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Mimics of Paediatric Musculoskeletal Infections and their Management

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Abstract

Musculoskeletal infections in pediatric and adolescent populations pose challenges due to heightened pathogen virulence and emerging antimicrobial resistance. Prompt diagnosis is hindered by conditions mimicking these infections, necessitating multidisciplinary approaches. Recent advancements in diagnostics facilitate accurate differentiation. Common mimickers include cellulitis, neoplasms, hematological disorders, inflammatory conditions and stress fractures. Overlapping symptoms demand thorough history-taking and clinical assessment. Laboratory investigations, including CRP and procalcitonin, aid diagnosis, alongside imaging modalities like MRI. Management involves collaborative efforts, emphasizing early recognition, antibiotic therapy, and surgical intervention as needed. Adherence to guidelines and vigilant monitoring optimize outcomes and mitigate risks. This article describes the common mimickers of MSK infection in children and the approach to reaching a correct diagnosis by thorough history taking, clinical examination, relevant laboratory investigations, and appropriate radiological investigations.

Keywords: Infection mimickers, Pediatric infections, MSKI, Blood markers, Multidisciplinary approach

Introduction

Musculoskeletal infections (MSKI), including osteomyelitis, septic arthritis, and pyomyositis, pose significant challenges in pediatric and adolescent populations due to the increased virulence of pathogens, immature innate immunity, and the emergence of antimicrobial resistance, particularly methicillin-resistant Staphylococcus aureus (MRSA). These infections often necessitate prompt diagnosis and urgent in place of early frequent early surgical intervention to prevent long-term complications and readmissions. Most often, the diagnosis of pediatric MSKI is straightforward, but many times, the diagnosis and, hence, prompt management is hindered by failure to recognize and rule out pathologies that mimic them closely. It has been reported that 50% of osteomyelitis cases in children are misdiagnosed as tumours [1].

In view of their varied presentation and common mimickers, the approach and management of MSKI demands a multidisciplinary approach. Recent advances in diagnostic modalities and therapeutic approaches offer promising ways for accurately distinguishing MSKI from their mimics, facilitating precise diagnosis and targeted treatment [2].

Common mimickers of MSKI in children

It is not uncommon for the management of pediatric malignancies and juvenile arthritis to be delayed because infection is thought to be the primary diagnosis and vice versa. Similarities in symptoms and signs makes it difficult for orthopedic surgeons to make an earlier diagnosis. A delay in diagnosis heightens parental anxiety, often prompting them to seek opinions from multiple hospitals. In some cases, they

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Table 1: Highlighted all mimickers of osteomyelitis	
I	**Neoplasms**
A	Osteoid osteoma
B	Leukemia/lymphoma
C	Langerhans cell histiocytosis
D	Ewings sarcoma
E	osteosarcoma
II	**Inflammatory and noninflammatory arthritis**
A	Juvenile rheumatoid arthritis
B	Reactive arthritis
C	Juvenile idiopathic arthritis
D	Charcot arthropathy
E	Pigmented villonodular synovitis
III	**Hematological disorders**
A	Sickle cell arthropathy
B	Hemophilic arthropathy
IV	**Miscellaneous conditions**
A	Scurvy
B	Stress fracture
C	Cellulitis
D	Transient synovitis
E	Chronic nonbacterial osteomyelitis

may even become lost to follow-up, which can lead to adverse outcomes for the child.[3]

To add to the complexity further, imaging features for the infections are not necessarily specific for osteomyelitis and also can be shared with multiple other conditions. Table 1 highlights the common mimickers of pediatric MSKIs.

Overlapping Clinical Features

Infections can be in the form of septic arthritis, osteomyelitis, and pyomyositis. Fever, pain, and swelling are the most common overlapping symptoms in all the differentials mentioned in table 1. Because of the overlapping clinical symptoms, it is very important to properly take history and do the clinical examination to find any differentiating feature.

In case of fever due to infections, bacteria can act as pyrogens, stimulating immune cells to release inflammatory cytokines such as interleukins and tumor necrosis factor-alpha, ultimately leading to fever. Similarly, certain tumors can also induce fever either by directly producing these cytokines or by prompting immune cells to do so. There is speculation that fever associated with tumors might exhibit different responsiveness to anti-inflammatory medications compared to that caused by non-neoplastic conditions [3].

Starting with acute osteomyelitis of long bones there is generally sudden onset, high-grade fever with severe pain in the involved part of the extremity. In comparison, the tumors are generally associated with insidious onset low-grade fever with long duration of symptoms and mild to moderate pain in early stages. Fever in low-grade chronic infections like tuberculosis is usually low grade and mainly exhibits a tendency to present in the evening time. A positive family history is also elicited in TB infections.

