Evaluation of the Child Who Has Hip Pain

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Children who have hip pathology can present in different ways, including complaints of pain, refusal to bear weight, limp or abnormal gait, or decreased movement of the lower extremity. The first thing to remember when considering lower extremity or gait complaints in skeletally immature patients is that patients who have hip pathology may present without complaining of hip pain. They may have a painless hip (developmental dysplasia of the hip, a shortened extremity) or complain of pain elsewhere (usually the knee or distal thigh). The pediatric population is challenging because some patients may be too young to complain of pain, and present with only decreased movement of the extremity or refusal to bear weight. Considering possible pathophysiologic categories during the evaluation can guide the clinician in the history taking, physical examination, and ordering of tests. The most common cause of lower extremity pain and limp in children is trauma; other categories to consider include inflammatory, infectious, developmental, and neoplastic processes (Table 1). Because developmental dysplasia of the hip does not usually present with pain in children, it is not covered here.

History

Obtaining a thorough history can be the most important part of the evaluation. Any recent traumatic events should be noted, and questions asked as to whether or not the child could ambulate after the trauma. Discovery of the onset, duration, severity, and location of the pain, and identifying factors that aggravate or alleviate the discomfort, can provide clues regarding etiology. Specific questioning should investigate associated systemic signs or symptoms, such as fever, sweating, and weight loss; and any recent infections or antibiotic usage should be recorded. To identify potentially serious causes of hip pain for which a timely diagnosis is essential, questions about night pain or rest pain should be asked. There are occasions in pediatric practice in which these questions are not answerable because of the patient’s age, especially if the inciting event is not witnessed. In these cases, physical examination, imaging, and laboratory studies are needed to elucidate the diagnosis. The goal of targeted questions in the history is to assess the possibility that the pain is related to an infectious or neoplastic process, where delay in diagnosis and treatment can result in increased morbidity.

“Knee pain equals hip pain” is a maxim to consider in the patient who is skeletally immature, and important to remember in formulating a differential diagnosis and focusing the physical examination and possible imaging studies. This referred pain is thought to be a consequence of Hilton’s Law—any nerve that passes over a joint sends some nerve fibers to innervate that joint. Thus the femoral nerve sends fibers to innervate the hip joint; and by way of referral pain pathways, hip pathology may present with the patient complaining of pain in the medial aspect of the thigh or knee, in the area of the terminal branch of the femoral nerve [1]. As an example, in one series up to 23% of patients who had slipped capital femoral epiphysis (SCFE) presented complaining only of knee pain [2]. Patients complaining of knee pain who are skeletally immature should be questioned specifically about associated hip or groin pain; and careful physical exam of the hips should be done, especially...
when the knee examination is benign or nonfocal. Pelvic radiographs are obtained on patients complaining of knee pain if there is also any history of groin or hip pain, or an abnormality on hip examination.

**Physical examination**

Physical examination of the patient who has hip pain begins with recording vital signs, especially temperature. If able to ambulate, the child should be observed walking up and down a long hallway. Observational gait analysis should specifically look at the foot progression angle, at pelvic and trunk balance, and for presence or absence of a limp. The child who refuses to bear weight should be examined to see if sitting or crawling is tolerable. Inability to sit comfortably may point to spinal pathology, and ability to bear weight through the knees proximally when crawling can localize the problem to the legs or feet. Range of hip motion examination is critical, particularly looking for diminished or painful inward rotation. The anatomy of the hip joint is such that maximal intracapsular volume is possible with the hip in a position of flexion, abduction, and outward rotation. A febrile infant holding the hip in this position at rest likely needs an aspiration and arthrogram to rule out pyarthrosis. Conversely, the hip joint accommodates less intracapsular volume with extension, adduction, and inward rotation. If these passive motions cause pain, suspicion for an intra-articular process is heightened. Children who have irritable hips often allow a gentle “log-roll” inward and outward rotation of the extended lower extremity to assess side-to-side differences in hip rotation and guarding. A useful physical examination maneuver to rule out significant hip pathology is a supine active straight leg raise against resistance. The muscle contractions necessary to raise the lower extremity cause the hip joint to be loaded, and thus patients who can perform this movement easily, without pain and with symmetric strength, are unlikely to have hip joint pathology. Squatting to the ground and rising is a simple, fast test of active lower extremity joint motion and strength. Alternate single leg hopping can sometimes demonstrate subtle differences in side-to-side lower extremity function. Thigh atrophy (measured at a standard distance above the patella) can also be a subtle marker of long-standing hip pathology. If the patient’s symptoms and physical examination signs are suspicious for hip pathology, laboratory studies and imaging may be indicated. Examination of other joints for swelling and skin examination for rashes can be helpful in identifying inflammatory or infectious causes of hip pain. Thorough palpation of the thigh is important to assess for any mass effect, and the inguinal area should be palpated also for any mass or lymphadenopathy.

