Fever and Knee Effusion in the Pediatric Patient

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Abstract: The pediatric patient with fever and knee effusion is always a cause for clinical concern. A thorough history and physical examination is required to guide appropriate diagnostic evaluation and management. Although pediatric knee effusions are common in the setting of trauma, the presence of fever should prompt consideration of infectious, rheumatologic, vasculitic, and malignant etiologies. This review covers the key components of the history, physical examination, diagnostic strategies, common etiologies, and initial management of the pediatric patient with fever and knee effusion.

Key Words: febrile knee effusion, fever, knee effusion, septic joint

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TARGET AUDIENCE

This CME review article is designed for physicians and advanced practitioners who care for pediatric patients in the emergency department or outpatient clinic setting.

LEARNING OBJECTIVES

After completion of this article, the reader should be better able to:

1. Delineate an approach to the assessment of the pediatric patient with fever and knee effusion.
2. Differentiate causes of febrile knee effusion using key features of the history and physical examination.
3. Describe the diagnostic evaluation, treatment, and initial management of the pediatric patient with febrile knee effusion.

ILLUSTRATIVE CASES

Case 1

A 5-year-old girl presents to the emergency department (ED) with 2 days of knee swelling and 1 day of refusal to bear weight. On arrival to the ED, she is tired appearing, febrile to 39°C, with a heart rate of 150, but otherwise normal vital signs. On examination, she has an erythematous, warm, swollen right knee, which she is holding in flexion. There is a visible loss of knee contours and a palpable knee effusion, with significant tenderness and limited range of motion. Initial x-rays of the knee show a large joint effusion without evidence of fracture. Laboratory results demonstrate an elevated c-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), and leukocytosis to 18, with 90% neutrophils. A joint aspiration is performed, and orthopedic surgery is consulted. Preliminary results of synovial fluid analysis include white blood cell (WBC) count of 60,000 with 80% neutrophils and a gram stain showing gram-positive cocci in clusters. She is started on empiric antibiotics for presumed septic arthritis.

Case 2

A 15-year-old boy presents to the ED with 10 days of knee swelling and 1 day of fever. He fell on the soccer field 1 month ago onto his left knee and reports intermittent dull, achy pain in the knee since that time. The pain occasionally wakes him from sleep. He then developed more visible swelling around the knee 10 days ago. He has no other significant medical history, has not traveled, does not own pets, or interact with livestock. He has not had a preceding illness. He does endorse some weight loss during the last month, but the remainder of review of systems is negative. On arrival to the ED, he is febrile to 38°C, with a heart rate of 90 and otherwise normal vital signs. On examination of the knee, there is suprapatellar fullness with moderate knee effusion and a tender, palpable mass in the distal femur; range of motion is normal, and he is able to bear weight with a limp. X-ray of the left knee shows a sclerotic lesion of the distal left femur with periosteal reaction and a joint effusion. Laboratory studies show an elevated lactate dehydrogenase, elevated ESR of 40 mm/hr, normal CRP, and normal WBC count. Pediatric oncology is consulted, and the patient is admitted for further evaluation and treatment of presumed Ewing sarcoma.

OVERVIEW

Knee complaints are a common reason for presentation to the pediatric ED. Although most pediatric patients presenting with knee effusion will have a traumatic etiology, the presence of fever in a patient with knee effusion should raise suspicion for nontraumatic etiologies, including infections, inflammatory processes, and malignancy. A thorough clinical assessment of the patient can guide the appropriate evaluation and management.

HISTORY

The differential diagnosis of the patient with fever and knee effusion encompasses a wide range of infectious, rheumatologic, vasculitic, and malignant diagnoses. Obtaining a thorough history is crucial in determining the risk factors for specific conditions and guiding subsequent evaluation. Although generally, the presence of fever in knee effusion raises the suspicion for a nontraumatic etiology, trauma and fever from separate etiologies may coexist. Thus, determining history regarding preceding injuries, including both traumatic and overuse, is helpful in guiding the differential diagnosis and workup. The clinician should obtain information about the duration, acuity, comorbid conditions, additional joint involvement, and signs and symptoms of systemic disease as well as risk factors for specific conditions.[1–3]

