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Solid Tumour Section

Mini Review

Soft tissue tumors: Ewing's tumors/Primitive neurectodermal tumors (PNET)

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Identity

Note: Ewing tumours form a histologically heterogeneous family belonging to the group of small round-cell tumours and derived from neural crests cells.

Classification

Ewing's tumors cover several distinct histological types:
- Peripheral neuroepithelioma,
- Esthesioneuroblastoma,
- Askin's tumour,
- Ewing's sarcoma of bones and soft tissues.

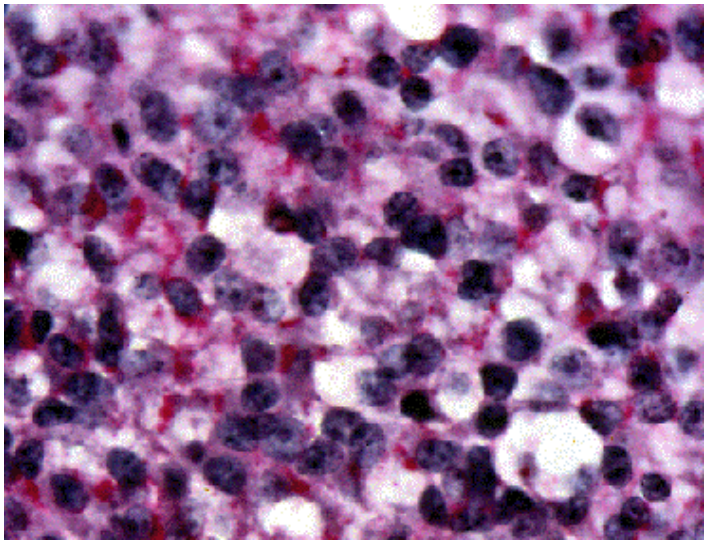
Clinics and pathology

Epidemiology

Peripheral neuroepithelioma is a very rare tumour (1% of all sarcomas); Ewing's sarcoma represents 5 to 15% of malignant bone and soft tissue tumours; two thirds of cases of Ewing's tumours occur before age 35 years, with a median age of 20 years.

Clinics

Peripheral neuroepithelioma typically occurs in the extremities (buttock and upper thigh, shoulder and upper arm);
Esthesioneuroblastoma probably develops from the olfactive placode, in the nasal vault;
Ewing's sarcoma of bones affects preferentially long bones (especially the femur), the pelvis, and the ribs;
Extraskeletal Ewing's sarcoma occur in the paravertebral region and chest wall, often in association with vertebrae and ribs, and in lower extremities;
Askin's tumour is a pediatric tumour affecting mostly the chest wall and ribs.



Ewing's tumor: the tumor is composed of blastematous tissue with some differentiated glomerular structures associated with mesenchymal tissue and tubules. Courtesy Pierre Bedossa.

Pathology

Peripheral neuroepithelioma shows sheets or lobules of small round-cells with a scarce cytoplasm; cells are often arranged in rosettes with a neurofibrillar center (Homer-Wright rosettes).
Esthesioneuroblastoma is histologically very similar to neuroblastoma; rosettes may be present.
Askin's tumour seems to be more related to neuroepithelioma than to Ewing's sarcoma.
Ewing's sarcoma forms sheets of uniform small round-cells, sometimes arranged in a lobular pattern; the cytoplasm is scanty, pale stained and often vacuolated (glycogen); Ewing's sarcoma is considered as the less differentiated form of the Ewing's tumours family.

Treatment

The treatment of Ewing's tumours is generally based on combined therapy with adjuvant chemotherapy, surgical resection and radiotherapy.

Prognosis

Combined therapies have largely improved the prognosis of Ewing's tumours in the recent years; the prognosis is mainly determined by the presence of metastases at the time of diagnosis (15 to 35% of the cases); the 5-year survival rate is 10-35% in patients with mestastases, and 54-74% for patients with a localised disease at presentation.