**Laboratory studies**

Laboratory studies are used primarily for screening when the differential diagnosis includes infectious, inflammatory, or neoplastic processes. Most frequently ordered are a complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and rheumatoid panel (rheumatoid factor, ANA). A Lyme disease titer should be considered in endemic areas. Each test has literature discussing its use in evaluating limping children [3]. Some important caveats from that body of knowledge that are helpful in evaluating children who have hip pain are:

- The ESR and CRP are acute phase reactants, and either infectious, inflammatory, or neoplastic causes can result in elevation above normal levels. The CRP will increase and decrease faster than the ESR, and so may be a better marker of day-to-day progress when treating infections. Of note, the ESR and CRP are better negative predictors than positive predictors for infectious processes. One study of septic arthritis in
children found that patients who had a normal CRP had an 87% probability of not having septic arthritis [4].

- The rheumatoid panel may be normal, yet the patient may still have an inflammatory condition.
- Leukemia must be considered in the differential diagnosis in children who have musculoskeletal pain. Patients who have an elevated ESR and associated anemia, neutropenia, or thrombocytopenia may benefit from consultation with hematology/oncology colleagues and from bone marrow aspiration to diagnose leukemia [5].
- If an infectious etiology is suspected, a blood culture should be drawn at the time of other laboratory studies, because often the blood culture is the only positive culture in patients who have musculoskeletal infection. Patients do not have to be febrile at the time the blood culture is drawn.

**Imaging**

Anteroposterior radiography of the pelvis is the standard first-line imaging, preferably taken with the patient standing, if age and physical function allow. A centered, good-quality pelvic radiograph provides much information about the health and development of the hip joint and allows comparison of symptomatic and asymptomatic sides. Lateral views of both hips may be needed, depending on the differential diagnosis, because some conditions, such as early slipped capital femoral epiphysis or Legg-Calvé-Perthes disease (LCPD), may be more evident on the lateral view. Advanced imaging is helpful in cases in which infectious or neoplastic processes are suspected, and may include magnetic resonance imaging (MRI), computed tomography (CT) or nuclear medicine studies (bone scan, positive emission tomography scan). Nuclear imaging was described frequently in the 1990s as a method to elucidate the cause of nonspecific lower extremity pain and limping in children [6], but these methods require intravenous access, entail exposure to radiation, give nonspecific anatomic detail, and are not fast. MRI scanning has replaced nuclear imaging studies for the most part, because it can be done faster, does not expose the child to radiation, and can give greater anatomic detail [7]. Coronal screening images from the lumbar spine to the ankles can be obtained rapidly, looking for infectious or inflammatory processes in limping children. The disadvantage of MRI is that young children may require sedation or general anesthesia to acquire quality images. CT scans allow the images to be acquired much faster, but expose the child to radiation, making CT a less desirable choice for screening. CT is excellent if a bone abnormality is suspected, or if the area to be studied can be localized by physical exam or plain radiography. Ultrasound of the hip can be used to assess for a hip effusion, but it does not provide information differentiating inflammatory or traumatic effusions from infectious arthritis. Ultrasound also can be used to guide aspiration of the hip joint.

