Identity

Note: Rhabdomyosarcoma (RMS) refers to a family of mesenchymal tumours related to the skeletal muscle lineage.

Classification

The two main histopathologic subtypes of rhabdomyosarcoma are:

- Embryonal rhabdomyosarcoma (ERMS)
- Alveolar rhabdomyosarcoma (ARMS)

Clinics and pathology

Embryonic origin

RMS is postulated to be derived from mesodermal tissues.

Epidemiology

RMS is the most common pediatric soft tissue sarcoma, representing ~5% of all malignancies among children and adolescents. The annual incidence is 4-5 per million. ERMS accounts for 70-80% of all RMS, and usually occurs in young children (median age of 6.5 years). ARMS accounts for the remaining 20-30% of RMS, and more often occurs in older children and young adults (median age of 12 years).

Clinics

RMS often presents as a painless mass. In other cases, the tumor may be discovered from symptoms produced by compression of structures at the primary site, such as diplopia (double vision) caused by RMS in the orbital region. The two histopathologic subtypes tend to occur at different sites. ERMS often occurs in the head and neck region, genitourinary tract, and retroperitoneum whereas ARMS often occurs in the extremities. All types of RMS are treated with a combination of surgery, radiation therapy, and intensive chemotherapy.

Pathology

In ERMS, the tumor cells range from small round cells to large elongated cells, and exhibit varying degrees of myogenic differentiation. There is often varying cell density with highly cellular areas alternating with low cellular areas in a loose myxoid stroma.

In ARMS, tumor cells are small with a round nucleus and scant cytoplasm. Aggregates of these tumors cells often become discohesive and produce spaces, reminiscent of lung alveoli.

An anaplastic RMS subset is recognized by large, lobated hyperchromatic nuclei and atypical mitoses. Anaplasia is more prevalent in ERMS and can be found as a focal or diffuse feature in the tumor.

The tumor cells of both subtypes of RMS variably express muscle specific proteins (such as desmin, myoglobin, muscle-specific actin, or the myogenic transcription factors MyoD and myogenin) that can be detected by immunohistochemistry.

Prognosis

Factors that influence the selection of therapy and the outcome of patients include primary site (orbit, superficial head and neck, biliary tree, vagina, and paratestis are considered favorable), size of primary...
tumor, extent of local spread, presence of nodal and distal metastases, and histologic subtype. Of the two histologic subtypes, ARMS has a poorer prognosis than ERMS.

**Genetics**

**Note**

Most cases of RMS occur sporadically without an apparent genetic predisposition. However, a small subset of RMS is associated with the following known genetic syndromes:
- Hereditary retinoblastoma syndrome (RB1)
- Li-Fraumeni syndrome (TP53)
- Neurofibromatosis type I (NF1)
- Costello syndrome (HRAS)
- Beckwith-Wiedemann syndrome (11p15 genes)
- Neviod basal cell carcinoma syndrome (PTCH)
- Rubinstein-Taybi syndrome (CREBBP).

**Cytogenetics**

**Cytogenetics Morphological**

Studies of cytogenetics and other acquired genetic changes in ERMS and ARMS have revealed significant genetic differences between these two subtypes.

Most ARMS cases are distinguished from ERMS and other solid tumors by the presence of one of two recurrent chromosomal translocations, which generate related fusion genes.
- t(2;13)(q35;q14) generates PAX3 - FOXO1 in ~60% of ARMS cases
- t(1;13)(p36;q14) generates PAX7 - FOXO1 in ~20% of ARMS cases

ERMS does not have recurrent structural chromosome rearrangements, but rather has frequent chromosome gains and losses. In addition, ERMS has a much higher frequency of loss of one of the two alleles of many chromosome 11 loci, particularly in the 11p15.5 region.

**References**


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