Duration of symptoms is particularly relevant in febrile knee effusion because chronic effusion raises suspicion for an inflammatory or malignant etiology, whereas an acute effusion is more

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suggestive of infection or trauma. The patient's history of specific comorbid disease is also relevant because underlying inflammatory bowel disease or rheumatologic disease increases the likelihood of an inflammatory etiology. Multiple joint involvement is likewise more suggestive of an inflammatory process or malignant infiltrative etiology, whereas single joint involvement is more likely infectious. Systemic symptoms of fever, weight loss, and malaise should raise the concern for inflammatory, malignant, and infectious etiologies. Previous history of joint damage, joint surgery, rheumatologic disease in the joint, or intravenous (IV) drug use should increase suspicion for septic arthritis. Other infectious risk factors and exposures should be assessed, such as travel or residence in an endemic Lyme disease region, which increases likelihood of Lyme arthritis; contact with farm animals and consumption of unpasteurized animal products, which prompts suspicion for *Brucella*; and a history of sexual activity, which increase likelihood of gonococcal arthritis and *Chlamydia trachomatis*–reactive arthritis.[1–4]

PHYSICAL EXAMINATION

In the patient with fever and knee effusion, the physical examination should first encompass a general assessment, noting any signs of systemic toxicity indicative of infection or rheumatologic disease. Cardiovascular examination should note the presence of murmurs (particularly new murmurs) because this could increase suspicion for acute rheumatic fever. Abdominal examination should note the presence of hepatosplenomegaly, and lymphadenopathy should similarly be noted because both of these findings can be seen in systemic inflammatory conditions and malignancy. A complete skin examination is warranted to identify any dermatologic findings that may point to specific inflammatory etiologies. Musculoskeletal examination should include a thorough assessment of the affected knee and adjacent bony and muscular structures, with attention to involvement of any additional joints. The patient's ability to ambulate and the presence of a limp should also be noted during the initial assessment because the ability to bear weight can help narrow the differential diagnosis. The knee examination should focus on delineating traumatic, septic, and rheumatologic effusions, which will help the clinician distinguish the underlying etiology.

KNEE EXAMINATION

Appearance

The initial assessment of the knee should involve a comparison to the unaffected knee joint, potentially making any gross swelling or deformity more readily apparent. The resting position of the joint should be noted because the patient with septic arthritis will typically hold the knee motionless with slight flexion. The presence of erythema overlying the entirety of the joint may indicate infection or inflammatory arthritis, whereas erythema involving only a portion of the joint may be more indicative of overlying cellulitis. The joint should also be inspected for presence of contusion, abrasions, and acute or healing open wounds, which increase suspicion for traumatic etiologies.

Palpation

Knee palpation is a crucial component of the assessment of the patient with fever and knee effusion. Warmth in the joint is consistent with infection and inflammation. Palpation for tenderness both in the joint line as well as surrounding bony structures and tissues is essential. Exquisite tenderness on knee palpation is expected with septic arthritis, whereas a joint that is subjectively painful but that has no objective findings of swelling or pain with palpation indicates arthralgia rather than a true arthritis. Periarticular processes such as cellulitis, bursitis, and tendonitis can produce redness, warmth, and tenderness; however these processes can be differentiated from an infected or inflamed joint because palpation of the joint line and maneuvers that stress the synovium (ie, flexion and extension) will not be painful. Clinicians should palpate the adjacent bony structures in their evaluation of the knee, including the distal femur, proximal tibia, and fibula because tenderness in these locations indicates fracture or osteomyelitis, whereas a palpable mass in these locations is consistent with tumor.