**Traumatic and mechanical causes of hip pain**

A history of trauma guides the physical examination and imaging studies to look for fractures, dislocations, muscle strains, or joint sprains. It is unusual for children to sprain or dislocate the hip joint, and fractures around the hip are caused typically by high-energy trauma and usually do not pose a diagnostic dilemma. An exception can be avulsion fractures of the pelvis, usually seen in older children and adolescents engaged in active sports. Focused examination reveals tenderness at sites of muscle attachment to the pelvis (anterior superior iliac spine – sartorius, anterior inferior iliac spine–rectus femoris, ischium – hamstrings) and pain on resisted strength testing of the involved muscles. Repetitive stress can also result in stress fractures of the femur that present with hip and thigh pain and may be confused with neoplastic processes such as Ewing’s sarcoma. This confusion is because of the typical location (femoral diaphysis) and radiographic findings (periosteal reaction) that stress fractures in children and Ewing’s sarcoma share. MRI can help distinguish between these two conditions, because stress fractures may have a visible disruption in cortical continuity and will not have an associated soft tissue mass or bone destruction, as is seen with sarcomas. Serial radiographic examinations reveal progressive healing of stress fractures after activity modification [8]. Repetitive motion of tendons over bone prominences can also cause symptoms, with snapping hip syndrome occurring from the psoas tendon abrading the pelvic brim and the tensor fascia lata/iliotibial band rubbing over the greater trochanter.

**Slipped capital femoral epiphysis**

SCFE is a disorder of the physis of the proximal femur, with the femoral neck slipping off the
proximal femoral epiphysis, which is contained within the acetabulum. SCFE is more likely to occur in older children and adolescents and is felt to be primarily of mechanical etiology because it is typically seen in obese patients. It tends to occur between the ages of 10 and 16 years and is more common in boys. It is bilateral in approximately 20% of patients at the time of initial presentation, and another 20% to 30% will develop a contralateral slip within 12 to 18 months of the initial slip. As noted earlier, it often presents initially as knee pain, which can cause a delay in diagnosis. This delay can have significant consequences, because the degree of slip can increase during the delay, increasing the risk for arthritis and perhaps even of osteonecrosis, the most feared complication of SCFE. Patients who have SCFE are classified as having a stable or unstable slip, based on whether or not they can bear weight on the involved extremity [9]. The major difference prognostically between the two groups is the risk for osteonecrosis, which is negligible in patients who have stable SCFE, but increases to almost 50% in patients who have unstable SCFE. The goal of evaluation of ambulatory patients who have SCFE is to identify them and treat them (in situ screw stabilization) to prevent progression to an unstable SCFE with its concomitant increased risk for osteonecrosis, and to prevent further deformity of the proximal femur with its increased risk for developing osteoarthritis. Patients who do not fit the typical profile of SCFE patients (younger age—less than 10 years—at presentation, body weight less than 50th percentile), should have an evaluation of renal and endocrine function, with hypothyroidism and growth hormone deficiency being the most common endocrinopathies associated with SCFE [10,11]. Patients who have SCFE usually have an asymmetrical outward foot progression angle on the involved side, have limited internal rotation, and may have obligatory outward rotation of the hip with flexion, to allow for clearance of the femoral neck, which would impinge on the anterior acetabulum with flexion in neutral rotation. The involved limb may be shortened. Radiographs confirm the diagnosis, with the lateral view being most sensitive for early slips of small magnitude. On the anteroposterior view, a line drawn along the superior femoral neck (Klein’s line) should intersect some portion of the femoral head. Other subtle early signs are asymmetrical physeal widening or blurring (blanch sign of Steel). In very suspicious cases by history and physical examination with normal initial radiographs, advanced imaging can be obtained (CT or MRI), or the patient can be placed on crutches with protected weight bearing and early return for repeat evaluation.

Inflammatory or infectious causes of hip pain

These two categories are presented together because the history and physical examination frequently leave these two as the leading possibilities, and clinical decision making in distinguishing between them is important, because the treatment needed is different.

When a child presents with an irritable hip, timely diagnosis is essential if the cause of the pain is septic arthritis of the hip [12]. An aphorism from Rang cautions the surgeon to “Never let the sun set on pus under pressure.” Intra-articular infection can result in permanent loss of hip function, with early arthritis as a result of loss of articular cartilage, a shortened limb as a result of damage to growth cartilage, a hip dislocation as a result of distension and destruction of the joint capsule, or osteonecrosis and complete loss of the femoral head and neck as the worst-case scenario. The differentiation of septic arthritis from transient synovitis can be difficult, and no combination of tests has been found to be foolproof. As the sequela of missed or late diagnosis can be severe, aggressive testing to rule out septic arthritis is favored, even though it is associated with some risks. Hip aspiration is regarded as the gold standard for diagnosis of septic arthritis, with positive findings on Gram stain and culture or the finding of greater than 50,000 white blood cells per mm$^3$ with a predominance of polymorphonuclear cells diagnostic. Because hip aspiration is painful, usually it is performed under sedation or general anesthesia; and it should be done under fluoroscopic guidance with arthrography or ultrasound confirmation to ensure that the hip joint is entered. A subadductor or anterior approach with a spinal needle can be used to enter the joint; and often in cases of septic arthritis, pus exits once the obturator is withdrawn. If synovial fluid is not encountered when the obturator is withdrawn and aspiration performed, the joint should be injected with radiographic contrast material to confirm intra-articular placement of the needle. Fluid that is withdrawn from the hip should be sent for cell count and differential, Gram stain, and culture. If no fluid is obtained on aspiration, the joint can be injected with a small amount (3–5 mL) of sterile saline, which is then reaspirated and sent for culture.

