ABSTRACT Clinically, Ewing sarcoma in the bone can look like osteomyelitis (both can cause fever, increased serum inflammatory markers, and bone pain) and on imaging tests (both may present with aggressive periosteal reaction, cortical destruction, and articular involvement). Indeed, it has been reported that up to 50% of subacute osteomyelitis cases in children are misdiagnosed as malignancies, according to reports. However, because therapy and result are fundamentally different, differentiate between these two entities promptly and accurately. The narrowing of the differential diagnosis is complicated by two additional factors. For starters, age does not assist restrict the differential diagnosis because primary bone tumours and osteomyelitis are more common in children and young people. Second, in rare circumstances, infection and tumour may coexist. As a result, a pain and swelling presentation’s underlying diagnosis may be confusing. Conventional radiology (CR), which permits examination of the biological behaviour of isolated bone lesions, is the foundation of the initial approach to disorders of the bones and joints. It usually shows the lesion’s location, internal matrix, borders, and accompanying periosteal reaction in great detail. Magnetic resonance imaging (MRI), which has a significant negative predictive value for malignant bone tumours, is now used as the primary diagnostic work-up for bone pain, particularly in children. If the MRI results are inconclusive, projection radiography or, in the case of overlapping regions, computed tomography (CT) must be used. The difficulty in identifying Ewing sarcoma from bone and soft-tissue infection was highlighted in this study. A thorough study is recommended given the similarity in age, anatomical location, and clinical symptoms of infections and malignancies. Because no single clinical, biochemical, or radiological sign or investigation can be relied on to diagnose Ewing sarcoma, practitioners should send such cases to an Ewing sarcoma multidisciplinary team even there is just a little suspicion of malignancies.

KEYWORDS Magnetic Resonance Imaging, Ewing Sarcoma, Osteomyelitis, Radiograph Study
differential diagnosis for osseous lesions in individuals with pain and/or swelling includes benign and malignant tumours, pseudo-tumours (eosinophilic granuloma), and osteomyelitis. Acute, subacute, and chronic osteomyelitis relate to infections lasting weeks, one to three months, or more than three months, respectively. In addition, purulent collections in the bone might develop into abscesses over time. In individuals with a soft-tissue mass, differential diagnoses include benign and malignant tumours, fluid collections (hematoma, abscess), and granulomatous infections [2].

The narrowing of the differential diagnosis is complicated by two additional factors. For starters, age does not effectively restrict the differential diagnosis because primary bone tumours and osteomyelitis are more common in children and adolescents. Second, in rare circumstances, infection and tumour may coexist. As a result, a pain and swelling presentation’s underlying diagnosis may be confusing. According to one study, 50 percent of all incidences of pediatric subacute osteomyelitis are misdiagnosed as tumours at first. Blood tests for the acute phase response, as well as imaging tests like radiography and magnetic resonance imaging (MRI), and, lastly, a biopsy with culture and histological examination are all common [3].

**Imaging of ewing sarcoma**

Conventional radiology (CR), which facilitates examination of the biological behaviour of isolated bone lesions, is the foundation of the initial approach to disorders of the bones and joints. It generally shows the lesion’s location, internal matrix, borders, and accompanying periosteal reaction in great detail. When these lesion characteristics are paired with the patient’s age, differential diagnoses of bone lesions are usually made [4]. Identifying and describing periosteal reactions is an important aspect of determining the behaviour and aggressiveness of such lesions. The classification of periosteal reactions is frequently divided into classical subtypes, and each of these categories might lead to the diagnosis of a disease or a specific type of malignancy. For example, the solid subtype of periosteal reaction strongly implies nonaggressive, slow-growing lesions, whereas the laminated (“onion skin”) subtype strongly suggests processes with intermediate aggressiveness. On the other hand, interrupted, spiculated, or complex periosteal reactions can suggest aggressive or fast-growing bone lesions, which have a bad prognosis [5]. Magnetic resonance imaging (MRI), which has a strong negative predictive value for malignant bone tumours, is now used as the primary diagnostic work-up for bone pain, particularly in children. However, if the MRI results are inconclusive, projection radiography or, in the case of overlapping regions, computed tomography (CT) must be used. On projection radiography/CT, peritumoral oedema and gadolinium enhancement are seen in the tumour. There is frequently a soft-tissue mass present. In contrast to osteomyelitis, MRI does not reveal specific signs that can include or exclude Ewing sarcoma [6].