Effusion Assessment

The first sign of a large effusion is a loss of normal knee contours, easily identified when comparing the affected knee with the unaffected knee. Large effusions, typically those exceeding 20 to 30 mL of fluid, will accumulate in the suprapatellar pouch leading to the appearance of fullness in this location. Several physical examination maneuvers can be used to assess for effusion: the ballottement test, the patellar tap, and the bulge sign. In the ballottement test, the clinician places 1 hand on the suprapatellar pouch, "milking" fluid down toward the patella. The clinician then presses down posteriorly on the patella and then releases; in the presence of an effusion, the patella should float upward hitting the examiner's fingers. The patellar tap uses a similar technique: initial milking of fluid from the suprapatellar pouch followed by posterior pressure on the patella. A palpable tap as the patella hits the femur is indicative of an effusion. Lastly, the bulge sign is useful in smaller effusions that may not be clinically apparent using the alternative maneuvers. For the bulge sign, the clinician milks joint fluid from the lateral to the medial side of the knee, then quickly presses against the lateral component of the knee and assesses for appearance of a fluid wave on the medial aspect of the knee.[1–3,5]

Range of Motion

The knee should be able to extend fully and symmetrically compared with the contralateral knee. The normal pediatric knee should be able to flex to at least 110 degrees.[1] Acute and subacute limitation in flexion may be secondary to traumatic etiologies including meniscal tear and intraarticular bony fragments as well as nontraumatic causes of large effusions. Limited flexion may also be secondary to other painful conditions of the knee that do not result in intraarticular effusions, such as cellulitis, contusion, or a Baker cyst. Significant limitation in range of motion secondary to pain or pseudoparalysis in a child with fever and joint effusion is concerning for septic arthritis.[1,4]

Neurovascular Status

Assessment of the neurovascular status of the extremity is particularly important in the setting of traumatic injuries because it dictates the urgency of intervention. For knee injuries, a thorough neurovascular assessment should include palpation of the dorsalis pedis and posterior tibial pulses, plantar flexion of the ankle to evaluate the posterior tibial nerve, eversion of the ankle to evaluate the superficial peroneal nerve, extension of the great toe to evaluate deep peroneal nerve, and assessment of sensation of the foot.[1–3,5]

Special Maneuvers in the Traumatized Knee

Typically, febrile knee effusion in a patient will not be caused by a traumatic injury unless there has been a complication of the initial injury. However, in the patient with a history of injury, special

maneuvers can be used to detect underlying traumatic pathology. The anterior drawer tests for integrity of the anterior collateral ligament and is performed by stabilizing the foot and pulling the tibia anteriorly with the knee at 90 degrees of flexion. If the maneuver produces 5 mm or greater of translation without a clear stopping point, the test is considered positive for anterior collateral ligament laxity. The posterior drawer assesses posterior collateral ligament integrity and is considered positive when the tibia may be posteriorly displaced using a posterior force on the tibia against the femur. Meniscal injuries can be assessed through the McMurray test, which is performed by rotating the tibia interiorly and exteriorly in a patient lying supine with the knee flexed. A positive test consists of pain and a palpable "clunk" as the torn meniscus is trapped in the joint space. The collateral ligaments can be assessed through application of lateral and medial stress on the joint in both full extension and 30 degrees of flexion. Greater than 30 degrees of translation with either medial or lateral stress indicates laxity of the lateral collateral ligament and medial collateral ligaments, respectively.

DIAGNOSTIC EVALUATION

Evaluation of the patient with fever and knee effusion should include an immediate assessment for potential life- and limb-threatening conditions including septic arthritis, osteomyelitis, and malignancy.[1,2] Compared with the afebrile patient with a traumatic knee effusion, who may only require standard radiographs of the knee, the patient with a febrile knee effusion will require additional diagnostic workup to ensure accurate and timely diagnosis and treatment.

Imaging

Approach to Imaging

Practically, initial evaluation of the febrile child with a knee effusion should start with a standard radiograph. In patients in whom a large effusion is present and concern for septic arthritis exists, joint aspiration is recommended without need for further imaging. In patients where a concern for osteomyelitis exists and ultrasound is readily available, ultrasound to assess the knee and for adjacent soft-tissue infection is a reasonable next step. However, if ultrasound is unavailable, or persistent concern for osteomyelitis exists in the face of a normal ultrasound, the clinician should proceed to obtain a magnetic resonance imaging (MRI) if the technology and appropriate sedation, if needed for age or anxiety, are available.[1,2,4]

