INTRODUCTION
Rhabdomyosarcoma is a malignant tumor of striated muscle origin. Approximately 90% of all cases of rhabdomyosarcoma are diagnosed in individuals younger than 25 years, and within this group, 60-70% are younger than 10 years. Rhabdomyosarcoma represents 3.5% of all malignancies in children aged 0-14 years, with approximately 250 new cases diagnosed each year. The head and neck are the most frequent (35-40%) sites of origin, followed by the genitourinary tract, extremities, trunk, retroperitoneum, and uncommon regions. In the head and neck, the most common sites are parameningeal and orbital locations.

HISTOLOGY
Rhabdomyosarcoma is divided into 5 major histologic categories: embryonal, alveolar, botryoid embryonal, spindle cell embryonal, and anaplastic.

Embryonal rhabdomyosarcoma
Embryonal rhabdomyosarcoma is the most common subtype observed in children, accounting for approximately 60% of all cases in this age group. The tumors can occur at any site, but they are most commonly observed in the genitourinary region or the head and neck region. On histologic examination, they have high cytologic variability, which represents several stages of skeletal muscle morphogenesis. They may range from highly differentiated neoplasms containing rhabdomyoblasts with large amounts of eosinophilic cytoplasm and cross striations to that of poorly differentiated tumor cells. Desmin and muscle specific actin are the typical stains used to identify rhabdomyosarcoma. Newer staining agents, such as myogenin and MyoD1, are more specific for skeletal muscle than older stains.

Embryonal rhabdomyosarcoma has unique molecular characteristics. Embryonal rhabdomyosarcoma cells show a loss of specific genome material from the short arm of chromosome 11. This consistent loss of the material from the 11p15 region may suggest the presence of a tumor suppressor gene, though the actual gene responsible for embryonal rhabdomyosarcoma is not yet known. Another molecular feature is its lack of gene amplification. In addition, the cellular DNA content of embryonal rhabdomyosarcoma is hyperdiploid (1.1-1.8 X normal DNA).

Alveolar rhabdomyosarcoma
The alveolar subtype makes up about 31% of all cases of rhabdomyosarcoma. It is most frequently observed in adolescents and in patients whose primary sites involve the extremities, the trunk, and the perianal and/or perirectal region. On microscopy, these tumors have the appearance of club-shaped tumor cells arranged in clumps and outlined by fibrous septa. In the center, the clusters are arranged loosely, and therefore, they appear in an alveolar pattern. These cells stain intensely with eosinophilic stain. Cross-striated malignant rhabdomyoblasts are observed in 25% of cases, which is less frequent than what is observed with the embryonal form.

Alveolar rhabdomyosarcoma has distinct molecular characteristics. A unique translocation occurs between the FKHR gene on chromosome 13 and either the PAX3 gene on chromosome 2 (70%) or the PAX7 gene on chromosome 1 (30%). Individuals with the PAX7 translocation are younger and may have longer event-free survival than those with the PAX3 translocation. Unlike embryonal rhabdomyosarcoma, alveolar rhabdomyosarcoma commonly demonstrates gene amplification, and its DNA content is typically tetraploidy.
Botryoid rhabdomyosarcoma

Botryoid type, a subset of embryonal rhabdomyosarcoma, accounts for 6% of all cases of rhabdomyosarcoma. This subtype characteristically arises under the mucosal surfaces of body orifices; therefore, it is most commonly observed in areas such as the vagina, bladder, and nares. It is distinguished by the formation of polypoid and grapelike tumor masses. On histologic study, botryoid rhabdomyosarcoma demonstrates malignant cells in an abundant myxoid stroma.

Spindle cell rhabdomyosarcoma

The spindle cell subtype of embryonal rhabdomyosarcoma accounts for 3% of all cases. It has a fascicular, spindled, and leiomyomatous growth pattern and can demonstrate notable rhabdomyoblastic differentiation. Some neoplasms show marked collagen deposition and have a nested, storiform growth pattern. This subtype occurs predominantly in the paratesticular region and is rare in the head and neck.