Cytogenetics

Cytogenetics, morphological

About 90% of Ewing's tumours, whatever their type, show a t(11;22)(q24;q12); the translocation results in the fusion of the EWS gene with the transcription factor gene FLI1, leading to a hybrid transcript and an oncogenic chimeric protein; in about 5% of the cases, the EWS gene is involved in variant translocations: t(21;22)(q12;q12) and t(7;22)(p22;q12), leading to fusions EWS-ERG and EWS-ETV1, respectively.

Additional anomalies

Additional anomalies in Ewing's tumours mainly consist in chromosome gains: +8 (45% of the cases) and, with a much lower frequency, trisomies 2, 5, 7, 9, 12 (between 10 and 15% of the cases); trisomy 1q, through unbalanced t(1q;16q), is observed in about 25% of the cases.

Genes involved and Proteins

Genes

EWSR1

Location: 22q12

Protein

RNA binding.

FLI1

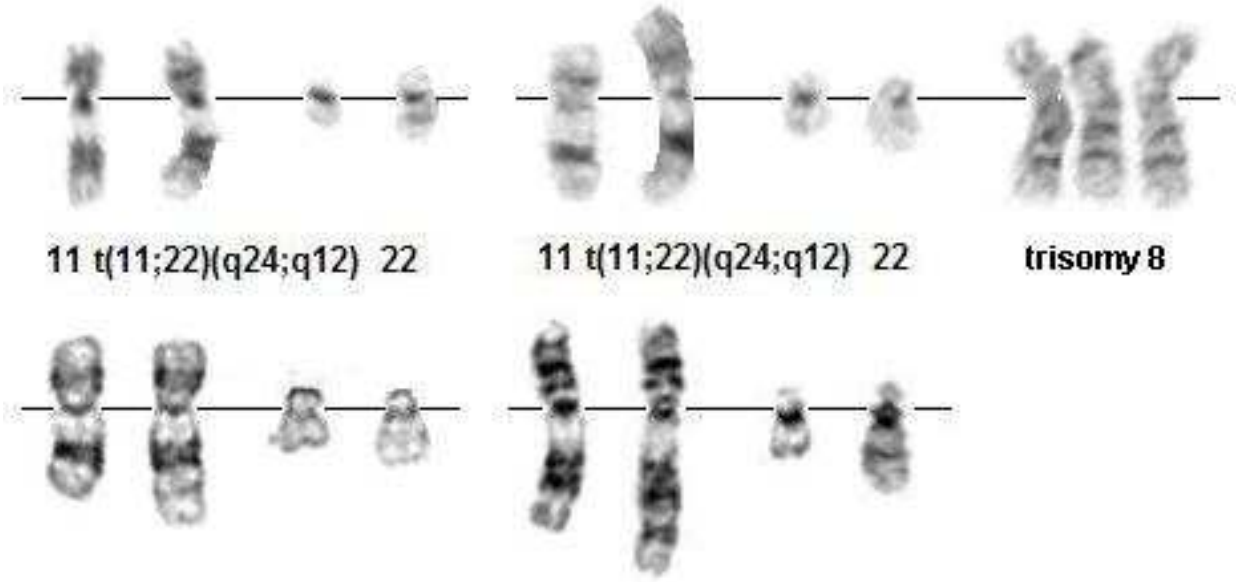
Location: 11q24

ERG

Location: 21q21

ETV1

Location: 7p22



t(11;22)(q24;q12) in Ewing sarcoma, G- banding - top: courtesy Jean Luc Lai (with trisomy 8 on the right); - bottom: courtesy G. Reza Hafez, Eric B.Johnson, and Sara Morrison-Delap, UW Cytogenetic Services.

Result of the chromosomal anomaly

Hybrid Gene

Description

The 5' EWSR1 is fused to parts of either FLI1, ERG, or ETV1.

Fusion protein

Description

N terminal domain of EWS protein with DNA binding domain of FLI1, ERG (ETS family genes).

Oncogenesis

Through transcription dysregulation.

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