Radiography

A standard knee radiograph series, including anteroposterior and lateral views, is indicated in the initial evaluation to assess for fracture, tumor, and potential signs of inflammation or infection. The lateral view is most helpful in identifying knee effusion and is identified through a separation of the suprapatellar and femoral fat pads of greater than 5 mm.[6] Additional views can be obtained to search for specific pathologies; the sunrise patella view is used to evaluate for patellar pathology, and the intracondylar view can be used to visualize osteochondral lesions.[2] Radiographs in acute infections of the knee and surrounding tissues will typically be normal because it takes approximately 50% bony loss and generally 10 to 14 days of symptoms before the appearance of radiographic changes in osteomyelitis.[4,6–10] However, in subacute and chronic infectious and inflammatory processes, radiographs can demonstrate bony erosion, epiphyseal enlargement, and joint space deformity.[4,7] X-rays can also show characteristic changes in malignancies: "onion skinning" periosteal reaction in Ewing sarcoma and calcified blood vessels or "sun bursting" in osteosarcoma. A patient with leukemia may demonstrate diffuse osteopenia, metaphyseal bands, lytic lesions, and mixed sclerosis and lysis.[10–12]

Ultrasound

Ultrasound can be a useful adjunct for assessment of knee effusion in the pediatric patient. Ultrasonography has superior sensitivity and specificity in the detection of knee effusion relative to the physical examination and is noninvasive, repeatable, and has no associated ionizing radiation.[13–15] Bedside ultrasound can be helpful in guiding joint aspirations, particularly in the patient with a small knee effusion. In the patient with juvenile idiopathic arthritis (JIA), ultrasound can also demonstrate signs of synovitis and associated inflammatory periarticular changes, thus assessing disease activity. In the patient with concern for osteomyelitis, ultrasound imaging can demonstrate bone-adjacent soft-tissue inflammatory changes, such as subperiosteal abscess, as early as 2 days after symptoms onset.[14–17] In subacute osteomyelitis (>7 days), ultrasound can also demonstrate findings of bony erosion and extension into the joint. However because ultrasound is unable to differentiate infectious from noninfectious causes of knee effusion, it often does not provide a definitive diagnosis for many patients with fever and knee effusion. Importantly, ultrasound cannot assess for early bony changes associated with osteomyelitis; thus, a negative study does not rule out this disease process.[13–17]

Magnetic Resonance Imaging

Magnetic resonance imaging is excellent in its ability to detect inflammatory and infectious changes in joint and cartilage.[17] In the patient with fever and knee effusion, the study should be performed with gadolinium enhancement to enhance sensitivity for infectious and inflammatory changes in the bone and synovium. For the diagnosis of osteomyelitis, MRI is the most sensitive and specific noninvasive test.[7,17,18] With septic arthritis, MRI can demonstrate evidence of joint effusion, synovial thickening, and potentially popliteal lymphadenopathy.[17,18] Magnetic resonance imaging can also be used to determine disease activity in patients with JIA, illustrating synovial thickening and nodularity, pannus formation, and inflammation in the infrapatellar fat pad. In the patient with long-standing inflammatory arthritis, MRI can also illustrate evidence of bony erosion, joint space loss, and ligament involvement.[18–21] In addition, in a patient with a suspected tumor or malignancy, MRI can characterize the intramedullary and extrosseus extent of the tumor to aid in tumor staging and treatment planning.[22]

Computed Tomography

Computed tomography (CT) is excellent at identifying bony pathology; however, it is not typically the imaging of choice with fever and joint effusion because of ionizing radiation and limited ability to visualize soft-tissue inflammation.[23] In osteomyelitis, specificity of CT is approximately 66% and sensitivity is approximately 97%.[24] If a bony tumor is detected on radiograph and is not clearly benign, CT can more accurately delineate the underlying pathology.[23,25]

Laboratory Studies

Laboratory studies are indicated as part of the evaluation for the patient with febrile knee effusion to help determine the risk of an emergent osteoarticular infection and assess for possible malignancy. Initial laboratory evaluation of a patient with a febrile knee effusion should include complete blood count (CBC), inflammatory

markers (ESR and CRP), and blood cultures.[1,2,4,26–28] A CBC with differential may be diagnostic in the patient with a hematologic malignancy; illustrate cytopenias in systemic lupus erythematosus (SLE), anemia, and thrombocytosis in JIA; and support the diagnosis of a bacterial osteomyelitis or septic arthritis if a significant leukocytosis is present. However, a normal WBC count does not exclude an osteoarticular infection because up to 80% of cases of osteoarticular infection will present with a normal WBC count.[29] Blood cultures should be obtained in all patients in whom an osteoarticular infection is suspected because they can identify an etiologic agent in the case of a negative joint fluid culture.[1,2,4,30]

