Review article:
Paediatric bone and joint infection

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ABSTRACT
Paediatric musculoskeletal infection remains an important cause of morbidity. Methicillin sensitive Staphylococcus aureus is still the most common organism although the incidence of methicillin resistant S. aureus in the community is rising. Osteomyelitis and septic arthritis due to Haemophilus influenzae is decreasing in incidence secondary to immunisation and in some units has been replaced by infections with the gram negative bacillus, Kingella kingae. Recent prospective studies indicate that uncomplicated osteomyelitis can be treated by three to four weeks of antibiotics. However, there is still a small group of children who will have overwhelming disseminated infection. These children require aggressive surgical and medical intervention. Two recent reports have identified an increased incidence of septic arthritis in children who have hemophilia and are HIV positive.

OSTEOMYELITIS
Acute haematogenous osteomyelitis is most common in childhood with a peak incidence in neonates. There is a seasonal variation, the hospital admission rate for osteomyelitis peaking in late summer and autumn in both the Northern and Southern hemispheres. The incidence is greater in boys than girls and the male to female sex ratio increases with age. The reported incidence has been falling around the world but remains high in Western Australia and New Zealand. This is due to an increased incidence in Aboriginal and New Zealand Maori children compared to European children in Australia and New Zealand.

Pathology
Infection almost always occurs by hematogenous colonisation of the bones by bacteria. The metaphysis of long bones is the most usual site. Theories to account for this fact include decreased blood flow in sinusoidal vessels in this area and relative paucity of phagocytic cells in this area. In animal models, isolated bacteremia does not lead to osteomyelitis but bacteremia plus a traumatic injury to the metaphysis produces significant osteomyelitis. Although many children give a history of minor trauma, it is very rare to see osteomyelitis complicating a closed fracture treated by non-operative means. Other features of the epidemiology including the male preponderance and peak incidence remain to be explained.

The pathological response to osteomyelitis is one of acute inflammation in the intra-medullary cavity of the metaphysis of the long bone. After 48 hours, pus accumulates sub-periosteally and then portions of the cortex may die as a result of the loss of blood supply forming a sequestrum and the abscess may rupture.
the periosteum. Occasionally, osteomyelitis can involve the epiphysis of a long bone and then is usually subacute although acute epiphyseal osteomyelitis has been reported.2,8

Clinical Setting
The most commonly affected long bones are the tibia and femur67 but involvement of almost every bone in the body has been reported.32,60 The hallmark of osteomyelitis is fever plus localised bony tenderness but in the immuno-compromised patient, such as the neonate, sepsis can be clinically silent until a large amount of pus has accumulated.71 Pelvic osteomyelitis is well known to mimic a number of other diseases including appendicitis, lumber disc prolapse and septic arthritis of the hip.4

Investigations
The white cell count is a relatively poor indicator of osteomyelitis. Prospective studies of children presenting with acute haematogenous osteomyelitis have shown that the WCC is elevated in only 35 to 40% of cases while the ESR is greater than 20 in 70 to 92% of cases.25 C-reactive protein is the most sensitive test, being elevated in up to 98% of patients at the time of admission.68 Blood cultures will be positive in 30 to 50% of patients24 and the organism detection rate is increased to 75% to 80% by aspiration of the affected bone.25

Plain radiographs are normal in the first 7 to 10 days. The earliest sign is deep soft-tissue swelling and loss of soft tissue planes at 48 hours but this can be difficult to detect. After 10 days, bony changes may become apparent including resorption of bone in the affected area and sub-periosteal new bone formation.10 Prospective studies have shown that only 70% of children with culture proven osteomyelitis will have bone changes at three weeks.45 In general the degree of bone change reflects the severity of the disease.

