PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "**Acute Osteoarticular Infections – CPS podcast"** These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Acute Osteoarticular Infections – CPS Podcast

Developed by Anupreet Rai and Dr. Matthew Magyar for PedsCases.com.
Jan 20, 2018

Introduction:

Hello everyone, my name is Matthew Magyar and I am a PGY4 undergoing subspecialty training in Paediatric Infectious Diseases at the University of Ottawa. This podcast was made in conjunction with PedsCases and the Canadian Pediatrics Society (CPS) and aims to summarize the recently published CPS statement on the Diagnosis and management of acute osteoarticular infections in children. This podcast was created under the guidance of Dr. Nicole Le Saux, a Paediatric Infectious Diseases specialist and Professor at the University of Ottawa, and lead author of the CPS statement.

The position statement focuses on children with clinical presentations that could be consistent with acute osteomyelitis (AO) and septic arthritis (SA) in previously healthy children. The statement does not focus on infections in the head and neck region, infections associated with artificial joints or prostheses, infections due to direct spread, for example such as secondary to trauma, infections with symptoms present for over one month or gonococcal infections.

By the end of the podcast, the learner should be able to:

1. Define and explain the pathogenesis of osteoarticular infections in children
2. Recognize the clinical manifestations of osteoarticular infections in children
3. Discuss the diagnostic investigations important for osteoarticular infections in children
4. Understand management principles and follow up for osteoarticular infections in children

Let's start off with a case.

You are a junior paediatric resident performing your first emergency rotation. The first patient you plan to see is Johnny, a 3 year old boy who is refusing to walk.

Upon discussion with his parents, you learn that Johnny has progressively been refusing to weight bear on his right leg for the last 3 days. The parents thought initially it was because he was tired but every time that they try to put him upright, he begins to cry and sits back down. There was no history of acute trauma but his mother reports that Johnny had fallen from his own height at the park 1 week prior to presentation. On further questioning, his parents relate that he was febrile for two days last week but this resolved and their main concern today is the refusal to walk.

Developed by Anupreet Rai and Dr. Matthew Magyar for PedsCases.com.
Jan 20, 2018

His family and past medical history are unremarkable. On physical exam, Johnny is non-toxic. His temperature was recorded at 38 degrees axillary. Otherwise, his vital signs are within normal limits. Upon placing Johnny upright, he begins to cry and refuses to put weight on his right leg. Upon inspection of the right leg, you do not find any swelling or erythema of the overlying skin. Palpation of the leg is remarkable for tenderness over the right proximal tibia. His knee, hip and ankle joints are normal. The rest of his exam was unremarkable.

As you are an astute junior resident, you read around acute refusal to weight bear and you come across osteomyelitis as a possible diagnosis. You have heard about osteomyelitis but have only seen it in adults in the past. Evidently you know that this is likely bacterial and that most cases in adults are due to *Staphylococcus aureus* so you do not want to miss this in a child.

Differential Diagnosis:

The differential diagnosis in a limping child is extremely important as it is unusual for a healthy, happy child to limp or not want to use one of their limbs. The document in the CPS practice point has a list of important diagnoses to consider in these children. The most common error that is made is to attribute this to an injury. However, the injury that causes inability to use a limb would be substantial and be associated with bruising and edema, with an associated fracture on plain imaging. Transient synovitis of the hip can also be part of the differential but in contrast to bacterial infections, they can usually weight bear. Other significant differentials to consider if the onset is more subacute are malignancies, such as leukemia and primary bone tumours. Lyme disease arthritis is characteristically much less painful than bacterial septic arthritis and the swelling is very significant compared to the pain. These children do not have fever as it is a later phenomenon. Compared to a cellulitis, osteomyelitis does not usually have skin and soft tissue findings unless there is an adjacent underlying periosteal abscess. One important aspect to remember is that osteoarticular infections due to *Kingella* spp. are sometimes subacute and are less fulminant compared to those caused by *S. aureus*.

