Osteosarcoma: Looking to a Stronger Future

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Background & Epidemiology

Osteosarcoma, although rare overall, is the most common primary bone cancer contributing heavily to paediatric cancer mortality [3].

Arises from primitive bone-forming mesenchymal cells that produce osteoid [3].

Commonly originates in the metaphysis of long bones, such the knee joint, during rapid growth [3].

RB1 and TP53 dysregulation leads to uncontrolled cellular proliferation and compromised DNA repair mechanisms [4].

Highly aggressive, typically metastasizing early in disease progression via hematogenous spread, most frequently to the lungs [1].

Incidence of about 4 to 5 cases per million per year in Canada [2]. Majority of cases in adolescence (ages 10–19) and older adults (over 60) [3].

A slight male predominance is commonly observed [2][3].

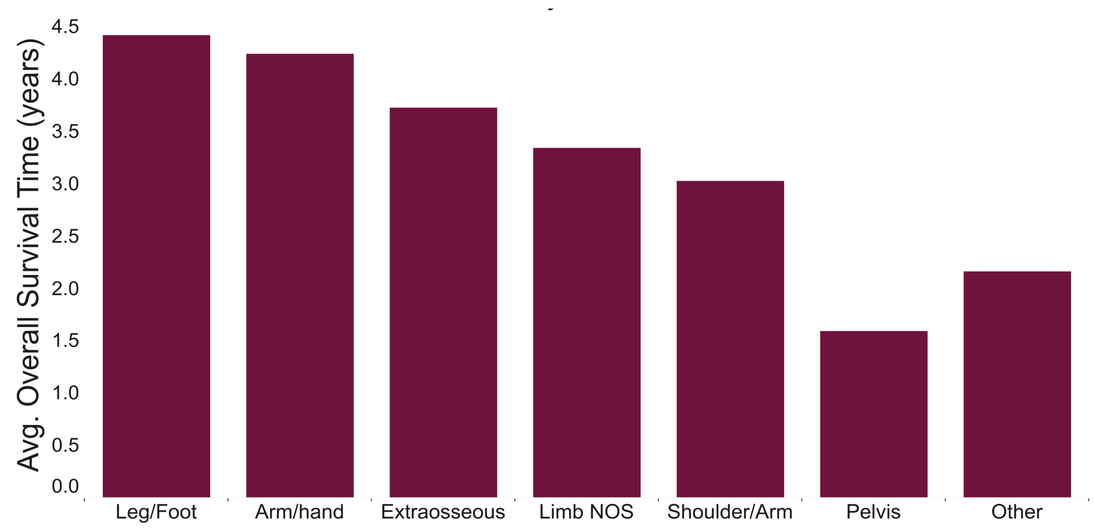

Figure 1: Site of primary tumour and survival time in TARGET dataset. More info at QR code.

Methods

This literature review examined current and developing practices in osteosarcoma treatment. A PubMed database search using key terms such as 'osteosarcoma,' 'targeted therapy,' 'nanoparticle drug delivery,' 'checkpoint inhibitors,' and other related terms was conducted with articles from 2008 to 2025 included. An infographic was then created with the findings and is shown here.

Clinical Presentation

Symptoms: Bone Pain & Joint Discomfort, Swelling & Palpable Mass, Warmth & Erythema, and Pathologic Fractures with Reduced Mobility [5][6].

Symptom Progression: Progressive, localized bone pain may be accompanied by systemic symptoms, including occasional low-grade fever or fatigue, particularly as condition advances [5][6].

- Initial imaging through X-rays, which may show findings such as a "sunburst" pattern or Codman's triangle. MRI used for evaluating soft tissue and marrow involvement, while CT assess bone destruction and detects lung metastases [6].
- Definitive diagnosis relies on biopsy to confirm malignant osteoid production by tumour cells and classify histological subtypes [6].

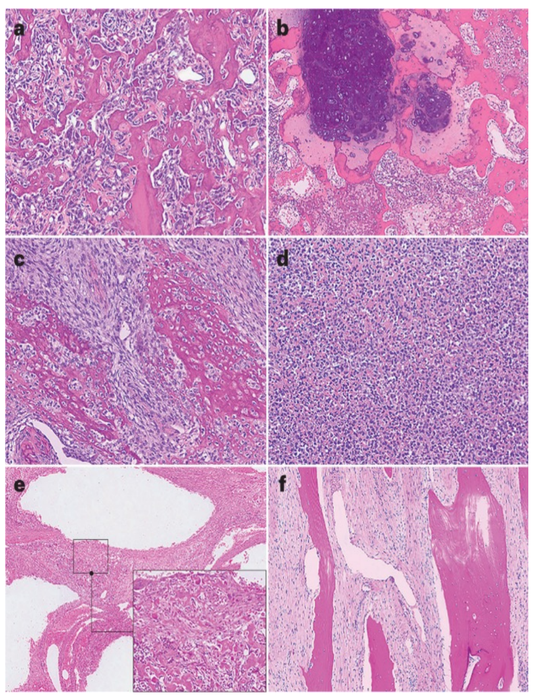

Figure 2: Osteosarcoma subtype histology (a) Osteoblastic, (b) Chondroblastic, (c) Fibroblastic, (d) Small-cell, (e) Telangiectatic, (f) Low-grade central [1].