The MRI provides more information about differential diagnoses. Choosing the correct sequences is critical: while the classic T1 and T2 contrast are required, proton-weighted and gradient-echo sequences are ineffective for tissue characterization. Ewing sarcoma appears as a solid tumour mass in bone on MRI, with a low signal intensity in T1 and a high signal intensity in T2. There is frequently a sharp transition zone in the bone portion of the tumour. Peritumoral oedema and gadolinium enhancement are seen in the tumour. There is frequently a soft-tissue mass present. In contrast to osteomyelitis, MRI does not reveal specific signs that can include or exclude Ewing sarcoma [6].

MRI is highly sensitive for detecting bone abnormalities because it can characterize bone marrow involvement, soft tissue invasion, and fluid content of lesions [4]. In addition, MRI has...
utility in detecting periosteal reactions. However, there was no significant difference in the utility of CR and MRI in detecting periosteal reactions. Our findings indicate that the two methods for detecting periosteal reactions have a high interobserver agreement. The interobserver agreement between CR and MRI for identifying aggressive periosteal reactions by subtype was variable, with a better agreement for the Codman’s triangle subtype and worse agreement for the laminated and spiculated subtypes. MRI had a high specificity and a low sensitivity for diagnosing periosteal reaction compared to CR [5]. The native T1 sequence—"trust in T1"—is best suited for determining resection height. Different sequences, such as T2 TSE and T1 TSE with contrast media and fat saturation, must be added to the protocol to address extraosseous tumour infiltration of adjacent vascular/nervous bundles or joint compartments. These findings will influence the extent and technique of local therapy [6].

The presence of a soft-tissue mass is the most significant MRI marker for separating Ewing sarcoma from osteomyelitis, according to Kasalak, Mer, et al., with diagnostic accuracies of around 80%. This feature can be used to tell the difference between Ewing sarcoma and other cancers and osteomyelitis and other benign diseases. The transition zone of the bone lesion was only good predictive, with diagnostic accuracies of around 60%. The penumbra sign, intramedullary and extramedullary fat globules, and diagnostic accuracy were all 50% [5]. In a small dataset, radiologists were 100 percent sensitive but only 55 percent specific and 73 percent accurate in identifying bone cancer using plain radiographs and MRI. Considering the limits of advanced imaging and the rarity of bone malignancies in clinical practice [4].

Ewing sarcoma has a heterogeneous appearance on MRI. It can be difficult to clinically diagnose in its earliest stages prior to the significant cortical destruction following spread beyond the bone marrow [4].

**Biopsy in ewing sarcoma**

The biopsy method of choice in Ewing sarcoma remains debatable. An open or core needle biopsy (CNB) is advised if Ewing sarcoma is suspected. Furthermore, if possible, suspected solitary bone metastases and lymph node metastases should be biopsied at the time of presentation. According to some published studies, the accuracy of open biopsies is close to 100%. CNB-reported biopsy success rates range from 50% to 98 percent in sarcoma patients. The success rate of needle biopsy may be lower than that of open biopsy, particularly in Ewing sarcoma patients. However, inexperienced centres, sampling errors may be as low as in open biopsies. Importantly, Ewing sarcoma can clinically and radiologically mimic osteomyelitis (fever, increased infection values, isolated bone pain). Therefore, the possibility of a biopsy material sampling error with merely reactively altered tissue must always be considered, and if in doubt, new sampling should be considered. Regardless of the biopsy method used, it is critical to avoid hematomas and contamination of neurovascular structures or joints because all contaminated tissue must be resected if Ewing sarcoma is diagnosed [6].

**Therapy of ewing sarcoma**

Patients with Ewing sarcoma require highly personalized local therapy. Therefore, patients and families should be allowed to investigate local treatment alternatives as soon as possible after being diagnosed, and local therapy decisions should be made in consultation with them. Expert interdisciplinary tumour boards are required to establish the optimal course of action in each case. The optimum technique for local control in Ewing sarcoma patients is governed by some parameters, including the patient’s age, tumour site, size, and local extension [6].

