Pediatric Sarcomas

Regan F. Williams, MD[a,*], Israel Fernandez-Pineda, MD[b], Ankush Gosain, MD, PhD[a]

KEYWORDS

- Rhabdomyosarcoma • Osteosarcoma • Ewing's sarcoma
- Nonrhabdomyosarcoma soft tissue sarcoma

KEY POINTS

- Pediatric sarcomas are best treated with a multidisciplinary team to include surgery, radiation, and oncology.
- Rhabdomyosarcomas (RMS) often occur in young children, whereas nonrhabdomyosarcomas occur in infants and teenagers.
- All patients with RMS receive chemotherapy.
- Low-grade osteosarcomas and low risk nonrhabdomyosarcomas are treated with surgery alone.

Pediatric sarcomas are a heterogeneous group of tumors and account for approximately 10% of childhood solid tumors.[1] Treatment is focused on multimodality therapy, which has improved the prognosis over the past 2 decades. Current regimens focus on decreasing treatment for low-risk patients to decrease the long-term side effects of chemotherapy and radiation while maximizing therapy for patients with metastatic disease in an attempt to improve survival. Pediatric sarcomas can be divided into soft tissue sarcomas and osseous tumors. Soft tissue sarcomas are further delineated into rhabdomyosarcoma (RMS), which affect young children and nonrhabdomyosarcoma, which are most common in adolescents. The most common bone sarcomas are osteosarcoma (OS) and Ewing sarcoma (ES).

RHABDOMYOSARCOMA

Epidemiology

RMS is the most common soft tissue sarcoma in children and adolescents, accounting for nearly 250 cases of childhood cancer in the United States each year.[2] RMS is a

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[a] Department of Surgery, University of Tennessee Health Science Center, 49 North Dunlap Avenue, Second Floor, Memphis, TN 38105, USA; [b] Department of Surgery, St Jude Children's Research Hospital, MS133, Room B3019, 262 Danny Thomas Place, Memphis, TN 38105-3678, USA
* Corresponding author.
E-mail address: rfwillia@uthsc.edu

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malignant soft tissue tumor of mesenchymal origin, accounting for approximately 3.5% of cancers among children aged 0 to 14 years and 2% of the cases among adolescents aged 15 to 19 years.[3] The incidence of RMS is 4.5 per million children, with one-half of cases seen in the first decade of life.[4] During the course of 4 consecutive Intergroup Rhabdomyosarcoma Study Group clinical trials, our understanding of RMS tumor biology has advanced, and the outcome for children and adolescents with RMS has improved significantly.[5–8] Five-year survival for RMS has increased, from 53% to 67% for children younger than 15 years and from 30% to 51% for adolescents aged 15 to 19 years.[9]

The incidence of RMS varies depending on histologic subtype.[2] Embryonal RMS patients are predominantly male (male = 1.5 × female), with a peak incidence in the 0- to 4-year age group (approximately 4 cases per million). Adolescents have a lower incidence, with approximately 1.5 cases per million. The incidence of alveolar RMS is relatively constant through childhood (1 case per million) and does not show a gender predilection.[9] Undifferentiated sarcoma is more common in infants less than 1 year of age, with increased numbers found in the trunk and abdomen and fewer in the parameningeal site as compared with noninfants.[10]

The most common primary tumor sites for RMS are the head, the genitourinary (GU) tract, and the extremities.[11] Extremity tumors are more commonly found in the hand and foot of older patients, and are more likely to display alveolar histology and metastatic spread.[12] Less frequently seen primary tumor sites include the trunk, chest wall, perineal/anal region, and abdomen (including retroperitoneum and biliary tract).

The majority of RMS cases are sporadic, with no identifiable risk factors.[2] Embryonal RMS is associated with high birth weight and infants that are large for gestational age.[13] The Li-Fraumeni syndrome (germline *p53* mutations),[14] pleuropulmonary blastoma (*DICER1* mutations),[15] neurofibromatosis type I,[16] Costello syndrome (germline *HRAS* mutations),[17,18] Beckwith-Wiedemann syndrome,[19] and Noonan syndrome are all associated with RMS.[20]

Prognosis

The prognosis for children with RMS depends on age, primary tumor site, tumor size, resectability, presence or absence of metastases, number of metastatic sites, presence or absence of regional lymph node involvement, histopathologic subtype (alveolar vs embryonal), and, in some cases, delivery of radiation therapy.[5–8,11,21,22]

In children with localized disease who receive combined-modality therapy, there is greater than 70% survival at 3 years.[8] Relapses are uncommon after this point, with a less than 10% late event rate through 10 years. However, children with gross residual disease in unfavorable sites after initial surgery and those who have metastatic disease at diagnosis are more likely to experience relapse.[23]

Patient- and tumor-specific factors with prognostic implications include the following:

- Age: Children aged 1 to 9 years have improved prognosis, whereas those less than 1 year and greater than 9 years have worse prognosis (5-year survival is 76% for patients <1 year, 87% for patients 1–9 years, and 76% for patients >10 years).[10] It is unclear if infants have poorer outcomes because of disease-specific factors or owing to adjustments that are made to therapy owing to their small size (eg, less chemotherapy because of intolerant bone marrow, less use of radiation therapy).[8,24] Additionally, adolescent patients seem to present with unfavorable tumor-specific factors, such as alveolar histology, regional lymph node involvement, and metastatic disease.[25] Finally, 5-year survival rates for adults are markedly worse than those for children.[26]