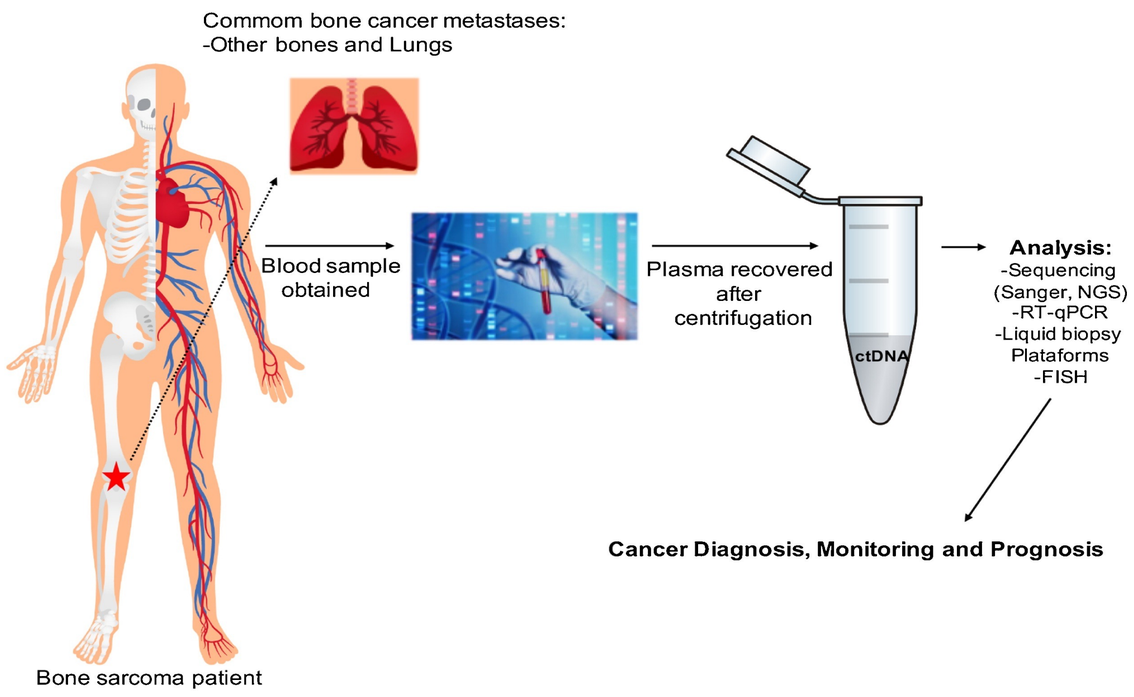

Figure 3: Peripheral blood samples are centrifuged to obtain plasma, which is then examined for ctDNA or other components. Liquid biopsy, utilizing techniques such as ddPCR, RT-qPCR, NGS, and Sanger sequencing, serves as a valuable tool for diagnosis and monitoring [7].

Standard of Care & Prognosis

Neoadjuvant & Adjuvant Chemotherapy: Commonly includes methotrexate, doxorubicin, and cisplatin to shrink the tumour before or eradicate microscopic disease after surgery [8].

Surgical Resection: To complete tumour removal with functional limb preservation. Limb-salvage procedures are often feasible unless neurovascular structures are compromised [9].

Radiation Therapy & Investigational Treatments: Used for inoperable lesions or palliation; novel therapies are under investigation in this area [1].

Prognosis: Localized disease, 60–80% five-year survival with surgery plus chemotherapy. Metastatic disease, five-year survival decreases to roughly 20–30% [1].

Treatments in Development

Immunotherapeutic Approaches:

Mifamurtide is an immune stimulant shown to enhance overall survival when combined with chemotherapy [10].

Preclinical cellular therapy exploring CAR T-cells and adoptive T-cell therapy have shown tumour-specific immune responses [11].