Anaplastic rhabdomyosarcoma

Anaplastic rhabdomyosarcoma, previously called pleomorphic rhabdomyosarcoma, is the least common of all subtypes. It most often occurs in patients aged 30-50 years. It is rarely observed in children. Anaplastic rhabdomyosarcoma is defined by large, lobate hyperchromatic nuclei and multipolar mitotic figures.

PROGNOSTIC FACTORS

Multiple clinical and biologic factors have been shown to influence the prognosis for a child with rhabdomyosarcoma. These include site of tumor origin, tumor size, nodal involvement, histology, and cellular DNA content.

The site of origin influences the patient's clinical outcome. For example, patients with head and neck rhabdomyosarcoma affecting the orbit and nonparameningeal area have a prognosis more favorable than that of patients with tumors in other sites in the body.

Another factor is tumor burden. Individuals with tumors smaller than 5 cm have an improved prognosis. Children with regional nodal involvement do worse than those without nodal disease. Children with metastatic disease have the poorest prognosis.

The final clinical factor affecting the patient's prognosis is the extent of disease following initial surgical resection.

Biologic factors can also influence prognosis. The literature often mentions that the alveolar subtype of rhabdomyosarcoma is associated with a prognosis worse than that of the other types. Cellular DNA content, or ploidy, does appear to have prognostic significance. Tumor cells with hyperdiploid have a better outcome than those with diploid or tetraploid DNA content.

STAGING INFORMATION

Group staging system

- Group I: 13% rhabdomyosarcoma are in group I. This group is defined by localized disease with complete surgical resection and no evidence of regional nodal involvement.

- Group II: 20% rhabdomyosarcoma are in group II.
  - Group IIA patients have grossly resected disease with microscopic residual disease and no regional involvement.
  - Group IIB patients have had complete resection with no residual disease, but they also have regional disease with involved nodes.
• Group IIC is a hybrid of groups IIA and IIB, containing patients with microscopic residual disease and regional nodal involvement.

• Group III: 48% rhabdomyosarcoma are in group III. This group is marked by incomplete resection or biopsy only; therefore, it is characterized as gross residual disease.

• Group IV: 18% rhabdomyosarcoma are in group IV. Individuals in group IV have distant metastasis at the time of diagnosis.

TNM staging system

• Stage I: Disease is localized and involves the orbit, the head and neck region (excluding parameningeal sites), or the nonbladder and/or nonprostate genitourinary region.

• Stage II: This stage includes any localized disease of any unfavorable primary site not included in the stage I category. The primary tumor must be less than or equal to 5 cm in diameter.

• Stage III: The criteria are the same as in stage II except the primary tumor is larger than 5 cm in diameter and/or it involves regional lymph nodes.

• Stage IV: Like group IV, stage IV implies metastatic disease at the time of diagnosis.

Risk classification

• Low risk: Patients have embryonal rhabdomyosarcoma at a favorable site (stage I), at an unfavorable site with complete resection (group I), or at an unfavorable site with microscopic residual disease (group II).

• Intermediate risk: Patients have embryonal rhabdomyosarcoma at an unfavorable site with gross residual disease (group III), metastatic embryonal rhabdomyosarcoma and are younger than 10 years, or any nonmetastatic alveolar rhabdomyosarcoma at any site.

• High risk: Those at high risk include any patient with metastatic disease unless he or she is younger than 10 years and has embryonal metastasis.

TREATMENT

Treatment of rhabdomyosarcoma is a multimodality effort. Initial efforts are aimed at surgical resection of the tumor, always followed by chemotherapy and typically ending with a standard course of radiation. The principles of surgical and radiation therapy are based on the site of involvement and the extent of disease, whereas the chemotherapeutic options depend on risk factors.