Both CRP and ESR are standard components in the assessment of the patient with a knee effusion to assess risk for underlying osteoarticular infection and inflammatory conditions. However, they are limited by a lack of specificity.[15,25,30,31] C-reactive protein both rises and falls more quickly than ESR and is generally considered to have greater sensitivity than ESR in detection of bone and joint infections. In a large prospective study of pediatric osteoarticular infections, ESR greater than 20 mm/h was 94% sensitive, CRP greater than 20 was 95% sensitive, and a combination of the 2 was 98% sensitive for pediatric osteoarticular infections.[32]

Given the lack of specificity of WBC count, CRP, and ESR, using these markers to distinguish septic arthritis/osteomyelitis from other inflammatory conditions is challenging. Several clinical prediction models to distinguish septic arthritis of the knee from alternative etiologies have been developed. The Kocher criteria (ESR > 40 mg/dL, WBC > 12×10^9 cells/L, non–weight bearing status, fever >38.5°C) were initially developed to evaluate the likelihood of septic arthritis of the hip; however, in clinical practice, they often are used to assess likelihood in additional joints including the knee. In a recent evaluation of the validity of the Kocher criteria to distinguish septic arthritis of the knee from transient synovitis, the criteria had poor sensitivity (~48.5%) in the presence of 3 or more criteria. The addition of CRP greater than 20 mg/dL improved the sensitivity of the criteria to 71.6%.[33] Baldwin et al[34] developed predictors to distinguish septic arthritis of the knee from Lyme arthritis. Criteria included pain with less than 30 degrees of movement, CRP greater than 4.0 mg/dL, patient-reported history of fever, and aged younger than 2 years. Three criteria were 84% predictive and 4 predictors were 100% predictive of septic arthritis. However, use of these should be cautioned in areas with very high Lyme disease prevalence.[34] Given lack of external validation of these criteria then, a useful pragmatic approach proposed by Pääkkönen et al[32] is that in a child with an acute red, swollen, and painful knee in the presence of fever with a CRP greater than 20 mg/L and ESR greater than 20 mm/h, joint aspiration should be performed with empiric treatment for septic arthritis.[31]

Additional infectious studies should also be obtained given the right clinical context. In the patient who resides in or has traveled to a Lyme disease–endemic region, screening with enzyme-linked immunosorbent assay with reflexive Western blot confirmation should be obtained. Serologic testing for *Brucella* can be considered in a patient with animal contact or who consumes unpasteurized animal products. Gonorrhea and chlamydia testing should be considered in patients with sexual activity; viral Hepatitis B/C serologies in patients undergoing chronic transfusions or with history of IV drug use can be helpful; tuberculosis (TB) testing (screening with purified protein derivative or an IFN-γ assay) may be helpful in the patient with chronic symptoms and TB risk factors. If reactive arthritis is suspected, stool-infectious PCR may be useful because results may be available in real time and aid in decision making. Stool cultures for *Salmonella*, *Shigella*, *Yersinia*, and campylobacter can also be obtained, although these will not influence management in the acute setting.[35]

When acute rheumatic fever or a reactive streptococcal arthritis is suspected, evaluation for concurrent or previous streptococcal infection can be performed with streptococcus culture/rapid antigen streptococcus testing and antistreptolysin/anti-DNAase antibodies. Antinuclear antibodies can be obtained in patients in whom systemic lupus erythematous is suspected because titers are elevated in 94% of children with SLE. However, antinuclear antibodies have poor predictive usefulness for SLE in nonspecialty settings and is not useful in the diagnosis of juvenile rheumatologic arthritis.[36]

