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Editorial Article

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Neonatal Osteomyelitis and Septic Arthritis

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The purpose of this editorial is to perform an extensive review of the relevant international literature about neonatal osteomyelitis and septic arthritis, to indicate the value of clinical suspicion and of regular osteoarticular examination for the early diagnosis and treatment of the disease in the septicemic neonate or in the preterm infant, even when initial empiric antibiotic therapy is used, and to present illustrative cases.

Acute osteomyelitis varies in its clinical characteristics according to the age group of the patient, so the three separate clinical entities, including osteomyelitis of the infant, child and adult, are attributed to the changing vascular arrangement at each age limit. The neonatal period, within the infant group, is particularly susceptible to osteomyelitis due to significant predisposing pathophysiologic factors and standard techniques of care of the newborn during birth and in the first weeks of life. Therefore, neonatal osteomyelitis, occurring during the first 2 months of life, should be distinguished and described separately from infantile osteomyelitis [1-4].

Fever or other signs of systemic infection in the newborn may be due to an underlying anatomic, metabolic or immune system abnormality. The hematology of neonates seems to render them more susceptible to infection. This may be related to hypofunction of the antibody, complement and phagocyte pathway, which is a temporary condition in the newborn [5, 6].

The source of bone infection in the newborn may be:

1. A congenital infection with onset in uterus,
2. An infection acquired during the birth process from the maternal genital tract and
3. An infection acquired during nursery (nosocomial/hospital-acquired infection) and household (community-acquired infection); nursery and household infections are spread through either human carriers or contaminated materials and equipment [7-9].

Complications of pregnancy, labor or delivery may precede the occurrence of neonatal osteomyelitis in one half of patients. Most cases of neonatal osteomyelitis arise as a consequence of bacteremia or in the course of neonatal septicemia. Neonates who develop bacterial sepsis often have specific risk factors. Among these factors is preterm birth at a gestational age less than 37 weeks, which is the most significant risk factor, respiratory distress syndrome, low birth weight (<1,500 grams), anemia, prolonged rupture of maternal membranes, maternal intraamniotic infection, traumatic delivery, fetal anoxia, etc [10-14].

Microorganisms may reach bones of the newborn by:

1. Hematogenous dissemination, which is the most common route of bone infection, defining acute hematogenous osteomyelitis,
2. Direct inoculation (ventilatory support, lumbar puncture, great toe or heel capillary blood sampling, umbilical and intravenous or intraarterial catheters, etc),
3. Extension from adjacent soft tissue infection (skull osteomyelitis from infected cephalhematoma, scalp abscesses, etc) or distant infection (pneumonia, meningitis, omphalitis, paronychia, mastitis, pustular dermatitis, purulent rhinitis, operative sites, intramuscular injections, etc) and
4. Maternal bacteremia with transplacental infection (syphilis is the most characteristic type) [3, 10, 15-18].

Metaphysis is the most vascular area of the long bones, while the nutrient artery is the main route for bacteria causing osteomyelitis. The capillaries adjacent to the growth plate, in its metaphyseal side, are the last ramifications of the nutrient artery. They reach, turning down in acute loops, large sinusoidal veins, so the blood flow slows down. Under these circumstances, pathogenic bacteria or cancerous cells may find the best conditions for development. In addition, there are relatively few phagocytic cells in the metaphyseal vessels. These anatomic findings may explain the predilection of osteomyelitis for the metaphysis of the long bones. The isolation of the epiphysis from the metaphysis, due to the growth plate, provides protection for both the epiphysis and the joint in children. However, transphyseal vessels appear to be present in many long bones during infancy. The transphyseal vascular barrier is first obvious at the age of 8 months and is definitely established at 18 months of age, although this varies from bone to bone and seems to be related to the appearance of the secondary ossification center. Therefore, considering the vascular anatomy, the infant becomes a child approximately at the age of 12 months [19-23].

The diagnosis of septicemia may be difficult because of the often nonspecific neonate's response to infection. The earliest signs may

be subtle. Changes in color, tone, activity and feeding patterns, poor temperature control or simply a general feeling that the neonate is 'not doing well' may only be evident. Other potential early signs are abdominal distention, apnea and jaundice. These signs may also appear at later stages but they may also be seen in healthy premature newborns. Late signs include grunting, dyspnea, cyanosis, arrhythmias, hepatosplenomegaly, petechiae, seizures, buldging fontanelles and irritability. Focal signs of meningitis or pneumonia may also be diagnosed [24].

