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Mini Review

Bone Sarcoma: Decoding the Biology, Diagnostic Challenges, and Evolving Therapeutic Landscape

Golenbock F, Wolenski S, Cardozo S, Wendell D, Ochieng D, Nakamura E

Institute of Oncology, Italy

***Corresponding Author:** Wendell D, Institute of Oncology, Italy
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Abstract

Bone sarcomas are uncommon malignant tumors arising from bone and represent a biologically diverse group of cancers with substantial differences in age distribution, molecular characteristics, clinical behavior, and response to therapy. The major primary bone sarcomas include osteosarcoma, Ewing sarcoma, and chondrosarcoma, alongside several rarer histological subtypes. Although advances in imaging, molecular diagnostics, multidisciplinary care, surgical techniques, chemotherapy, and radiotherapy have improved outcomes for many patients, early recognition remains challenging because initial manifestations such as localized pain, swelling, or reduced mobility may resemble benign musculoskeletal disorders. Contemporary diagnosis increasingly integrates radiological assessment with histopathology and molecular profiling to establish an accurate tumor classification and guide treatment selection. Surgical resection with adequate oncological margins remains a cornerstone of management, while systemic therapy and radiotherapy are selected according to histological subtype, tumor location, stage, and biological characteristics. Emerging research has focused on targeted therapies, immune-based approaches, novel drug combinations, precision oncology, and biomarkers capable of predicting treatment response or resistance.

Introduction

Bone sarcoma comprises a heterogeneous group of malignant tumors originating primarily within bone. Although these tumors account for a relatively small proportion of overall cancer diagnoses, they can produce substantial morbidity because of their effects on the skeletal system, surrounding soft tissues, physical function, and quality of life.

Bone sarcomas may develop in individuals across the age spectrum. Osteosarcoma and Ewing sarcoma are more frequently encountered in children, adolescents, and young adults, whereas several forms of chondrosarcoma predominantly occur in adults. Tumor location, histological subtype, grade, biological behavior, and metastatic status strongly influence prognosis and therapeutic decision-making.

Major Types of Bone Sarcoma

Osteosarcoma

Osteosarcoma is characterized by malignant cells producing osteoid or immature bone. It commonly develops in the metaphyseal regions of long bones, particularly around the knee and proximal humerus. Conventional high-grade osteosarcoma is among the most frequently diagnosed primary malignant bone tumors in younger individuals.

Ewing Sarcoma

Ewing sarcoma is a highly malignant small round cell tumor that frequently affects children, adolescents, and young adults. It may arise in the pelvis, long bones, ribs, and other skeletal locations

Unlike osteosarcoma, Ewing sarcoma is strongly associated with characteristic molecular alterations involving the EWSR1 gene, most commonly through fusion with an ETS-family transcription factor. Molecular confirmation can therefore play an

important role in distinguishing Ewing sarcoma from morphologically similar tumors.

Chondrosarcoma

Chondrosarcoma is characterized by malignant cartilage production and is more frequently diagnosed in adults. It may arise in the pelvis, proximal femur, shoulder region, ribs, and other locationsUnlike conventional osteosarcoma and Ewing sarcoma, many conventional chondrosarcomas demonstrate limited sensitivity to conventional cytotoxic chemotherapy and radiotherapy. Consequently, complete surgical excision is particularly important when technically feasible.

Clinical Presentation

The clinical manifestations of bone sarcoma depend on tumor location, size, growth rate, and involvement of adjacent structures.

Common symptoms include:

- Persistent or progressive localized bone pain
- Swelling or a palpable mass
- Reduced joint movement
- Functional limitation
- Unexplained limp
- Pathological fracture in advanced lesions
- Occasionally systemic manifestations such as fever or fatigue

Pain that persists despite conventional treatment, progressively worsens, occurs at rest or at night, or is accompanied by swelling should prompt further clinical evaluation.

Molecular Biology of Bone Sarcoma

The molecular landscape of bone sarcomas varies considerably among histological subtypes.

Osteosarcoma is frequently associated with complex genomic alterations, including abnormalities affecting tumor suppressor pathways. In contrast, Ewing sarcoma is characterized by relatively specific chromosomal rearrangements that generate oncogenic transcription-factor fusions.

Chondrosarcoma can exhibit alterations involving pathways associated with cellular metabolism, epigenetic regulation, and growth signaling. Some tumors contain mutations affecting IDH1 or IDH2, particularly in specific chondrosarcoma contexts

Conclusion

Bone sarcoma represents a diverse group of rare malignancies requiring specialized diagnostic and therapeutic expertise. Persistent bone pain, swelling, or unexplained functional impairment should not be dismissed when symptoms are progressive or atypical. Modern diagnosis increasingly combines imaging, biopsy, immunohistochemistry, and molecular testing to establish precise tumor classification.

Surgery remains fundamental to local disease control, while chemotherapy and radiotherapy have important roles depending on histological subtype and disease characteristics. Despite improvements in multidisciplinary care, metastatic and recurrent disease continues to present major challenges. Future progress will likely depend on molecularly informed treatment, biomarker discovery, innovative immunotherapeutic approaches, and collaborative clinical research.

Ultimately, the evolution of bone sarcoma care is moving from a predominantly morphology-based approach toward integrated precision oncology, in which tumor biology, clinical characteristics, imaging, and patient-centered outcomes collectively guide treatment decisions

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