Urinalysis can evaluate for pyuria, such as in the case of serum-sickness–like reactions or genitourinary infections. Microscopic hematuria can be a sign of intrinsic kidney disease such as from lupus nephritis or can occur from an acute vasculitis such as Henoch-Schönlein purpura. If significant muscular tenderness is present, a creatinine kinase can be obtained to assess for muscle breakdown, such as in the case of a myositis.[1,2,35]

Joint Aspiration

Most patients with a clinically significant knee effusion and fever will require a joint fluid aspiration for diagnostic purposes. Analysis of synovial fluid is capable of distinguishing underlying etiology by identifying specific causative agents such as infectious organisms, crystals, or malignant cells. Normal synovial fluid is clear, straw colored, acellular, has a protein concentration similar to that of plasma, and glucose concentration ⅓ of plasma. Synovial fluid should be sent for WBC count and differential, Gram stain, microscopic examination, lactate dehydrogenase, protein, glucose, culture, and if available, PCR detection for *Kingella kingae* and Lyme disease.[2,37]

The presence of 50,000 or more WBC/μL with greater than 90% polymorphonuclear leukocytes is classically considered to be suggestive of septic arthritis.[1,2,26,37] However, recent studies have demonstrated synovial fluid cell count alone cannot differentiate septic arthritis from other inflammatory conditions such as Lyme arthritis and JIA.[38–42] A pragmatic approach outlined initially by Arson et al[43] is to consider a synovial fluid WBC count greater than 50,000 WBC/μL as positive for pyogenic arthritis; WBC count of 25,000 to 50,000 as equivocal and consider the clinical context and alternative etiologies such as TB, Lyme, gonorrhea, etc; and WBC count less than 25,000 as negative for pyogenic arthritis.[43,44]

Importantly, although a positive bacterial synovial fluid culture definitively confirms septic arthritis, negative synovial fluid cultures do not rule out septic arthritis because 50% to 70% of children who have clinical signs of the disease have negative joint fluid cultures.[37,45,46] Synovial fluid can also be sent for crystal analysis, although crystal arthropathies are rare in children, and should be considered primarily in those with underlying metabolic conditions (ie, Lesch-Nyhan disease). Arthrocentesis is contraindicated in patients with overlying cellulitis or neutropenia because of risk of bacterial seeding in the joint in these instances.[2]

MANAGEMENT OF COMMON ETIOLOGIES

Septic Arthritis

Children with septic arthritis of the knee typically have fever, an exquisitely painful joint, restricted joint movement, and joint effusion. Symptoms are typically present 2 to 5 days before presentation, and additional symptoms may include malaise and poor appetite. Approximately 20% of patients will have a preceding history of fall or other minor trauma before symptom onset. Leukocytosis is present in 30% to 60% of patients, and CRP and ESR (as previously discussed) are elevated in most patients. All patients

with suspected septic arthritis will require blood cultures and joint fluid aspiration. Blood cultures will be positive in 40% of patients, and synovial fluid cultures in 50% to 70% of patients.[25,30,31,37,45,47]

Septic arthritis is an emergent condition necessitating prompt evaluation and treatment to reduce associated morbidity and mortality. The knee is the most frequently affected joint in septic arthritis in children, comprising approximately 37% to 54.5% of cases.[1,15,37] The clinical presentation varies widely by patient age, severity, causative organism, and the underlying conditions of the patient. Most pediatric septic arthritis cases occur in healthy children, with the highest frequency in boys and those aged younger than 4 years. Additional risk factors include immunocompromised states, hemoglobinopathies, low birthweight, bacteremia, and recent IV therapy.[10,30,31,45] The most common pathogens include *Staphylococcus aureus* (both methicillin-sensitive and methicillin-resistant) and *Streptococcus pyogenes*; however, increasing prevalence of the fastidious gram-negative bacillus *K. kingae* has been noted, particularly in children aged younger than 4 years. Classically, *Kingella* septic arthritis is less severe in presentation, and the organism is often difficult to isolate in traditional cultures. Additional pathogens should be considered depending on the patient's age and underlying risk factors. In neonates, Guillain-Barré syndrome and gram-negative enteric bacteria are important pathogens. Gonococcal arthritis (discussed in the next section) should be considered in sexually active patients, and *Salmonella* is an important etiologic agent in those with hemoglobinopathies. In immunocompromised patients, *Mycobacterium tuberculosis*, *Bartonella henslae*, *Streptococcus pneumoniae*, and fungal etiologies should also be considered.[25,30,31,45]

