Sarcomas

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KEYWORDS

• Soft-tissue sarcoma • Rhabdomyosarcoma • Nonrhabdomyosarcoma • Bone • Ewing's • Osteosarcoma

KEY POINTS

- Osteosarcoma and Ewing sarcoma are the 2 most common malignant bone tumors of pediatrics, with peak incidence during the adolescent years.
- Rhabdomyosarcoma is the most common soft-tissue sarcoma of childhood, with a bimodal age distribution of 2 to 6 years and 15 to 19 years of age.
- Sarcomas are best treated with multimodality treatment that often includes chemotherapy, surgery, and/or radiation therapy.
- Children with localized sarcoma fare well with multimodality treatment, whereas those with metastatic or recurrent disease have poor outcomes.
- Improved molecular understanding of these diseases has led to the possibility of using new molecular targeted agents in the setting of clinical trials.

INTRODUCTION

Osteosarcoma (OS) and Ewing sarcoma (EWS) are the 2 most common malignant bone tumors in children and adolescents, and make up approximately 6% of all childhood malignancies. Rhabdomyosarcoma (RMS) and nonrhabdomyosarcoma soft-tissue sarcomas (NRSTS), the 2 major classes of soft-tissue sarcoma, account for another 7% of all childhood malignancies. Optimal comprehensive care of patients with either bone or soft-tissue sarcoma requires a multidisciplinary team, which includes an oncologist, a surgeon, a radiation oncologist, a pathologist, and a radiologist. Treatment is multimodal, with the overall goal being to achieve local control with surgery and/or

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radiation and to use chemotherapy to control metastatic disease, even though it may not be clinically detectable. Over the last 4 decades improvements in chemotherapy regimens, surgery, radiation, and the use of collaborative group clinical trials have led to significant improvements in outcome for patients with sarcoma; this is particularly true for patients with localized tumors, most of whom now survive their disease. However, patients with metastatic and recurrent disease continue to have poor prognoses despite various attempts at intensifying chemotherapy. Furthermore, sarcoma patients who survive have one of the highest risks of developing long-term treatment effects, many of which can be life-threatening. Better treatments are therefore still needed to improve the outcomes of patients with sarcomas, especially for those with metastatic and recurrent disease, and to limit long-term complications for those who survive. Uncovering the key vulnerabilities, developing ways to target these key molecular pathways, and improving the risk stratification to better predict outcome are developing areas that it is hoped will improve the outcome for children with these diseases.

PATHOLOGY AND BIOLOGY

Osteosarcoma

OS is a malignancy that derives its origin from mesenchymal cells. The pathologic hallmark is the production of malignant osteoid by pleomorphic malignant cells within a connective tissue matrix. OS can be divided into several subsets defined by location (appendicular vs axial, central vs surface), histologic grade (low, intermediate, or high), and the predominant matrix type.[1] Most OS tumors are conventional OS, a high-grade OS made up of 3 major subtypes based on the predominant mix of cartilage matrix and fibrous tissue: osteoblastic, chrondroblastic, and fibroblastic. The remainder includes low-grade OS, parosteal OS, periosteal OS, and telangiectatic OS, which are less common (**Box 1**). Although the presence of malignant osteoid is necessary to confirm a diagnosis of OS (**Fig. 1**A), radiographic appearance of the tumor is helpful in arriving at the diagnosis. Immunohistochemistry and cytogenetics are not diagnostic of OS. There are no consistent chromosomal or gene abnormalities described in OS; however, several genes have been implicated in OS pathogenesis following the observations of increased frequency of OS seen in patients with cancer predisposition syndromes, including Rothmund-Thomson syndrome, Bloom syndrome, Werner syndrome, Li-Fraumeni syndrome, and hereditary retinoblastoma (**Box 2**).[2,3]

Box 1
Pathologic subtypes of osteosarcoma

- Conventional
  - Osteoblastic
  - Chondroblastic
  - Fibroblastic
- Secondary
- Telangiectatic
- Small cell
- Periosteal
- High-grade surface
- Low-grade intramedullary
- Parosteal