Infants treated in neonatal intensive care units usually suffer from unifocal osteomyelitis and the femur is the most frequently affected bone. However, multifocal (polyosteal) disease is also quite common and it is frequently unsuspected [25]. Osteomyelitis of the newborn infant may appear as two distinct clinical syndromes [26]. The severe form presents with systemic manifestations of sepsis, including multiple sites of osteoarticular and visceral involvement. The diagnosis of the osteoarticular infection in the severely ill infant may be easily missed or underdiagnosed. The benign form, which is the most common type, may also involve one or more skeletal sites. It is due to a mild transient bacteremia that arises peripherally and causes only minimal inflammation and suppuration. The clinical diagnosis of osteomyelitis and/or septic arthritis is difficult even when infection is localized in the distal extremities. There is usually little or no clinical evidence of infection, apart from local swelling or disuse [27, 28]. Disability, following both syndromes, may be indicated by abnormal posture, pain on passive movement and diminished spontaneous or reflex movement of the affected extremity, either because of pain (pseudoparalysis) (Figure 1) or because of weakness caused by an associated neuropathy (Figure 2). Cases with unusual localization or clinical presentation have also been encountered [29-39].

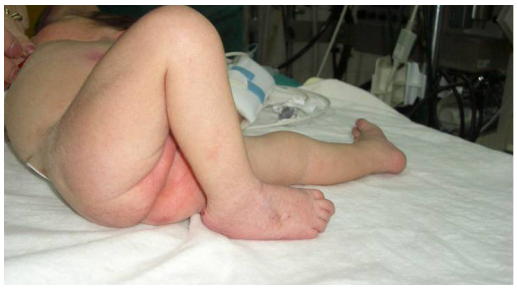

Figure 1: Clinical appearance of a 7-day-old girl with pseudoparalysis of the left leg due to septic dislocation of the hip.

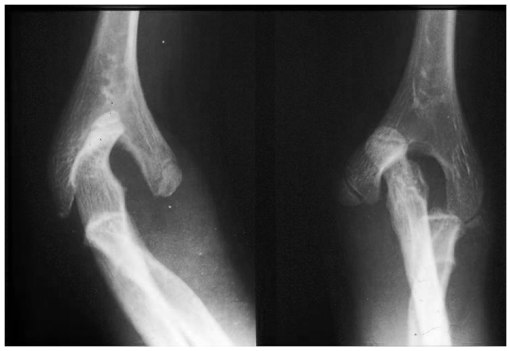

Figure 2: Radiographs of an 11-year-old boy who suffered from multifocal neonatal osteoarticular infection. It was complicated by complete deformation of the left elbow, both humeral condyles are grossly deformed, and paralysis of the radial nerve. The radiographic appearance of the distal humerus is consistent with a fish-tail deformity. Fishtail deformity of the distal humerus has rarely been reported as a complication of trauma in children but it has never been previously recorded as a sequel of acute osteoarticular infection.

Septic (pyogenic) arthritis may occur via:

1. Hematogenous invasion,
2. Extension from an adjacent metaphysis through the growth plate, via vascular channels, into the epiphysis and further in the joint space,
3. Erosion of the thin metaphyseal cortex in an intraarticular metaphysis (particularly of the proximal femur, humerus and radius as well as of the distal lateral tibia) and
4. Direct inoculation through penetrating injuries, especially of the knee joint.

Presenting signs and symptoms may differ from those encountered in older children. They may be mild or there may be complete lack of systemic signs, especially if antibiotics have masked the signs, resulting in diagnostic challenge or significant delay. Septic arthritis is a real emergency in neonates and infants. Joint aspiration is mandatory in children with a suspected joint infection, whatever the age of the patient [40-48]. On the other hand, the absence of aspirable fluid contents in the hip joint does not rule out septic arthritis in neonates, while in cases with false-negative aspiration, a delay in appropriate surgical treatment is typical [49].

Laboratory tests (C reactive protein, erythrocyte sedimentation rate, white cell count, blood and joint cultures) and conventional radiographic studies play a crucial role in evaluating diagnosis of neonatal osteomyelitis and septic arthritis. It may be prudent to suggest that every septicemic neonate should have a pelvic radiograph to exclude occult hip sepsis [50] or even a complete skeletal survey to seek additional silent areas of involvement [51]. Ultrasonography, arthrography, computed tomography, magnetic resonance imaging (MRI) and radionuclide studies can all contribute to establishing the diagnosis due to the relatively late appearance of the primary radiographic signs of infection [52-55].