Because it is often not clear on presentation if infection is the cause of hip pain, the office eval-
ulation of the child who has an irritable hip involves clinical decision making along the lines of threshold modeling described by Pauker and Kassirer [13]. The primary objective is to identify and treat all patients who have septic arthritis of the hip. The clinician has three options: (1) make a presumptive diagnosis of transient synovitis and order no further tests (observation threshold, treat with analgesics or anti-inflammatories), (2) order further testing (testing threshold) to elucidate the diagnosis (laboratory studies, imaging), or (3) proceed to invasive testing or treatment (test-treatment threshold) with hip aspiration/arthrogram or arthrotomy if suspicion for septic arthritis is high. Multiple studies have attempted to define factors that can be used to differentiate septic arthritis from transient synovitis of the hip. Noted factors include a history of fever, refusal to bear weight on the involved extremity, an elevated white blood cell (WBC) count in the peripheral blood, an elevated ESR, side-to-side differences in the width of the apparent hip joint space on radiographs, prior visits to a health care provider, and an elevated CRP [14–17]. Clinical decision rules based on these factors have a reported likelihood of identifying septic arthritis as high as 99% when a combination of these factors is used [14].

Transient synovitis of the hip is probably the most common cause of hip pain in children. Retrospective and prospective studies from large referral children’s hospitals attempting to develop clinical algorithms to differentiate transient synovitis from septic arthritis have found patient populations that consist of two thirds with transient synovitis and one third with septic arthritis [14–16]. Patients who have septic arthritis tend to be younger on average; but there is a wide overlap, and septic arthritis of the hip can occur at any age. Transient synovitis typically occurs between the ages of 3 and 8 years, presenting with hip pain and a limp or even refusal to bear weight. It may be preceded by a viral illness or minor trauma, and it can have an acute or insidious onset. The child is usually not toxic in appearance, and typically does not have a high fever. Motion of the hip is usually possible in the midrange, with pain at the extremes. It is a benign, self-limited condition, with no known long-term sequela. There are times, however, when patients present with fever, refusal to bear weight, and pain with any motion of the hip; and distinguishing transient synovitis from pyarthrosis is challenging.

Children who have septic arthritis of the hip usually appear ill, have a fever or a history of fever, refuse to bear weight, and guard against any movement of the involved hip. Transient bacteremic episodes are believed to result in deposition of bacteria within the hip joint and subsequent infection. Patients often have a history of mild antecedent trauma, which can be misleading; and some investigators have hypothesized that minor trauma may predispose the area to infection, as has been shown for osteomyelitis [18]. Again, the challenge is that patients who have septic arthritis may present early in the infectious process and not manifest the classic signs and symptoms.

Kocher and colleagues sought to provide a clinical decision-making algorithm based on a retrospective review of patients at Boston Children’s Hospital over 17 years [14]. They identified four independent multivariate predictors of septic arthritis of the hip: a history of fever, inability to bear weight, an ESR of 40 mm/h or greater, and a serum WBC count greater than 12,000 cells/mm³. Patient who had three of four predictors had a 93% chance of having septic arthritis, and those who had all four had a 99% likelihood of pyarthrosis.