Another symptom common to most of the pathologies in Table 1 is pain. Pain in acute infections is moderate to severe and aggravated by movement, so the child assumes a posture of pseudo-paralysis. Pain in inflammatory conditions like rheumatoid arthritis is usally more in the morning hours and gets better as the day progresses. Pain in osteoid osteoma generally is present in the nighttime and is relieved rapidly by taking NSAIDs.

The site of pathology also helps to differentiate infection as infections are generally metaphyseal except for tubercular infections which are diaphyseal and closely resemble tumors like Ewings sarcoma. Certain neoplastic mimickers like Ewings sarcoma, Langerhans cell histiocytosis, Leukemia, and lymphoma exhibit a propensity for diaphyseal involvement of long bone with a relatively pain-free motion of adjoining joints.

Local appearance of the pathology also helps in differentiation. Cellulitis very closely resembles septic arthritis but exhibits more swelling, edema, and redness. Swelling in cases of osteomyelitis is usually uniform across the circumference of the extremity while swelling in certain malignancies like osteosarcoma and Ewings sarcoma is eccentric because of the involvement of adjoining soft tissues.

Diagnosing an acutely irritable hip in a child presents a unique challenge. There are various potential causes for this hip discomfort, including septic arthritis, transient synovitis, fractures, slipped capital femoral epiphysis, inflammatory joint conditions, and tumors. A common mimicker in such a condition is hemarthrosis because of sickle cell disease and hemophilic arthropathy. They can be ruled out by a properly elicited history of bleeding tendency, familial disposition, and frequent need for blood transfusions.

Children less than 18 months age, because of the presence of transphyseal vessels, can have epiphyseal and joint involvement in femoral osteomyelitis. After taking a proper history and examination, two most similar etiologies left are septic arthritis and transient synovitis of the hip. Kocher's criteria (Table 2)

Table 2: Kocher criteria to determine risk for paediatric septic joint

Kocher Criteria to Determine Risk for Pediatric Septic Joint	
Non-weight bearing on affected side	*Probability of Septic Arthritis*
ESR > 40 mm/hr	• 4/4 = 99%
Fever	• 3/4 = 93%
WBC > 12,000	• 2/4 = 40%
	• 1/4 = 3%

TABLE 3
Blood markers
Complete blood count
Haemoglobin
Platelets
Total leucocyte count
Differential leukocyte count
Peripheral blood smear
ESR
CRP
LDH
PROCALCITONIN
Neutrophil: lymphocyte ratio
IL- 6
RA factor
ANA
Factor VIII
Synovial fluid/ tissue diagnosis
Synovial fluid - TLC
Tissue culture
Tissue biopsy

help us differentiate between these two. In general, septic arthritis patients have a toxic look compared to transient synovitis.

Involvement of other joints also gives a clue for other diagnoses. Septic arthritis is usually monoarticular, unlike juvenile arthritis and acute rheumatic fever, which are oligo or polyarticular.

Laboratory investigations

Earlier, only ESR (Erythrocyte sedimentation rate) and white blood cell count (WBC) were used as acute phase reactants (APR), but both of these were found to be less specific for infection. Newer modalities like C-reactive protein (CRP), procalcitonin, and IL – 6 have been added (Table-3) to the diagnostic battery of tests [4].

Studies have shown that only 36% of children with osteomyelitis will have an elevated WBC but the combined use of ESR and CRP gives a 98% diagnostic sensitivity. In addition, CRP also acts as a prognostic tool in infection. It rises within 4-6 hours of infection and its serial monitoring helps to see the response of infection to treatment [5].

Apart from infections, the ESR, WBC, and CRP also rise in inflammatory arthritis, certain tumors like Ewings sarcoma, and traumatic events. Newer markers like procalcitonin, IL – 6, Platlet count, and Neutrophil Lymphocyte Ratio (NLR) have been added [4] (Table 3).

Just like CRP, procalcitonin also rises rapidly within the body and also shows treatment response within 72 hours. The only limitation is its cost. Multiple studies have shown its benefit over CRP and WBC count [6].

Although not yet widely adopted in pediatric MSKI, the NLR has gained attention in research for its ability to detect infections sensitively and predict disease severity. For instance, in hospitalized patients with fever of unknown origin, NLR levels were higher in those with bacterial infections compared to viral infections. Additionally, NLR has shown superiority over Crp, WBC count as an early predictor of septicemia [7].