Definition and Pathogenesis:

First, let's start off by defining osteomyelitis and septic arthritis. Osteomyelitis is defined as inflammation of bone and bone marrow most often due to infection. AO is defined when symptoms last less than 4 weeks while chronic osteomyelitis refers to symptoms for over one month. Septic arthritis is infection of the joint space.

Children, unlike adults, commonly acquire AO through hematogenous spread, the source of which is usually not clinically evident. So in actual fact, not having a recognizable site of infection (such as an infected wound or otitis) in a mildly febrile child who is limping actually increases the probability that this is an osteoarticular infection. Typical microbial pathogens causing AO and SA are often common skin and respiratory tract colonizers, suggesting these are the most likely portal of entries. *Staphylococcus aureus* is the most common cause of AO in children. *Kingella kingae*, a common colonizer of infants, occurs most often in children less than 3 years of age. Other causative pathogens include *Streptococcus pneumoniae* and *Streptococcus pyogenes.* In the past, before we had *Haemophilus influenzae* type B vaccines, *Haemophilus influenzae* would be a common bacteria in the pharynx, but vaccines have eliminated this, so this is now a rare cause of childhood osteoarticular infections.

AO can occur in any bone but the most common site is the metaphysis in the long tubular bones such as the femur, tibia or humerus. The predominance of AO in children is presumably due to

the rich vascular supply of their growing bones. Infecting organisms enter the bone through the nutrient artery, where at the metaphysis, ends in small arterial loops that empty into venous sinusoids. It is thought that at this site, the bacteria translocate into the pooled blood of the bone and begin to proliferate, release toxins and create an inflammatory response that promotes bony destruction. When suppuration occurs in the metaphysis of bones, infection can extend to adjacent sub-periosteal area and subsequently to the overlying soft tissues.

The age-related differences in bone anatomy and its blood supply plays an important factor in the clinical manifestations of AO in children. For example, in children less than 2 years of age, there are transphyseal vessels that crosses the metaphysis to the epiphysis, creating a connection that allows bacteria to infect the joint space. In addition, joints like the hip, elbow, ankle and shoulder in children have joint capsules that insert below the epiphyseal growth plate and predispose to adjacent SA. Therefore, it is not uncommon for children with AO to have adjacent SA.

Clinical Manifestations:

Children presenting with osteomyelitis or septic arthritis should be suspected in patients who have reluctance to use an affected extremity, otherwise known as pseudo-paralysis. Pain may be the only symptom elicited by the patient. Fever may be present, but is not required for the diagnosis. Less common complaints are anorexia, malaise and vomiting.

When the metaphyseal infection progresses to involve the periosteum to form an abscess and is superficial enough to the skin, children may present with focal swelling, tenderness, warmth and erythema on physical exam. If the predominant symptoms are skin and soft tissue pain, swelling and erythema, acute cellulitis or fasciitis need to be considered in the differential diagnosis.

Features of SA often overlap with osteomyelitis when it is near a joint area. SA alone presents with acute swelling, joint effusion, erythema, warmth and pain on movement of the joint. External physical findings may be absent when the hip is involved, however while examining the hip joint, certain maneuvers that increase intracapsular pressure such as compression of the head of the femur into the acetabulum, elicits pain which is suggestive of joint involvement. Similarly, in patients with bacterial arthritis of the sacroiliac joint, maneuvers that twist the pelvis cause pain whereas gentle hip motion does not. You should be cautious when pain is the buttocks or near the pelvic area as physical findings are very difficult to elicit, even in the presence of osteomyelitis in the pelvic bones or ileum.

If AO or SA are suspected, they will often need to be referred to a hospital and should be assessed by an orthopaedic surgeon or a pediatrician.

The past history and the immunization status are clinically important factors in determining if other possible organisms may be involved. Always consider *H. influenzae* type b osteoarticular infection in unimmunized children. Enterobacteriaceae or fungi are uncommon causes of acute osteomyelitis, but they do occur in special populations, such as neonates, immunocompromised individuals or in cases of exposure to unique environments. Children and adolescents with sickle cell disease are prone to infections with *Salmonella* species in addition to *S. aureus*.

Investigations:

The gold standard for diagnosis of AO remains pathological assessment of a bone specimen;

but this may not always be necessary if a clinical diagnosis can be supported by other investigations.