Several imaging modalities are available to diagnose osteomyelitis. Bone scans in acute haematogenous osteomyelitis have a sensitivity of 84% to 100% and a specificity of 40% to 96%.1,14,66 The sensitivity of bone scans is least in the first 48 hours due to the transitional period between decreased and increased activity. Scintigraphy is most helpful in the assessment of the young child, where localisation can be difficult and in detecting multiple foci of disease.2,23 Gallium-67 citrate scans have a higher diagnostic accuracy than technetium 99m but involve more radiation and should not be used on a routine basis.6 Indium labeled white cell scans are most useful in the postoperative situation but have relatively poor localisation, making it difficult to distinguish between deep and superficial infection.7

Ultrasound has been proposed as a useful investigation in the diagnosis of early osteomyelitis.48 The role of ultrasound in the diagnosis of early osteomyelitis has been studied by Larcos et al.21 They found that the sensitivity of ultrasound was only 63% and the diagnostic accuracy 58% with two false positives. Thus ultrasound can be misleading in early osteomyelitis. There is more support for the use of ultrasound to diagnose subperiosteal collections of pus.1,31,64 Another useful role for ultrasound may be in the differentiation between vaso-occlusive crisis and osteomyelitis in patients who have sickle cell disease.47,54

Magnetic resonance imaging (MRI) is the most sensitive test for osteomyelitis and is particularly helpful for infections in the pelvis and spine. The sensitivity of MRI is 97–100% and the specificity is 73–92%.35,70 Differentiation of tissue oedema from early abscess formation remains difficult in some cases.7,35,70 The cost for an MRI is significant and we therefore do not routinely use it for the diagnosis of osteomyelitis but reserve it for deep infections in the spine and pelvis or where the question of a subperiosteal collection is raised.

Treatment
Staphylococcus aureus remains the most common infecting organism although in neonates, infections with gram-negative organisms and Group B Streptococcus are common. The incidence of Haemophilus influenzae as a pathogen in children under four years is decreasing with the use of vaccination against H. influenzae B.8,45 Since this decline in H. influenzae osteomyelitis and septic arthritis in children under the age of 3 years, there has been an increasing prevalence of gram negative organisms such as Kingella kingae.5,34,71 Invasive Group A streptococcal disease can present with osteomyelitis and children with varicella infection are particularly prone to Group A streptococcal infection of bone or joint [Schreck et al. 1996, Doctor et al. 1995].

Penicillinase resistant penicillins such as oxacillin and fluclouxacin remain the mainstay of treatment; however in neonates, cefotaxime should be added to cover gram negatives. There is still a role for antibiotic coverage for Haemophilus in the child under four in areas where vaccination is not widespread or where invasive Haemophilus influenzae is still prevalent. Methicillin-resistant S. aureus (MRSA) is becoming a community organism and we have recently reported
a 20% incidence of MRSA in community acquired staphylococcal infections in our hospital. Other units are also experiencing an increase in musculoskeletal infections with methicillin-resistant S. aureus. Clindamycin has excellent bone and joint penetration and is our first line antibiotic of choice for methicillin-resistant S aureus.

The length of antibiotic treatment for osteomyelitis is largely empiric and recommendations have been evolved based on clinical experience. A total of three to four weeks of antibiotics is agreed to be the minimum length of treatment required for uncomplicated osteomyelitis that has not required surgical intervention. In the older orthopaedic literature, this was usually given intravenously for the whole period of treatment. Over the last twenty years, a number of retrospective series have reported good results with sequential-intravenous and oral therapy. This has been confirmed by a recent prospective study carried out in Finland. Fifty children with culture-proven osteomyelitis were treated with intravenous antibiotics for an average of 4 days followed by oral antibiotics for an average of 23 days. There were no adverse sequelae at one year and the need for one surgical procedure did not adversely affect outcome. In these children, the C-reactive protein had resolved to normal by an average of 9 days while the ESR took an average of 29 days to normalise.

Waiting for normalisation of the ESR is an overly cautious end-point and the initial length of treatment with intravenous antibiotics should be determined primarily by the clinical response over the first week. In uncomplicated osteomyelitis the C-reactive protein often normalises by day 8. However, antibiotic treatment should be continued orally for a total of 3–4 weeks, as an antibiotic duration of less than 3 weeks is associated with increased recurrence rate. Bactericidal levels have been promoted for use in monitoring oral medication but have not been widely used due to problems in interpretation. Nelson has pointed out that measured antibiotic levels may not always reflect true serum levels.