The management of pediatric septic arthritis involves initiation of empiric antibiotics and either joint aspiration or irrigation. Empiric antibiotics for most patients should be an antistaphylococcal penicillin (ie, nafcillin or oxacillin) or a first-generation cephalosporin (ie, cefazolin) to cover methicillin-susceptible *Staphylococcus aureus*, *S. pyogenes*, and *K. kingella*.[30,37,47] Clindamycin is an alternative for those with penicillin and/or cephalosporin allergies. Addition of methicillin-resistant *Staphylococcus aureus* (MRSA) coverage is only recommended with previous history of MRSA and in communities with high MRSA prevalence, recent hospitalization, intensive care unit admission, or immunocompromised state. Intravenous antibiotic therapy is the initial treatment; however, typically after an initial course of parenteral therapy, patients can transition to oral therapy for the duration of treatment course. Treatment course ranges from approximately 2 to 4 weeks depending on presence of concomitant osteomyelitis, clinical improvement, and normalization of inflammatory markers. Additional coverage for unusual pathogens (ie, *M. tuberculosis*, *B. henslae*, fungal organisms) may be required given the patient's underlying risk factors and presentation.[25,30,31,37,45,47]

Osteomyelitis

Acute osteomyelitis is bacterial or fungal infection of bone that results in bony inflammation and, ultimately, bony destruction. Most pediatric osteomyelitis occur hematogenously after a transient bacteremia.[48] The condition can also result from penetrating injuries or spread from adjacent tissues, although these are less common mechanisms in children. The condition occurs in approximately 8 in 100,000, with higher rates in male children and those aged younger than 5 years.[49,50] The most frequent sites of acute hematogenous osteomyelitis involve the lower extremity, with the femur involved in 27% and tibia in 22% of cases. Contiguous spread to the adjacent joint occurs in 33% of cases overall, and with even higher frequency in neonates.[49,51] The microbiology of pediatric osteomyelitis is similar to that of septic arthritis, with *S. aureus* as the most common bacterial organism followed by *S. pyogenes.* Microbiology varies by age group and additional risk factors; *K. kingae* is an increasingly recognized pathogen in the preschool age group. Neonates may have GBS or enteric gram-negative bacteria, and those with immunocompromised states may have fungal, mycobacterial, or other atypical pathogens. In traumatic osteomyelitis, infections are often polymicrobial, including both aerobic and anaerobic bacteria. Osteomyelitis stemming from human or animal bites may involve *Pasturella multocida* and *Eikenella corrodens*, and puncture wounds are associated with *S. aureus* and *Pseudomonas aeruginosa.*[47,50]

Clinically, patients with acute osteomyelitis of the lower extremity typically present with painful limp, fever, and malaise. Symptoms are typically present 3 to 4 days before presentation and tend to be more insidious than those of septic arthritis, particularly in the case of *Kingella* osteomyelitis.[47,50] In distal femur osteomyelitis and proximal tibia/fibular osteomyelitis, a reactive effusion or concomitant septic arthritis can result in knee swelling. In addition, patients may have restricted movement of the extremity, tenderness over the affected bone, and overlying erythema/edema. As discussed previously, standard radiographs in acute (early) osteomyelitis will often be normal, with evidence of bony destruction not present until 10 to 14 days after symptoms onset. White blood cell, CRP, and ESR levels are often elevated, although in *Kingella* osteomyelitis, these markers may be normal in a significant proportion of cases.[52] Magnetic resonance imaging is the diagnostic tool of choice for osteomyelitis, with the ability to characterize both bone and adjacent soft-tissue inflammation as early as 2 to 5 days after symptom onset.[26] If a significant joint effusion is present, joint aspiration to assess for concomitant septic arthritis is recommended. Blood cultures should be obtained in all patients and are positive in 30% to 50% of cases.[53]