The primary radiographic signs of osteomyelitis are not pathognomonic. The first sign is swelling due to oedema within the soft tissues. Periosteal reaction may appear within 3 days of the onset (Figure. 3). Periostitis may rapidly become exuberant. In the early stages of septic arthritis, a distention of the shadow of the articular capsule, which is an intramuscular plane, may be observed in the radiographs. A convexity of the fat pad, implying distention of the hip joint with fluid, is usually evident on the hip ultrasonography [56, 57].

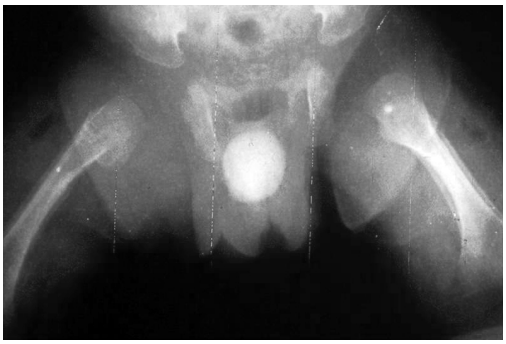

Figure 3: Radiograph of a 2-month-old boy, suffering from septicemia, multifocal neonatal osteomyelitis and bilateral hip septic arthritis. Periosteal reaction and new bone formation on both sides of the femoral shafts is evident.

Imaging investigation of the hip, further than plain radiographs, is recommended before the appearance of the ossific nucleus of the femoral head to differentiate septic arthritis from congenital hip dislocation, from neonatal separation of the proximal femoral epiphysis secondary to obstetric trauma [58, 59] or from a pathologic epiphyseal separation due to osteomyelitis or septic arthritis [60, 61].

In cases with pseudoparalysis, the clinical course and the radiographic examinations are generally sufficient to rule out diseases with muscular imbalance, whether paralytic (poliomyelitis) or spastic (cerebral palsy). Congenital syphilis, which is an intrauterine infection that usually manifests shortly after birth, may also present with pseudoparalysis or joint swelling. The radiographic findings of congenital syphilis, usually including diaphysitis and metaphyseal changes (Figure. 4), are frequently indistinguishable from bone alterations observed in infants with multicentric pyogenic osteomyelitis [62, 63]. Similar radiographic osseous changes have also been noted at birth in infants with congenital tumors or leukemia [64].

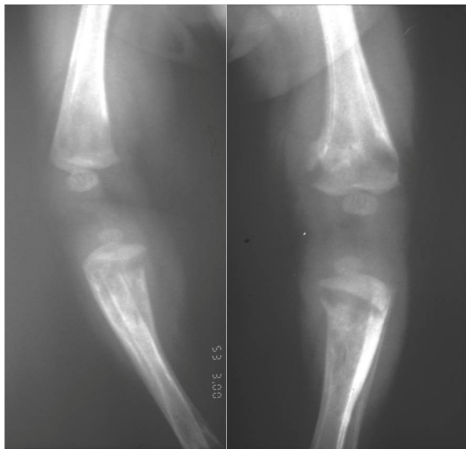

Figure 4: Radiograph of a 5-month-old girl with congenital syphilis showing bilateral femoral periosteal reaction and metaphyseal symmetrical erosions in the upper tibiae (Wimberger's sign) and distal femora. Exuberant callus formation is evident on the medial side of the left distal femoral metaphysis.

Joint aspirate and/or blood culture should be obtained before starting antibiotic treatment. In the newborn, staphylococcus aureus, hemolytic streptococci and aerobic Gram-negative rods are most commonly found. The increasing prevalence of methicillin-resistant staphylococcus aureus is an emerging problem in pediatrics [65-75].

The recorded differences of the normal skin flora between premature infants and full-term babies may be due to the higher temperature and humidity that surrounds the skin in the former as well as to the plentiful supply of nutrients. The skin at this age is most likely to be immature without many of the natural defenses. In most cases, the contaminating organisms are the major components of the strains that are usually isolated from the flora of the nose, skin or umbilicus. In hospital environments, there are generally more potential pathogens in the surroundings and so, less common organisms could colonize various areas and multiply, at least for a short time [76-81].