In cases of certain mimickers like leukemia, lymphoma and sickle cell disease, peripheral blood film is also important. Sometimes, hemoglobin percentage helps in reaching a diagnosis as it is chronically low in conditions like TB, sickle cell disease, and in certain malignancies like Ewings sarcoma and osteosarcoma [8].

A common mimicker of septic arthritis, i.e., transient synovitis, can be ruled out by synovial fluid TLC analysis. TLC count of $\geq 50{,}000/mm^3$ in the synovial fluid and a positive Gram stain are considered to be the best predictors of septic arthritis over transient synovitis [9].

Last but not least, tissue diagnosis remains the mainstay of diagnosing any MSK infection and their mimickers in children. Many times septic hip/TB hip needs to be differentiated from inflammatory arthritis or idiopathic chondrolysis of the hip. Taking a tissue sample and getting a culture as well as a biopsy is considered to be the gold standard in such scenarios [8].

Radiological parameters

Imaging is an important step to identify the pathology. Studies say that the ability of the orthopedic oncologist to correctly predict infection based upon clinical examination and radiological features is 60%, and in addition, if we get a musculoskeletal radiologist's opinion it improves the predictive ability to 72% [8].

X-ray in an acute septic joint is usually unremarkable apart from increased joint space due to synovial effusion and distension because of pus. In metaphyseal osteomyelitis, the earliest tissue feature is the loss of normal tissue planes, which requires a high-quality X-ray for its detection. Diaphyseal lesions like Ewings and osteosarcoma very commonly mimic osteomyelitis because of periosteal reaction. The periosteal reaction in Ewings sarcoma is typically fusiform with onion peel appearance, while in osteosarcoma, many a times Codmanns triangle is evident. In chronic osteomyelitis, apart from

Table 4: Demonstrating differentiating MRI features amongst various mimickers of infections	
Osteomyelitis	T1 - hypointense
	T2- hyperintense
	With peripheral enhancement with the central necrotic area showing hypointensity
Osteoid osteoma	Nonspecific marrow edema
	CT- central nidus
Tumour	Soft tissue mass- solid and more discrete
	Sharper and more defined margin
	Moth-eaten, destructive in malignant lesions
Chronic recurrent multifocal osteomyelitis	Periphyseal location with mild marrow edema
Stress injuries	Disruption of cortex – T1
	Periosteal and endosteal marrow edema- hyperintense – T2
	Poorly demarcated abnormal signal confined to bone
Sickle cell crises	Well-defined serpentine rim – hypointense T1
	Double rim sign

periosteal reaction there would be areas of osteolysis mixed with osteosclerosis. In late cases, a sequestrum or involucrum may also be evident. A typical diaphyseal mimicker like osteoid osteoma can be well differentiated from other conditions by a CT scan, which shows a typical nidus formation. X-ray findings in suspected cellulitis are usually normal [8, 10].

The next radiological investigation, which is often important but not essential, is MRI. It helps to differentiate osteomyelitis from the rest of the mimickers. A few points that we have to keep in mind while looking at MRI are the location of the lesion, cortical involvement with thickening, periosteal reaction, the presence of cystic/necrotic aspects, presence of contrast-enhancing soft tissue mass, the presence of a solid bone lesion with defined margins or signs of a sharp transition zone between normal bone and edematous/affected bone and relationship of the lesion to the adjacent physis and joint.

To understand the MR imaging appearances of infection mimics, it is important to know the classic appearances of infection. In MRI marrow changes are demonstrated as areas of low and high signal intensity on T1W- and T2W-weighted images, respectively, and show enhancement after intravenous administration of gadolinium chelates. Areas of necrosis appear hypointense on T2W images and do not show enhancement. The majority of the tumors, on contrast MRI show a uniform uptake of dye; however, it has been observed that in the case of tuberculosis, only the peripheral rim of cells shows an enhancement. A solid bone lesion with defined margins and a sharp transition zone between normal bone and edematous/affected bone could be depicted in all patients with Ewing sarcoma [10].

After a thorough evaluation of all studies, it was found that the presence of a soft-tissue mass is the most valuable MRI sign for discriminating Ewing sarcoma from osteomyelitis with diagnostic accuracies of around 80% [1]. The diagnostic accuracies for various other MRI signs, such as the transition zone of the bone lesion, intramedullary and extramedullary fat globules, and the penumbra sign, were found to be relatively low, making them less reliable for distinguishing between the two conditions.

An interesting observation was made regarding the measurement of soft tissue mass diameter perpendicular to the long axis of the involved bone. Larger diameters were found in Ewing sarcoma compared to osteomyelitis, suggesting that this measurement could be useful in differentiation. Table 4 describes the typical MRI findings in various MSKI mimickers.