Unless emergency surgery is required at the time of diagnosis, such as spinal cord compression, definitive surgery normally follows neoadjuvant chemotherapy. Patients should be referred to a reliable hospital for their procedure, which is critical. The duration of neoadjuvant chemotherapy is the primary determinant of the timing of local surgical therapy. It is also influenced by the availability of the required technical devices (e.g., custom-made implants, scheduling an irradiation appointment) as well as the most experienced interdisciplinary surgical and/or radiation therapist team. It may look desirable to maintain high-dose intensity by scheduling 1-2 extra cycles of chemotherapy before adequate local treatment to obtain the optimal logistical and technical execution [6].

Reconstructive surgical procedures should be performed wherever possible, although oncological control should take precedence over limb preservation. Bone reconstruction surgery is required in most patients undergoing local surgical therapy. Biological reconstruction with bone grafts is one option, which is particularly beneficial in intercalary bone lesions where the original joint must be preserved. Allografts, vascularized fibula grafts, and irradiated autografts are all common procedures. These excel at various advantages and disadvantages in terms of complexity or reconstructive survival [6].

Primary amputation is rarely required in Ewing sarcoma due to tumour reduction after neoadjuvant chemotherapy and the availability of definitive RT as a viable option to surgery. However, patients with severe postoperative complications and tumours in which limb salvage would jeopardize the required surgical margin, such as extended infiltration of the neuro/vascular bundle, cases of tumour progression during neoadjuvant treatment, or very young patients under the age of 3–6 years with lower extremity tumours, should have ablative surgery performed. Local recurrence or periprosthetic infection are the most common reasons for subsequent amputation. In comparing the quality of life of patients who underwent amputation or limb-salvage surgery, no long-term outcomes were discovered. Rotationplasty is a type of lower-leg amputation that allows patients to preserve a functional hip and a modified knee joint. This procedure is most suited for children under six [6].

**Sarcoma or infection process**

Sarcomas are rare malignant tumours of the mesenchymal type that make up less than 1% of all malignant neoplasms. The most common signs of bone and soft tissue sarcomas are pain and swelling. These are, however, the hallmarks of inflammatory, benign neoplastic, and infectious illnesses, making clinical diagnosis challenging. As a result, numerous clinical specializations are required for prompt and correct diagnosis [2].

A study of bone and soft tissue infections that mirror sarcoma infections was published by J. R. LEX et al. When patients were referred for a probable bone sarcoma, the rate of osteomyelitis was rather high, at 2.1 percent, compared to 0.7 percent for soft-tissue infections that were initially assumed to be soft-tissue sarcomas. In addition, patients with osteomyelitis are 18 years old on average, compared to 46 years for patients with soft-tissue infections [2].
The pain was the most common symptom in patients with osteomyelitis, whereas swelling was the most common symptom in soft tissue infections. On the other hand, soft-tissue infections were frequently associated with discomfort (70 percent), but soft-tissue sarcomas are typically painless masses. The systemic disturbance occurred in just 9.0 percent and 7.4 percent of individuals with bone and soft-tissue infections, respectively. These signs and symptoms are very common in sarcoma. As a result, based on clinical presentation and anatomical location, it is impossible to distinguish sarcoma from infection [2].

Inflammatory markers were more likely to be increased in the soft-tissue group. Radiological tests could not distinguish between tumour and infection in 59.7% of osteomyelitis patients and 81.5% of soft-tissue infection cases. No organism was detected in 64.9 percent of patients who received a percutaneous biopsy culture [2].

**Osteomyelitis**

A bone infection causes osteomyelitis, with bacteria being the most prevalent causative agent (Staphylococcus aureus). In children, hematogenous osteomyelitis is the most common cause, with trauma, surgery, or infected adjacent soft tissue being less common [2]. Acute osteomyelitis affects roughly eight children per 100,000 each year. In nearly half of the instances, children under five are afflicted, with a male/female ratio of 2:1. Acute osteomyelitis is nearly twice as prevalent as septic arthritis, and its incidence is on the rise (due in part to the increasing prevalence of antibiotic resistance among Staphylococci) [7].