Early recognition of the osteoarticular infection in neonates, and prompt institution of surgical drainage and parenteral antibiotic treatment minimizes permanent damage. Antibiotics cannot replace surgical drainage in cases with pus collection due to osteomyelitis or septic arthritis. Pyogenic pus is severely injurious to cartilage. The risk for long-term complications is greatest if the physeal plate is damaged. Septic arthritis, especially when it is associated with osteomyelitis or when early decompression by open surgical arthrotomy and irrigation are delayed, can cause severe complications and permanent disability (Figure. 5, 6, 7). In the hip, complications may include cartilage necrosis, ischemic necrosis of the proximal femur, pathologic fractures, premature symmetrical or asymmetrical closure of the proximal femoral growth plate, hip subluxation or dislocation (Figure. 8a), acetabular dysplasia (Figure. 8b), premature closure of the triradiate cartilage (Figure. 9) and premature joint degeneration [82-84]. Damage to the triradiate growth plate of the acetabulum in suppurative arthritis of the hip in neonates is a reliable indication that the femoral head has been destroyed [85, 86]. On the other hand, in the shoulder, late diagnosis is associated with deformation of the humeral head and shortening of the humerus causing marked cosmetic abnormality but negligible functional loss (Figure. 10) [87-89].

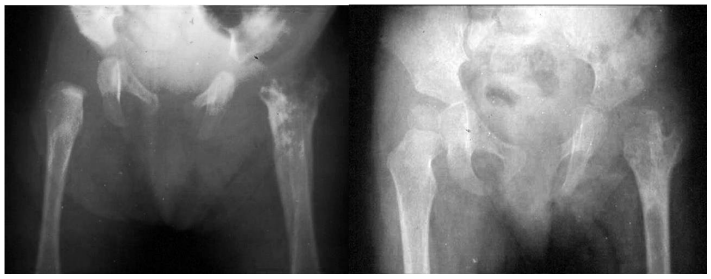

Figure 5: Radiograph of a 4-month-old girl with neonatal osteomyelitis and septic dislocation of the left hip treated by open drainage and irrigation. Complete destruction of the proximal femur and extensive periosteal reaction with considerable new bone around the femoral shaft is evident.

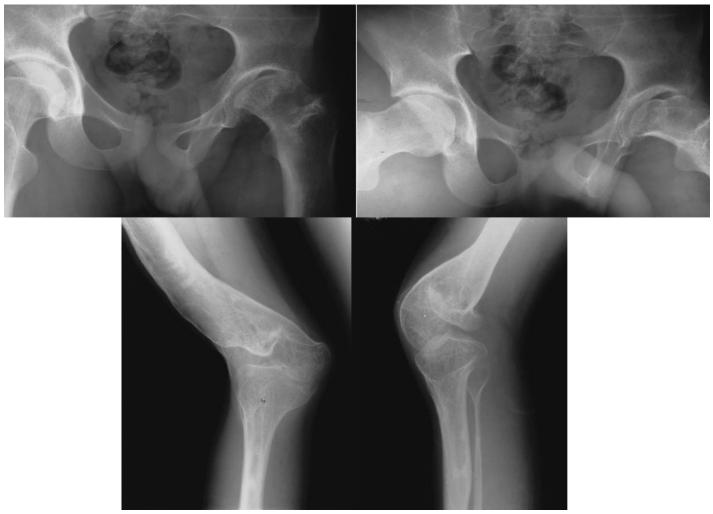

Figure 6: Radiographs of a 17-year-old boy who suffered from multifocal neonatal osteoarticular infection. Hip, knee and shoulder septic arthritis was treated surgically. The left femoral head is flattened and considerably deformed. Complete destruction of the lateral femoral condyle and severe valgus deformity of the left knee is evident.

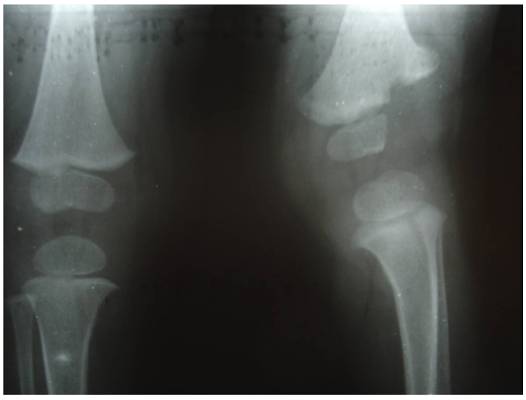

Figure 7: Complete destruction of the lateral part of the lower femoral epiphysis and severe valgus deformity of the left knee due to multifocal neonatal osteoarticular infection.