Luhmann and colleagues [16] then looked at these four variables retrospectively in their patients from St. Louis Children’s Hospital who underwent arthrocentesis for an irritable hip over an 8-year period and found that the presence of all four Kocher predictors in their patients predicted septic arthritis only 59% of the time. In their patients, statistical analysis revealed the three best predictors of septic arthritis were a history of fever, a serum WBC greater than 12,000 cells/mm³, and a previous health care visit, with a probability of septic arthritis 71% of the time when all three variables were present. They questioned whether clinical decision algorithms developed in one center were valid if applied in a different health care setting. Jung and colleagues [17] performed a similar study to the retrospective study of Kocher and colleagues, and they identified five independent predictors of septic arthritis: a temperature of 37°C or greater, an ESR of 20 mm/h or greater, a CRP of greater than 1.0 mg/dL, a serum WBC of greater than 11,000/mm³, and an apparent medial joint space difference of greater than or equal to 2mm on radiographs. Kocher and colleagues followed up their original study with a prospective study to validate their clinical prediction rule and found good diagnostic performance in these new patients. Patients who had zero of the four predictors had a 2% probability of septic arthritis, one of four 9.5%, two of four 35%, three of four 72.8%. Patients who had all four predictors present had a 93% probability of septic arthritis [15].

The clinical prediction rules of Kocher and colleagues are not meant to supplant clinical judg-
ment, but they may be used to determine thresholds for clinical decision making as described by Kassirer and colleagues. Those patients who have three or four predictors may pass the test-treatment threshold and warrant hip aspiration/arthrogram. Experienced pediatric orthopedic surgeons believe there is no area more treacherous or more in need of a skilled and wise assessment than the evaluation of a child who has possible musculoskeletal infection about the hip. Patients who have hip pain can have an infectious etiology and not have septic arthritis; the other sites of possible infection are the bones and muscles around the hip joint. Proximal femoral or pelvic osteomyelitis can present similarly to septic arthritis, although often the patients will still bear weight and allow some passive range of motion of the hip (less irritable). Osteomyelitis in either location around the joint can eventually erode into the joint and cause concomitant septic arthritis. This situation needs more timely diagnosis and treatment, because the effects of infection on articular cartilage can have more severe and irreversible effects than infections isolated to the bone. As noted previously, patients who have musculoskeletal infection may have had minor preceding trauma, which may predispose them to infection by providing an area of hematoma or injured tissue for bacteria to invade [18]. Pyomyositis, in particular, can mimic septic arthritis; and it should be kept in mind if hip aspiration or arthrogram is negative and the patient continues to manifest signs of infection (fever, positive blood cultures). Deep muscles around the pelvis can become infected (psosas, obturator internus, adductor brevis, gluteus minimus, and others) and present with pain around the groin, guarding against hip motion that stretches the involved muscle, and often fever or systemic illness. Typically ESR and CRP are elevated. MRI scanning is the best imaging study to assess for intramuscular abscesses, although CT scans can also be diagnostic [19,20].

Other infectious causes of hip pain include Lyme disease, although hip involvement is rare. It should be suspected in patients who have a history of a bull's-eye rash, a tick bite, or being in an area endemic for Lyme disease. Diagnosis is made by measurement of serum Lyme disease titer.

Inflammatory causes of childhood hip pain from juvenile rheumatoid arthritis, ankylosing spondylitis, or Reiter syndrome are uncommon. Family history of inflammatory or autoimmune conditions should be sought, and other joints should be examined for any signs of inflammation. Hip involvement in juvenile rheumatoid arthritis is uncommon except in the systemic form.

Reiter syndrome and ankylosing spondylitis rarely manifest in children and are more common in adolescents and young adults.

Vascular causes

LCPD is idiopathic osteonecrosis of the proximal femoral epiphysis. It is most commonly seen in children aged 4 to 8 years, and it occurs more often in boys. Some associations have been noted with delayed bone age, hyperactivity, and passive smoke inhalation. Some controversy exists regarding the presence of thrombophilia in patients who have LCPD, with conflicting studies published. It frequently presents initially with a painless limp, but then patients may develop pain, typically in concert with femoral head collapse. Patients may complain of pain in the hip, thigh, or knee. Patients often have pain at the end range of motion, especially abduction and internal rotation, with less painful midrange motion. Symptoms and limp severity are usually worse at the end of the day. The diagnosis of LCPD is made based on the radiographic appearance, with the earliest signs being a decreased size of one proximal femoral epiphysis, or increased density of one epiphysis. The lateral radiograph of the hip is more likely to show a crescent sign, a subchondral fracture that correlates with the extent of necrotic bone. Bilateral involvement is uncommon in patients who have LCPD; and when it is bilateral, there is usually sequential involvement. In patients who have symmetric flattening or fragmentation, multiple epiphyseal dysplasia or spondyloepiphyseal dysplasia should be considered. Prognosis for patients who have LCPD is most closely associated with age at presentation, and treatment generally follows containment principles [21].