A complete blood count may show elevated white count but may not always be present. CRP performed at presentation will often be elevated and is a good inflammatory marker. ESR is often performed in conjunction with the CRP but is not essential. Both of these inflammatory markers are acute phase proteins and may be abnormal in other infectious, hematological and neoplastic processes. The CRP may increase initially with the start of therapy. It is often used to help guide therapy when the overt clinical symptoms have improved.

X-rays for the diagnosis of AO are often not helpful to confirm the diagnosis as the classical signs of lytic lesions and localized periosteal lifting may not be apparent for the first 7-21 days after the onset of infection. They are more useful in the early presentations to rule out other important pathological lesions.

Magnetic resonance imaging (MRI) with gadolinium enhancement is the most sensitive and specific noninvasive test for diagnosing AO. MRI is useful in identifying early changes of bone marrow edema. MRI also provides information on associated soft tissues and growth plate involvement, and can help differentiate other etiologies from osteomyelitis. Although an MRI does not entail radiation, many patients presenting with AO may require general anesthesia.

Radionucleotide bone scans are used when radiographs appear normal, MRI cannot be performed, when multifocal bone involvement is suspected or when the site of the infection cannot be localized. Children often do not require sedation to perform this test. Computed tomography is used when MRI and radionucleotide bone scans are not available. It is less sensitive at detecting bone marrow edema.

When diagnosing SA, the optimal method is aspiration of the joint. The cell count and culture are used to determine the presence of inflammation and potential microbial pathogens. Consultation with interventional radiology or an orthopaedic surgeon may be required. If joint aspiration is not possible, then ultrasound can be used to confirm the presence of joint effusion and MRI will help confirm that the fluid is inflammatory.

When it comes to identifying a pathogen, blood, bone and joint fluid often test negative (an estimated 30-90% of the time). Efforts should be made in children who are hemodynamically stable to achieve blood cultures with adequate volume prior to initiating antibiotics. If blood cultures are positive, they should be repeated after 48 hours of antimicrobial therapy to ensure clearance. If a patient presents with *S. aureus* bacteremia with no source, AO must be ruled out. *S. aureus* bacteremia should never be considered a contaminant. When surgery of a joint or bone is required at presentation and the child is otherwise stable, delaying antibiotics for cultures may be appropriate. Many microbiology laboratories can now perform molecular tests to identify *Kingella kingae* since this bacteria does not grow well on standard media. It is worthwhile to save some joint fluid for additional testing if the standard cultures are negative.

Management and Follow-Up

In Canada, the majority of previously healthy fully immunized children may be started on empiric antibiotics with a first generation cephalosporin, such as cefazolin. The rationale is that the majority of cases of AO and SA are caused by Methicillin-sensitive *Staphylococcus aureus* (MSSA) and *K. kingae*, both of which are susceptible to the above mentioned antibiotic.

Developed by Anupreet Rai and Dr. Matthew Magyar for PedsCases.com.
Jan 20, 2018

Cefazolin at a dose of 100-150 mg/kg/day divided every 6-8 h should be the empiric intravenous (IV) antimicrobial choice. In areas where there is high prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) or if the child is known carrier, vancomycin should added to the initial cefazolin as empiric therapy until cultures are available. In children who are less than 4 years of age and are unimmunized, the use of cefuroxime for empiric therapy to cover for *H. Influenza* type B is an option. In these two cases, cefazolin would be inadequate coverage for these organisms. When a pathogen is identified, antibiotics should be modified to the most narrow and most appropriate antibiotic to target osteoarticular infection. Usually, this decision will be performed in consultation with a paediatric infectious diseases specialist.

Transitioning to oral therapy is indicated when there is a clinical response to treatment and a decrease in CRP. For most uncomplicated cases of acute osteomyelitis, current recommended treatment length is for a total of 3 to 4 weeks of antimicrobial therapy, compared with the 6 weeks recommended previously. For septic arthritis, the usual duration is 3 to 4 weeks, but most clinicians still recommend a total duration of 4 to 6 weeks of therapy if the hip is involved.