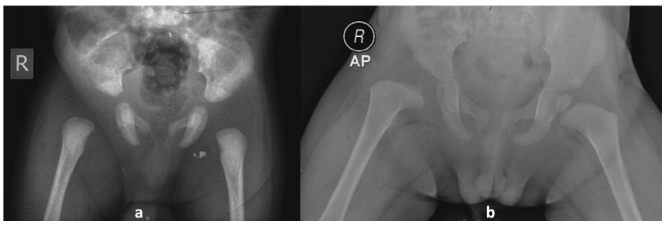

Figure 8: Radiograph of a 1-month-old boy showing upward and lateral displacement of the right femur and increased medial gap due to neonatal septic arthritis of the hip. There is no evidence of acetabular dysplasia (a). At 1-year there is residual deformity of the proximal femur associated with delayed right acetabular growth, leading to acetabular roof deficiency (flat/horizontal acetabulum), which may be defined as secondary, postinfectious, acetabular dysplasia (b).

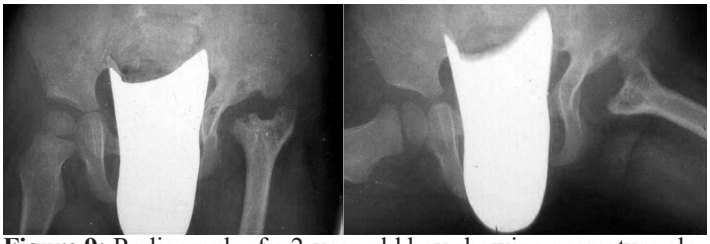

Figure 9: Radiograph of a 2-year-old boy showing premature closure of the left triradiate acetabular growth plate due to neonatal osteomyelitis and septic arthritis of the hip. There is complete destruction of the femoral head and trochanteric overgrowth.

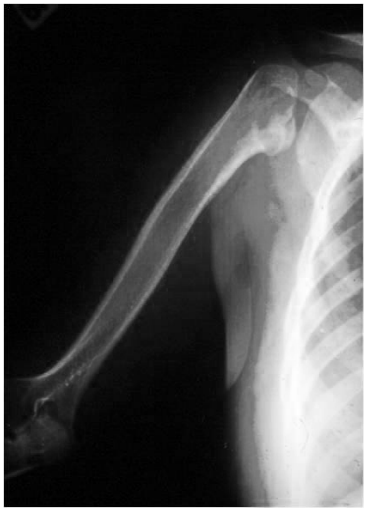

Figure 10: Radiograph of a 20-year-old female with complete deformation of the right humeral head and shortening of the humerus. She suffered from multifocal neonatal osteomyelitis and septic arthritis of the shoulder, which was treated surgically. Growth abnormalities were due to premature arrest of the proximal humeral growth plate.

Before the advent of antibiotics, the incidence of infection of the long bones was 10% in infants with bacteremia. A marked decrease followed early recognition and effective empiric antibiotic therapy to prevent bacterial sepsis in the preterm infant. However, the incidence of moderate to severe handicaps in survivors remained unchanged at around 20% [90]. The prognosis for the skeletal lesions among survivors of the severe form is not different from the prognosis for the benign form. The improved survival rate directed greater attention to a high incidence of residual joint deformities, particularly with hip and knee involvement or with delayed diagnosis. All patients should be followed till skeletal maturity to observe for growth arrest, destruction of the epiphysis and disturbance of joint development leading to premature joint degeneration [8, 91-93]. Restitution of the epiphysis and growth disturbance is unpredictable on the basis of radiographic findings during infancy [94]. The full clinical consequences of neonatal osteomyelitis may not be apparent for months to years (Figure. 11a). Although the initial infection may be frequently believed to be successfully treated in the neonate, its clinical effect on the growth plate cannot be fully appreciated (Figure. 11b) [95]. In the proximal femur and

humerus, damage to the physeal plate may be due either to the abscess formation or to ischemia following occlusion/tamponade of the major intraarticular arterial pathways [96]. The value of MRI to visualize significant insult to the growth plate following osteoarticular infection has already been documented, so as preventable measures may be undertaken to avoid the catastrophic long-term alterations of longitudinal growth producing angular deformities [97]. On the other hand, a remarkable potential for recovery and regeneration has been observed in patients with involvement of the distal femoral or the proximal tibial epiphysis [98-101]. Therefore, it might be prudent to treat these bony epiphyseal defects expectantly since the initiation of reossification can begin several years after the infection [102]. Arthrograms have been used to evaluate accurately the epiphyseal shape and volume [103].