Initial management of pediatric acute osteomyelitis requires timely initiation of empiric IV antibiotic therapy. Prompt initiation of antibiotics may prevent progression of disease to abscess formation and prevent need for surgical debridement.[48] Empiric antibiotic choice is similar to that of septic arthritis, with a staphylococcal penicillin such as nafcillin, oxacillin, or first-generation cephalosporin such as cefazolin as the first choice in most patients. Alternative antibiotic regimens may be indicated depending on patient age and specific underlying risk factors. If subperiosteal abscess or concomitant septic arthritis are present or the patient fails to respond to empiric therapy and culture, surgical debridement may be required. Duration of antibiotic therapy is typically several weeks, and patients will often be transitioned to oral antibiotics to complete the antibiotic course.[48,50]

Lyme Arthritis

Lyme arthritis is a frequent cause of knee effusion in pediatric patients in Lyme-endemic regions of the United States. Lyme disease is caused by the spirochete *Borrelia burgdoferi*, and transmitted to humans through the bite of the Ixodes tick.[54] Early localized disease is marked by the classic bull's eye erythema migrans rash, and may be accompanied by fever, fatigue, or arthralgias. Left untreated, approximately 60% of pediatric patients with early Lyme disease with develop Lyme arthritis. It is important to note that most patients with Lyme arthritis cannot identify a history of erythema migrans, and this should not be used as a variable in assessing likelihood of disease. The knee is the most frequently involved joint, comprising 90% of Lyme arthritis in children. Clinically, Lyme arthritis in children typically presents with a large knee effusion and associated limited range of motion. The knee may be red and warm, and fever is present in 25% to 50% of cases. The pain of Lyme arthritis is variable, although typically is less

than that of septic arthritis, and many children can still bear weight. Untreated episodes of Lyme arthritis typically follow a relapsing-remitting course, with recurrent episode affecting the same or different joints.

Significant clinical overlap exists between septic arthritis and Lyme arthritis. White blood cell count, ESR, and CRP are typically higher in patients with septic arthritis when compared with those with Lyme arthritis. In addition, children with Lyme arthritis are less likely to have pain with micromotion of the joint as compared with those with septic arthritis.[34,38] Synovial fluid WBC count does not reliably differentiate Lyme arthritis from septic arthritis, and thus cannot be used in isolation to differentiate the 2 entities.[38,55] If a suspicion for Lyme arthritis exists, screening with enzyme-linked immunosorbent assay is recommended, followed by reflex confirmatory study with Western blot for IgG/IgM antibodies. Most patients with Lyme arthritis will have positive serologies. In addition, patients with suspected Lyme arthritis should undergo a screening electrocardiogram given potential for coexisting Lyme carditis, and those with neurological signs and symptoms warrant evaluation with lumbar puncture to assess for Lyme meningitis. First-line treatment for Lyme arthritis without concurrent cardiac or neurologic manifestations is a 28-day oral course of amoxicillin, cefuroxime, or doxycycline.[38,54,55] Although doxycycline was previously only recommended for patients aged 8 years and older because of concerns regarding bone deposition, this age restriction has subsequently been lifted.[44] Although untreated Lyme arthritis may resolve spontaneously, antibiotic treatment can prevent long-term joint damage and hastens resolution of symptoms and is therefore indicated on diagnosis.[27,28] However, families should be counseled that symptoms often do not immediately resolve on the initiation of antibiotics, and a waxing-and-waning course is not unusual. Ninety percent of patients will ultimately completely respond to an initial treatment with oral antibiotics alone within approximately 3 months.[54]

SUMMARY

The pediatric patient with fever and knee effusion requires an expedient and thoughtful evaluation in the ED. Initial assessment should be targeted toward evaluation for emergent infectious etiologies including septic arthritis and osteomyelitis. In the patient with chronic symptoms, a broader differential must be considered, including chronic infectious, vasculitic, inflammatory, malignant, and traumatic etiologies. Standard radiographs along with CBC, blood cultures, and inflammatory markers are indicated as initial workup in most patients. Empiric treatment with IV antibiotic(s) is indicated in patients with concern for septic arthritis or osteomyelitis. Specialty consultation will likely be indicated in those with concern for malignancy and chronic inflammatory arthritis to guide further workup and treatment plans.

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