Although magnetic resonance imaging (MRI) is the most sensitive imaging modality for identifying osteomyelitis, imaging characteristics can be deceiving, frequently mimicking severe infiltrative malignancies. In addition, the overlapping clinical characteristics of osteomyelitis and skeletal tumours, such as localized pain, fever, and high inflammatory markers, complicate the diagnosis. In the past, osteomyelitis has been reported as a skeletal neoplasm that mimics Ewing sarcoma, chordrosarcoma, and other skeletal neoplasms. Radiographic misinterpretation of osteomyelitis is widespread in children, with 50% of all instances of subacute osteomyelitis being misdiagnosed as malignancies. Extrasosseous marrow fat in the location of marrow signal abnormalities is a specific observation in acute and aggressive osteomyelitis that may help in imaging-based separation of these entities. Acute supplicative reaction to medullary bacterial proliferation can cause an increase in intramedullary pressure, rupturing the cortex and causing medullary fat to be expelled into the surrounding soft tissues [7].

CRMO is a rare idiopathic inflammatory condition characterized by recurring episodes of non-infectious osteomyelitis. The slow onset of nonspecific pain, swelling, and discomfort over an afflicted joint characterize CRMO. CRMO is characterized by musculoskeletal pain that alternates between exacerbation and improvement. The average age at which symptoms first appear is between 8 and 14 [8]. Radiographs are the most common type of first imaging, and they can be normal or show abnormalities near the metaphysis and growth plates. Lesions can be entirely osteolytic, mixed lytic and sclerotic, or solely sclerotic, depending on the chronicity. The lesions have a symmetrical appearance, involving the metaphyses and epiphyses of long bones. Clinical and temporal symmetry are typically absent in lesions. The femur and tibia are the long bones that are most typically impacted. The spine, pelvis, mandible, hands, and feet are potential involvement locations. CRMO is distinguished from other procedures because it involves the clavicle [8]. The presence of osseous involvement on imaging that is not clinically evident distinguishes CRMO. As a result, whole-body imaging, such as Tc-99 bone scintigraphy or MRI, is routinely done to aid in finding asymptomatic lesions and establishing a baseline of disease burden. Increased uptake is visible in radionuclide investigations, with early uptake indicating inflammation and late uptake indicating bone sclerosis. Bone scans are not conducted as often as they used to be because of absorption in the growth plates and patient radiation exposure. Because it does not expose the patient to radiation and provides more accurate anatomy and soft tissue assessment, whole-body MRI has become the recommended investigation. An MRI can reveal marrow oedema, periostitis, soft tissue inflammation, transphyseal illness, and joint involvement. Acute signs on MRI are hyperintense and increased with contrast on fluid-sensitive sequences.

On the other hand, chronic lesions are hypointense on both T1 and T2 due to lesion sclerosis. The limited examination of the ribs and skull due to the considerable slice thickness is one of the potential limitations of MRI. Increased costs and the requirement for general anaesthesia, usually required in children [8], are further drawbacks. The clinical course and radiological and histopathological picture of ES and osteomyelitis are so similar that objectively distinguishing these two diseases is difficult. A biopsy may provide a more accurate diagnosis, but it has limitations. The diagnostic utility of FTIR (Fourier Transform Infrared) spectroscopy helps distinguish between these two clinically significant diseases. The chemical composition of normal, osteomyelitis, and ES bone tissue was determined using FTIR spectroscopy. The greatest differences in the osteomyelitis group were related to maximum absorbance values in the FTIR region, which corresponded to lipid functional groups. The altered lipid content could be due to increased lipid hydroperoxide (LOOH) concentration. This enzyme is a marker of oxidative stress because it is responsible for the oxidative degradation of lipids to reactive aldehydes like malondialdehyde and 4-hydroxynonenal [8].

**Conclusion**

This study emphasized distinguishing Ewing sarcoma and bone and soft-tissue infection difficulties. A thorough investigation is recommended given the similarities in age, anatomical location, and clinical features of infections and tumours. Because no single clinical, biochemical, or radiological feature or investigation can be relied on for diagnosis, clinicians should refer such cases to an Ewing sarcoma multidisciplinary team if there is a little suspicion of malignancies.

**Declarations**

**Ethics approval and consent to participate**

All consents have been taken.

**Consent for publication**

Informed consent has been taken.

**Competing interests**

The authors declare that they have no competing interests.

**Author’s contribution**

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