Osteonecrosis of the proximal femoral epiphysis may also occur following fractures or dislocations of the hip, or after surgery around the hip. Other causes of osteonecrosis of the hip include hemoglobinopathies, such as sickle cell disease or thalassemia, leukemia, lymphoma, and hemophilia.

Neoplastic conditions

Several neoplastic conditions can present with hip pain. Most concerning of these are malignant neoplasms, particularly osteosarcoma and Ewing’s sarcoma. Patients who have night or rest pain, systemic symptoms, or palpable masses should be evaluated with laboratory studies and imaging to assess for
neoplasms. Benign neoplasms (bone cysts, fibrous dysplasia) that compromise the structural integrity of the bone may present with mechanical pain; and benign aggressive neoplasms, such as osteoid osteoma or chondroblastoma, may present with night pain and pain with weight bearing [22].

Leukemia is the most common malignancy in childhood and often presents with musculoskeletal complaints. One study noted the hip as the most frequent site of pain [5]. Thus, leukemia should be included in the differential diagnosis of limping children or patients who have hip pain, especially in patients who are initially believed to have an infectious etiology but do not improve during standard therapy for septic arthritis or osteomyelitis. Bone and joint pain is believed to be caused by the mass effect of malignant blast cells within the medullary canal. As malignant cells occupy the marrow space, the production of normal blood components is decreased and can offer diagnostic clues when assessing a patient who has hip pain on laboratory studies. Leukemic patients often have a very elevated ESR, with associated anemia, neutropenia, or thrombocytopenia. Often radiographs are normal, but MRI scans show the marrow replacement.

**Summary**

Evaluation of hip pain in children can be challenging, because there are several diagnoses to consider and differentiating among them can be difficult. Patients who have traumatic or mechanical causes of hip pain are not usually as difficult to diagnose, as long as the potential pitfall of referred pain to the knee is recognized, and appropriate radiographs are ordered and interpreted correctly. The diagnostic dilemma most commonly encountered involves identifying the etiology of the irritable hip in a child in whom the differential includes infectious, inflammatory, and neoplastic categories. A systematic approach based on the level of intensity of presenting circumstances can be helpful to guide the workup, allowing for clarification of the diagnosis without excessive use of testing that can be anxiety-provoking and costly and entails some risk to the patient. This approach is similar to the levels proposed by Wenger for evaluation of back pain in children [23]; and the predictors identified by Kocher and colleagues [14,15] are helpful, as long as it is recognized that they may not apply to every patient and may not be as predictive in settings outside Boston [16].

Patients who do not have systemic symptoms or signs and who on examination are considered to have a mild to moderately irritable hip may not pass the observation threshold. They are provisionally diagnosed as having transient synovitis and can be managed with analgesics and anti-inflammatory medications. Parents are given explicit instructions to return night or day for fever or increasing pain, and the patient is rechecked in 24 to 48 hours. Transient synovitis typically improves rapidly, and patients are often better within days. The course can be prolonged in a few patients, lasting up to three weeks. Those patients who do not improve rapidly may need more testing, particularly radiographs to look for subtle signs of LCPD disease. Patients who have two or more Kocher predictors, or a more irritable hip on examination, exceed the testing threshold; and laboratory studies and radiographs are obtained. Normal range findings on the ESR and CRP are supportive of a noninfectious etiology. Patients who have three or more Kocher predictors, systemic signs, or a severely irritable hip on examination pass the test-treatment threshold. Laboratory studies and radiographs are ordered, and clinical judgment determines whether the findings of all data gathered lead to advanced imaging (if the findings are not specific enough to the hip) or if the patient proceeds directly to aspiration-arthrogram and possible arthrotomy of the hip. Patients who have classic signs of septic arthritis who do proceed to arthrotomy and have either unimpressive findings at arthrotomy or negative cultures, should be evaluated with further imaging (pyomyositis, osteomyelitis) or even bone marrow aspiration (leukemia), if the patient does not improve on antibiotics.

**References**


