid matrix.

Tumour cells generally show positivity for vimentin, S-100 protein, occasionally for EMA, and negativity for cytokeratin.
A subset of tumours display neural or neuroendocrine differentiation as shown by positive immunohistochemical reactivities to neural or neuroendocrine markers such as neuron-specific enolase, synaptophysin, chromogranin A, and PGP9.5; tumours are mostly negative for markers (collagen type II, X, proteoglycan aggrecan) for the chondrocytic cell lineage.
Ultrastructurally, at least one third of the tumours demonstrate microtubular aggregates within dilated rough endoplasmic reticulum; neurosecretory granules (80-170 nm diameter) are occasionally identified.

Treatment

Treatment: surgical excision, with adjuvant chemotherapy in case of lymph nodes or metastasi.

Cytogenetics

Cytogenetics Morphological

Cytogenetic studies have demonstrated the presence of a recurrent translocation t(9;22)(q22;q12); it results in the fusion of the EWSR1 gene on chromosome 22 with NR4A3 (TEC, CHN, or NOR1) gene on chromosome 9.
Recently, a variant translocation t(9;17)(q22;q11) and t(9;15)(q22;q21) have been identified, fusing the gene NR4A3 to gene TAF15 (TAF2N, TAFII68, or RBP56) and gene TCF12 (HTF4), respectively.

A variant fusion gene, TFG-NR4A3, has also been identified recently.

Genes involved and proteins

NR4A3 (TEC)

Location
9q22
DNA / RNA
Transcripts: 2.6 kb and 3.7 kb.
Protein
Orphan nuclear receptor; signaling mediator; activate the c-fos promoter; role in growth and differentiation processes of hematopoietic tissues.

EWSR1

Location
22q12
DNA / RNA
17 exons; 2.4 kb mRNA.
Protein
RNA-binding protein; transcription repressor.

TAF2N

Location
17q11.1-q11.2
DNA / RNA
16 exons; alternative splicing; 2.2 kb bp mRNA.
Protein
RNA-binding protein; part of theTFIID and RNA polymerase II complex.

TCF12

Location
15q21
DNA / RNA
370 kb; 21 exons; 4 kb mRNA.
Protein
Transcription factor; a basic helix-loop-helix protein.

TFG

Location
3q11-q12
DNA / RNA
39.51 kb; 8 exons; 1.9 kb mRNA.
Protein
Putative signal transducer; positive regulator of I-kappaB kinase/NF-kappaB cascade.

Result of the chromosomal anomaly

Fusion Protein

Description
The EWSR1/NR4A3 (TEC, CHN) gene fusion encodes a fusion protein in which the C-terminal RNA-binding domain of EWSR1 (EWS) is replaced by the entire NR4A3 (TEC) protein. NR4A3 (TEC) is a member of the steroid/thyroid receptor gene superfamily; the EWSR1/NR4A3 (EWS/TEC) fusion protein is a potent transcriptional activator.
The TAF15 (TAF2N, TAGII68 or RBP56)/NR4A3 (TEC) fusion, in which exon 6 of TAF15 (TAF2N, TAFII68, or RBP56) is fused to the entire coding region of NR4A3 (TEC), is structurally and functionally very similar to the EWSR1/NR4A3 (EWS/TEC) fusion.
In the TCF12/NR4A3 fusion, the first 108 amino acids of the N terminus of TCF12 are fused in-frame upstream of the entire NR4A3 sequence.
The TFG/NR4A3 fusion, in which exon 6 of TFG is fused to the entire coding region of NR4A3.

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