Failure to respond to intravenous antibiotics after 48 to 72 hours indicates either antibiotic resistance or the development of a sub-periosteal abscess that will require surgical drainage. In general, surgical incisions to drain osteomyelitis should be extensile and not directly over the subcutaneous surface of a bone. We routinely close the wound after the first drainage procedure but if repeat procedures are required, will leave the wound open, although the bone should not be directly exposed.

A requirement for an additional surgical drainage procedure after the initial one is predictive of an adverse outcome as is an axillary temperature >37.4°C for >7 days, marked swelling or warmth >10 days, local pain or decreased mobility >10 days, and more than one focus of osteomyelitis or septic shock. A C-reactive protein level above 80 mg/litre on day 5 of admission also predicts a complicated course or poorer outcome. In these cases, intravenous antibiotics should be continued until all the clinical findings are resolved and the duration of total antibiotic treatment extended to 6 to 12 weeks.

A small number of children will have overwhelming disseminated infection and will require return to the operating room at 48 hour intervals for drainage of pus and progressive debridement of inflammatory tissue and dead bone. Toxic shock syndrome, staphylococcal pneumonia and/or endocarditis and septic thrombosis of the inferior vena cava have all been reported in association with staphylococcal musculoskeletal infection and should be looked for in any critically ill child. In these children, intravenous antibiotic treatment will need to be prolonged for 3 to 6 months and coupled with early intensive care monitoring. Despite early antibiotic administration and drainage of sub-periosteal collection as required, adverse sequelae such as pathological fracture and development of chronic osteomyelitis with sequestrum and draining sinuses are still seen in this group of children (Fig. 1). Interestingly, delays in diagnosis or antibiotic or surgical management do not explain why some patients develop sequelae suggesting that interactions between the host immune system and infecting organisms are also important in determining the outcome.

ACUTE SEPTIC ARTHRITIS

This may occur at any age and in any joint but is particularly common in children in the hip and knee. The incidence has been reported to be 6.5 per 100,000 in Finland with a peak incidence in the early years of the first decade. Immuno-compromised hosts may have a higher incidence, particularly those suffering from inflammatory arthritis of any type. Two recent articles have also reported an increased incidence of septic arthritis in children who have haemophilia and are HIV positive.

Pathology

There is an acute inflammatory reaction with an outpouring of white cells into the joint fluid and release of proteolytic enzymes. Degradation of the articular
Figure 1 13 year old boy with multi-focal osteomyelitis involving left proximal femur and hip treated by athrotomy and washout. (a) Antero-posterior radiograph of the pelvis six months after the disease onset shows lytic changes in the femoral neck consistent with proximal femoral osteomyelitis. (b) Anter-posterior radiograph of the pelvis at fourteen months shows extensive bone loss in the proximal femur and development of an adduction contracture. (c) CT scan at fourteen months shows the extent of the bone and articular cartilage loss in the left proximal femur.
cartilage begins within 8 hours of infection manifested by glycosaminoglycan and collagen breakdown mediated via polymorphonuclear cells and cytokines secreted by the chondrocytes. Antibiotic treatment alone, even instituted as early as eight hours, fails to totally prevent articular cartilage degradation in animal models. Joint washout and antibiotics is therefore the gold standard of management. In certain anatomical sites the bony metaphysis is intra-capsular and bone infection may lead to a septic arthritis, e.g., upper end of femur, proximal humerus. In neonates, metaphyseal osteomyelitis is often associated with septic arthritis due to the presence of transphyseal blood vessels that disappear by age 6 to 12 months. Sixty to 100% of neonates with septic arthritis will have adjacent osteomyelitis.

Clinical Picture

The most important feature is a hot, swollen joint which is painful on any movement. Such a finding indicates a septic arthritis until proved otherwise. In the neonate this disorder will present as a so-called pseudo-paralysis of one limb and this invariably should give rise to suspicion of a septic arthritis particularly in the shoulder or hip.