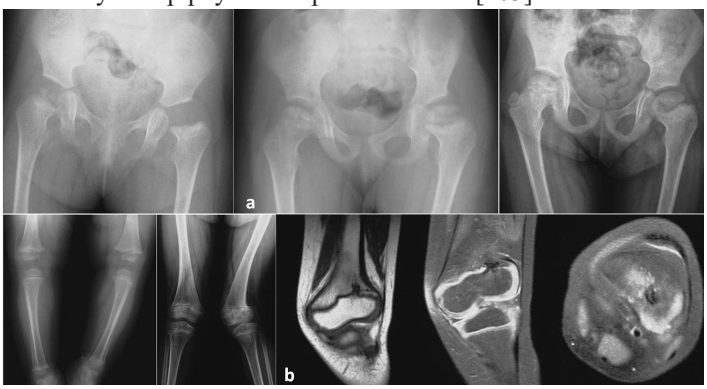

Figure 11: A girl, former preterm baby, who received initial empiric antibiotic therapy, which potentially obscured the diagnosis of neonatal osteoarticular infection. Hip radiographic evaluation at 11 months indicated absence of the ossification nucleus of the left femoral head and two ossification centers of the right femoral head. Radiographs at 5 years of age indicated almost complete recovery of the right femoral head and deformation, due to ischemic necrosis, of the left proximal femur (a). No obvious abnormality is evident on the knee radiograph at 11 months of age. Radiograph indicating valgus deformity of the left knee at 5 years of age. A physeal bridge is evident in the lateral aspect of the distal femoral growth plate on the MRI (b).

Various surgical modalities are currently available to reduce and stabilize the damaged proximal femur and to reconstruct its articulation with the acetabulum. Arthrodesis, usually undertaken with a moderate amount of valgus, has been extensively used in the past. Open reduction should be performed if there is sufficient femoral head and neck to achieve a stable reduction. Otherwise, a trochanteric arthroplasty seems the procedure of choice followed by a proximal femoral varus osteotomy, in cases with progressive subluxation. If successful, it will provide a stable joint, less length discrepancy and a limited motion, which seems preferable than accepting a high iliac dislocation. In addition, joint replacement will be easier to perform, if indicated at a later age [104-106]. However, any surgical treatment for severe sequelae must be regarded as a measure that temporarily improves clinical function and delays the more definitive procedures, which are reserved for adult patients [107]. Other results suggest that reconstructive efforts following hip joint sepsis, designed for relocation of an inadequate femoral head, for persistent dislocation or for transference of the greater trochanteric epiphysis into the acetabulum, may not yield results superior to nonoperative treatment [108].

It should be emphasized that it is wise to encourage activity, as much as possible during childhood, as this will stimulate growth at the lower femoral epiphysis. Thus, undue shortening, following premature distal femoral growth plate fusion from prolonged attempts at treatment and immobilization at too early an age may be avoided [40].

Late reconstructive surgery is difficult and does not always give the desired functional and anatomical improvement. Therefore, the most important factor influencing the end result is the time between beginning of symptoms and treatment. This is the only factor that can be changed to improve the ultimate outcome of neonatal osteomyelitis and septic arthritis [109, 110].

Conclusion

In conclusion, a wide variety of risk factors predispose neonates to bone and joint infection. In neonates, osteomyelitis and septic arthritis usually occur at the same time. Fever and other presenting signs and symptoms, commonly encountered in older children, may be minimal or absent. This occurrence may be associated with a significant diagnostic challenge or delay. The clinical suspicion of a potential osteoarticular infection and the subsequent regular clinical examination of the skeletal system are of outmost importance in the septicemic neonate as well as in preterm infants, even when initial empiric antibiotic therapy is used. Early diagnosis and adequate treatment are the most important prognostic factor to achieve a favorable outcome. It should be emphasized that significant residual deformities, especially of the hip, detected on the radiographs are not commonly associated with clinical symptoms of proportional severity in children but they worsen significantly in adulthood. Therefore, it may be prudent to consider that the pediatric orthopaedic surgeon should focus on the clinical rather than on the radiographic findings, and that all children with a history of neonatal osteomyelitis and/or septic arthritis should be followed till skeletal maturity and even longer.

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