When the patient fails to improve clinically within the first few days on antibiotics, it is important to consider repeat imaging to identify bone or joint fluid collections, soft tissue abscesses and to reconsider surgery. Obtaining a specimen for bacteriological and pathological diagnosis is important because it may yield a pathogen not covered by empiric therapies (e.g., MRSA or another bacterial or fungal pathogen).

Clinical evaluation is necessary before discontinuing antimicrobial treatment. A normal CRP should be documented unless it has normalized previously. Although baseline radiographs at diagnosis should usually be obtained, routine radiographs at the end of therapy are only clearly indicated when the growth plate is involved, and/or a large lytic lesion presents initially. A radiograph at the end of therapy typically shows sclerosis and changes consistent with healing, with the lytic lesion usually still evident.

Surgical intervention may be required upon presentation. Children with suspected SA should be evaluated promptly by an orthopedic surgeon for consideration of urgent arthrocentesis and irrigation of the joint. For AO, the role of surgery depends on the size of the infection, the location within the bone and the response to therapy. An orthopedic follow-up is required in cases where the infection involved the growth plate or an immediately adjacent epiphyseal or metaphyseal region.

Case Conclusion:

Back to the case!

As Johnny presented with acute refusal to walk, he had low-grade fever and has no skin changes on exam to suggest skin and soft tissue infection, you decide with your staff that AO of the tibia seems to be the most important and likely diagnosis on the list of differential diagnoses. Your preliminary blood work shows a normal WBC count, an elevated CRP at 75 and blood cultures that are pending. An x-ray of the right tibia is also normal, which is expected given the early presentation of the illness. You and your staff are concerned enough that you decide to admit Johnny to the wards for further investigations with an MRI and start on empiric cefazolin 150 mg/kg/day IV divided q6h. Over the following days, MRI confirms osteomyelitis of the right tibia metaphysis and he steadily improves on antibiotic therapy. After 5 days he is walking with minimal pain, the medical team steps him down to oral therapy and he is followed up with the

paediatric infectious diseases team at your local tertiary hospital.

Summary:

Let's take a moment to summarize the key take home messages on acute osteoarticular infections:

- Acute osteomyelitis and acute septic arthritis should be considered in all children who present with pain involving a bone or joint and/or pseudo-paralysis of an extremity.
- The most common pathogens causing acute osteomyelitis and septic arthritis in children are *Staphylococcus aureus* and *Kingella kingae.*
- MRI is the most sensitive and specific non-invasive test for the diagnosis of osteoarticular infections.
- In Canada, we recommend empiric Cefazolin at a dose of 100-150 mg/kg/day after obtaining blood cultures.
- Children with suspected septic arthritis or with acute osteomyelitis complicated by an abscess should be evaluated promptly by an orthopedic surgeon.
- Transition from intravenous to oral therapy can be performed once there is clinical improvement and decreasing inflammatory markers.
- For uncomplicated cases of acute osteomyelitis and septic arthritis, duration of antimicrobial therapy is generally 3 to 4 weeks (4 to 6 weeks for hip septic arthritis) rather than the 6 weeks previously recommended.

Thank you for listening to this PedsCases podcast! We hoped that you enjoyed it and will stay tuned for more podcasts to come.

References:

1. Kliegman, R., Stanton, B., St. Geme, J. W., Schor, N. F., & Behrman, R. E. (2016). Nelson textbook of pediatrics (Edition 20.). Philadelphia, PA: Elsevier. Chapter 684. Osteomyelitis; p. 3322-3327.
2. Long S, Prober CG, Fischer, M. Principles and Practice of Pediatric Infectious Diseases. 5th Ed. Philadelphia, PA. Elsevier; c2018. Chapter 76. Osteomyelitis; p480-487.
3. Gutierrez, K. (2005). Bone and Joint Infections in Children. *Pediatric Clinics of North America*, [online] 52(3), pp.779-794. Available at: http://www.sciencedirect.com/science/article/pii/S0031395505000325.

Developed by Anupreet Rai and Dr. Matthew Magyar for PedsCases.com.

Jan 20, 2018