Investigations

The investigations are similar to those required in osteomyelitis. However, plain X-rays and bone scans are less helpful. Four clinical features and lab investigations have been shown to discriminate well between a septic hip and an irritable (or non-infected) hip. These are severe spasms, localised tenderness, pyrexia greater than 38°C and ESR greater than 20. A combination of any two of these produces a specificity of 91% and a sensitivity of 95% for sepsis. The use of ultrasound has been reported to be helpful in identifying effusions in deep joints such as the hip. However, McGoldrick et al. have reported false negatives in the only blinded trial in the literature. As well, ultrasound cannot distinguish between a sterile effusion and infected fluid. Neither the quantity nor the echogenicity of the joint fluid are good indicators for infection and therefore, aspiration is always required to exclude infection.

Treatment

Aspiration and washout of the joint is essential. A white cell count of greater than 40,000 in the synovial fluid exceeds 90% sensitivity and specificity in differentiating septic arthritis from other forms of arthritis. However, acute monarticular inflammatory arthritis can also have a white cell count of greater than 50,000. Measurement of glucose concentration, protein and lactate levels in the synovial fluid are of limited diagnostic value. Equivocal cell counts can be seen when the patient has already been treated with antibiotics or very early in the disease process and it is our policy to wash out any joint in which turbid fluid is aspirated from the joint. Washouts of deep joints such as hip and shoulder should be by open arthrotomy. However, a case can be made for arthroscopic washout of the knee. Synovial biopsies should be taken at the same time, as sometimes organisms can be grown from these or an alternative diagnosis made based on histology.

The infecting organisms are similar to those detected in acute osteomyelitis. The antibiotic management is similar to that of acute osteomyelitis, and again there is evidence from retrospective studies that sequential intravenous-oral antibiotics for 3 to 4 weeks produces satisfactory long-term outcome.

The prognosis of septic arthritis diagnosed early remains good. However, neonatal sepsis continues to have a poorer outcome with sequelae such as avascular necrosis, limb shortening and angular deformity. Long term follow-ups of neonatal sepsis have shown that growth disturbance may not be evident until a mean age of nine years.

DISCITIS

Discitis is defined as infection in the disk space. However, MRI imaging has shown that the signal changes are not only in the disk but also in the end plates of adjacent vertebrae. It is thus better thought of as a vertebral osteomyelitis with spread to the adjacent disc. The lumbar spine is most commonly involved, although thoracic and cervical spine involvement has been reported. The child is usually below the age of five although discitis has been reported at all ages.

Clinical Setting

Discitis can present as refusal to walk, general irritability or abdominal pain in an otherwise well child. An elevated temperature occurs in only a minority. The white cell count is often normal but in over 90% of children, the ESR will be elevated. In older children, complaints of back, lower extremity or neck are more common. Due to the vague nature of
the presentation, it is common to see a delayed presentation, with the diagnosis being delayed by up to 2 months in some studies.\(^9\)

Pathology

Discitis represents a concomitant two-level anterior vertebral osteomyelitis with disk involvement. Infection begins in the metaphyseal bone near the vertebral end-plate and spreads via vessels that communicate with the intervertebral disc and with vessels from adjacent vertebrae at the periphery of the disk.\(^9\) Lytic destruction of disc material is seen, which is similar to the destruction of bone seen in acute osteomyelitis.

Investigations

Plain X-rays of the spine should be the first investigation. Often there is disk space narrowing at the affected level by the time of presentation, but in early presentations, a bone scan is very helpful in localising the disk space involved. An MRI scan can show dramatic changes including disc prolapse but these findings do not require surgical management in the absence of hard neurological signs. In general the findings on an MRI are indistinguishable from those observed in adult patients with the diagnosis of vertebral osteomyelitis.\(^9\) The infecting organism is usually Staphylococcus aureus and current literature agrees there is little need for disk space aspiration.\(^9\)

Treatment

Treatment is usually intravenous followed by oral antibiotics for four to six weeks. The back can be immobilised in a brace for comfort but most children do not require this. Most will go on to have persistent disk space narrowing or fusion but the long term sequelae are few.\(^9,92\)

REFERENCES