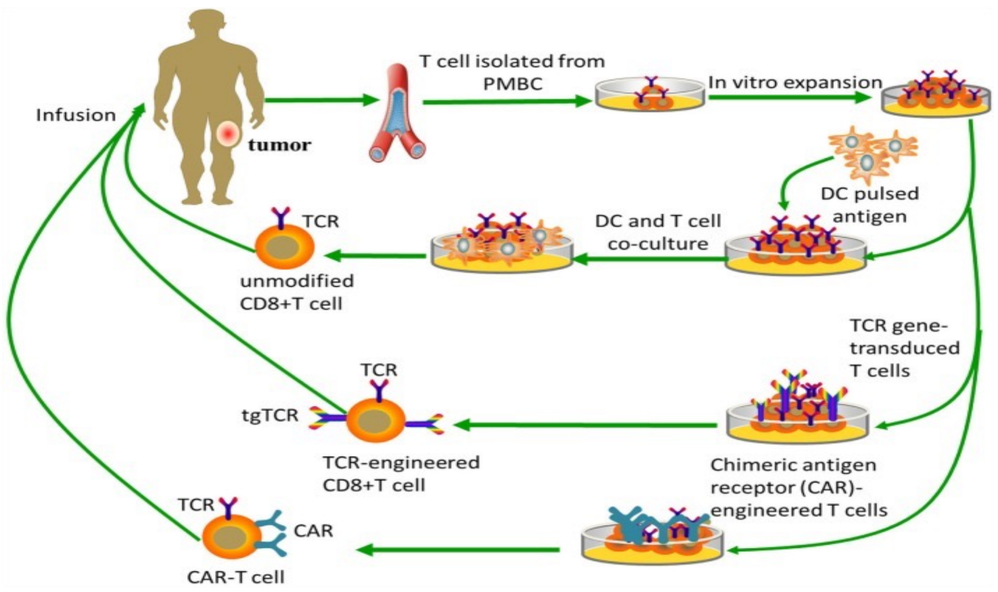

*Figure 4: T cells are isolated from the patient's peripheral blood mononuclear cells and expanded in vitro. The expanded cells undergo genetic modification, **produce T-cell receptors** or chimeric antigen **receptor (CAR)-T cells**. All cell types are infused back into the patient to destroy tumour cells [12].*

Biomarkers:

ctDNA can serve as a non-invasive real-time biomarker allowing early detection of metastatic or recurrent disease [7].

Collaborative Clinical Trials & Real-World Evidence:

Large-scale collaborative trials (EURAMOS-1) work to refine chemotherapy regimens by comparing intensified protocols with poor histologic response [12].

The Children's Oncology Group clinical trials have show promising results exploring the efficacy of denosumab, to improve survival with recurrent or refractory osteosarcoma [13].

Advances in Surgical & Reconstruction Techniques:

Patient-specific 3D-printed surgical implants allowing for more precise resections and customized reconstructions [14].

Advances in limb-salvage procedures have led to use modular endoprostheses with better durability and prostheses for paediatric patients which accommodates growth [15].

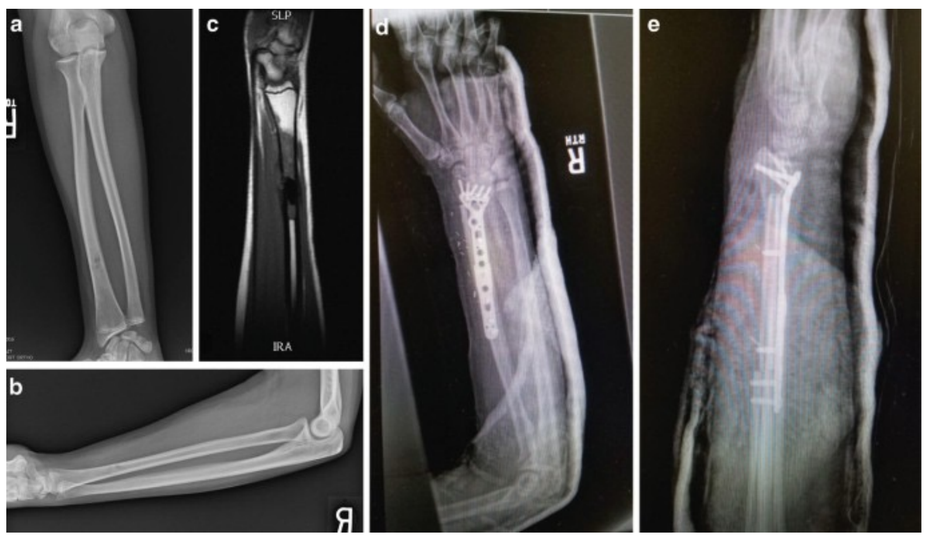

Figure 5: (a, b) X-ray shows an osteosarcoma-related lesion located at the distal radius. (c) The extent of tumour is depicted by an MRI scan. (d, e) Postoperative radiographs show successful reconstruction of the region using a vascularized fibular graft [15].

Conclusion

This literature review and infographic highlight the gap in current osteosarcoma treatments especially given its high mortality. While new treatments are being researched, work and funding must be put to bring effective treatment to all patients.

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