Management

Pediatric MSKI management involves a team approach, integrating various medical specialties for optimal care. This collaborative effort includes emergency medicine, pediatric intensive care, infectious disease, pediatric orthopedic surgery, radiology, and others. Early recognition, prompt antibiotic therapy, and close monitoring are key priorities in emergency department management. Admission to the ICU is often necessary for critically ill patients. Communication between teams facilitates seamless transitions and ensures timely interventions. Standard laboratory tests and imaging studies guide diagnosis and treatment. In the ICU, ongoing monitoring and treatment adjustments are crucial for favorable outcomes.

For initial resuscitation, administer up to 20 mL/kg boluses of crystalloids supplemented by colloids over 5 to 10 minutes, aiming for normal clinical parameters. Regarding the initiation of antibiotics, the timing of initiating antibiotic therapy for musculoskeletal infections hinges upon the clinical status of the pediatric patient. In instances where the child is unstable, immediate commencement of empirical intravenous antibiotics is imperative. The selection of antibiotics should be informed by local microbiology protocols and subsequent culture findings, along with sensitivities.

Conversely, if the child's condition is stable and surgical intervention is imminent, the administration of antibiotics can be delayed to facilitate deep tissue sampling. Subsequent management is contingent upon the specific pathology. Septic arthritis mandates prompt surgical drainage, either arthroscopically or by arthrotomy, within a 24-hour window of diagnosis, representing one of the few paediatric orthopaedic emergencies necessitating such expeditious intervention [11].

Conditions such as osteomyelitis, pyomyositis, and discitis typically require an extended course of intravenous antibiotics (often spanning 4-6 weeks). IV antibiotics are necessary initially because they ensure rapid delivery of the medication directly into the bloodstream, allowing for maximum effectiveness in combating the infection. Transitioning to oral agents to be considered upon clinical improvement, settled pyrexia and normalization of inflammatory markers [12]. This protocol is not only convenient for the patient but also reduces the duration of hospital stay. Surgical intervention may also be warranted for debridement or drainage in select cases.

Adherence to local guidelines and collaboration with microbiology specialists is paramount in ensuring judicious antibiotic selection. The distribution of pathogens affecting

various age groups varies, and so does the choice of empirical antibiotic. As neonates, having immature immune system, they are prone to acute hematogenous infections due to group B streptococci, E. coli, staphylococci, etc. hence the empirical treatment must comprise oxacillin with aminoglycoside [13]. In children older than three months, to cover MSSA, S. pyogenes, and K. kingae, antistaphylococcal penicillin such as nafcillin or oxacillin or a first-generation cephalosporin such as cefazolin should be used. Furthermore, vigilant monitoring of the patient's clinical response and periodic reassessment of the necessity for ongoing antibiotic therapy are crucial for optimizing outcomes and mitigating the risks of antibiotic resistance and adverse effects [13, 14].

Surgical intervention plays a pivotal role in the treatment of musculoskeletal infections.Surgical intervention is necessary for joint decompression to excise devitalized tissue, fluid collections, and abscesses. Surgery also helps in tissue diagnosis, identifying the pathogen, and guiding the specific antibiotic to be used based on the sensitivity. Surgical decompression not only reduces the pathogen burden but also relieves the pain, and allows better penetration of antibiotic at the site of infection [12, 15]. Moreover, in cases with joint involvement, surgical drainage of the joint reduces the risk of complications such as avascular necrosis of the bone and permanent cartilage damage due to increased intra-articular pressure and results in a better outcome. While arthrotomy has conventionally been favored, arthroscopic techniques yield comparable outcomes. Alternatively, serial ultrasonography-guided joint aspirations offer a safe and effective non-surgical option, as evidenced by studies demonstrating avoidance of surgery in select cases. This strategy is particularly advantageous for patients deemed unsuitable for surgical intervention [2, 16].

Conclusion

Recognizing conditions, both benign and malignant, that mimic infections is vital for accurately assessing differential diagnoses and initiating appropriate investigations. Although laboratory tests and imaging results provide valuable insights, they often overlap. Biopsy procedures, such as bone or soft tissue sampling, or synovial fluid/tissue aspiration, may be essential, especially in ambiguous cases, to validate the diagnosis. It's imperative to consider the potential of a malignant tumor when infection is suspected, and biopsy protocols must be followed rigorously. Successful diagnosis and management of these infections hinge on robust clinical-radiologic-pathologic correlations and collaborative efforts within a multidisciplinary medical team.

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