

## Short therapy in a septic arthritis of the neonatal hip

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### Abstract

Septic arthritis (SA) is a serious joint infection associated with significant morbidity that can cause permanent damage with articular cartilage destruction, osteonecrosis and lifelong deformities if not diagnosed and treated promptly. In neonates, because of the paucity of signs and symptoms, SA is difficult to diagnose. The treatment for SA in children is empirical antibiotic for weeks, initially intravenously, and surgical (arthrotomy) in particular for the hip and shoulder because of the high risk of sequelae in these joints. Actually, there isn't a consensus about the duration of antibiotic treatment, because of the lack of powered studies, and a variable period from 2 weeks to 4 months has been suggested in the literature. Data in the neonatal population are very limited. We describe a case of neonatal hip arthritis with a good outcome treated with a short antibiotic course of 2 weeks.

### Introduction

Septic arthritis (SA) is a serious joint infection associated with significant morbidity that can cause permanent damage with articular cartilage destruction, osteonecrosis and lifelong deformities if not diagnosed and treated promptly.<sup>1</sup>

In neonates, because of the paucity of signs and symptoms, SA is difficult to diagnose. In the literature the incidence of SA in children younger than age 3 months is reported only for a South African population, 1 in 20,000,<sup>2</sup> in the US infants aged up to 1 year 3.1 to 12.5 per 100,000,<sup>3</sup> and in India, 1 in 1,500 newborns, including also patients with osteomyelitis.<sup>4</sup>

The causative organisms most commonly identified are: *Staphylococcus aureus* in neonates and children above 2 years of age, *Hemophilus influenzae* type b (Hib) is the most common organism detected in children younger than 2 years of age.

With the introduction of conjugated vaccine for Hib Gram-positive organisms, particularly *S. aureus* became the predominant in all age groups.<sup>5</sup> Sreenivas *et al.* in a descriptive study in a neonatal population with septic arthritis described Gram-negative as more common causative agents with *Klebsiella pneumoniae* in 9/29 patients.

The treatment for SA in children is empirical antibiotic for weeks, initially intravenously, and surgical (arthrotomy) in particular for the hip and shoulder because of the high risk of sequelae in these joints. Actually, there isn't a consensus on the duration of antibiotic treatment, because of the lack of powered studies, and a variable period from 2 weeks to 4 months has been suggested in the literature depending on patient age, causative agent, and localization of the infection. Data in the neonatal population are very limited. We describe a case of neonatal hip arthritis with a good outcome treated with a short antibiotic course of 2 weeks.

### Case Report

A 6-day-old term male infant was brought to the emergency department by his parents for evaluation of irritability on passive movement of the right hip.

The infant was born via spontaneous vaginal delivery to a 28-year-old gravida 2 para 1 mother at 38 weeks. Pregnancy was complicated by group B *Streptococcus* colonization which was not known during the delivery so no antenatal prophylaxis was performed. He was 2800 g at birth, and received routine care in the delivery room. Metabolic screening tests and bilirubin controls were performed as routine by heel samples and were normal. Physical examination revealed an instability of the left hip, and he was discharged from the hospital after 72 hours with the indication to anticipate the ultrasound of the hips within the second month of life.

On the day of presentation, his parents noted a reduction of the movements of the lower right limb, so they referred him to the emergency department. Physical examination at the time of presentation revealed an afebrile infant, with vital parameters in the rule except for the absence of active movement and irritability to passive mobilization of the lower right limb. The baby was holding the right leg flexed with slight abduction and external rotation. The right hip was also noted to be slightly swollen without skin hyperemia or heat to the touch.

The complete blood count was unremarkable, hematocrit 44%, platelets

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273,000/L, and white blood cell count 13180/L, C-reactive protein was 13.3 mg/L (normal values <10 mg/L). The presence of fractures was excluded by radiography of the pelvis and the right femur. Ultrasound documented an intra-articular circumferential effusion, with echogenic content, in the right coxo-femoral area, with a maximum thickness of 3.4 mm (Figure 1).

The baby was admitted to the general pediatrics service for additional evaluation and management. After blood and urine cultures were obtained, antibiotic therapy was started with endovenous amikacin and cef-tazidime. A magnetic resonance was performed confirming the presence of endo-articular effusion in the right coxo-femoral area with articular capsule relaxation and signal characteristics compatible with the presence of corpusculous component. No sign of adjacent bone or soft tissue infection was present. These findings were suggestive for arthritis, so, during the second day of hospitalization, ecoguided drainage of intrarticular fluid was performed with the suction of 1 mL of serous fluid.

The culture of the articular fluid was positive for *Staphylococcus epidermidis* 500 UFC/mL, while the urine culture was positive for group B *Streptococcus* 500 UFC and the blood culture was negative. From the third day of hospitalization, there was a clear improvement in the right hip objectivity, with complete normalization of mobility and disappearance of joint effusion

at the ultrasound repeated after 7 days of antibiotic therapy. The C-reactive protein was negative at the 6th day of hospitalization. Antibiotic therapy with endovenous amikacin and ceftazidime was stopped after 14 days and the infant was resigned with orthopedic follow-up. At 1 week, 1 month, 3 and 6 months follow-up visit after discharge his conditions were good with normal right hip objectivity without pain or irritability to active or passive mobilization of the lower right limb.

## Discussion

Neonates have a high risk of hip SA for their particular anatomic characteristics of this joint, in particular because transphyseal vessels carry blood directly in the joint via the metaphysis and in the epiphysis, favoring the entry of bacteria from the blood vessels in this joint.<sup>6</sup>

The diagnosis is very difficult in neonates because the mild clinical symptoms and physical signs are often subtle and the laboratory data may be within normal limits. At this age the clinical evaluation may not be helpful because they may present only irritability, anorexia and mild or absent limitation of movement. The fever is not always present because neonates may have hypothermia. Narang *et al.* described a population of 25 neonates, mean gestational age 34.5 (range 27-40) weeks and mean birth weight 2269 (range 990-4750) gms, with diagnosis of septic arthritis/osteomyelitis and reported that the limitation of movement (64%) and local swelling (60%) were the most common presentation.<sup>4</sup>

Sreenivas *et al.* reported a population of 29 neonates with SA, mean age at presentation was 23.8 days with a female predominance (58.6%), the common symptoms were fever (100%), involved limb in position of ease/pseudo-paralysis (69.0%), swelling (79.3%) and warmth (75.9%).<sup>7</sup>



Figure 1. Joint effusion.

A timely diagnosis and an effective treatment are the most important variables for achieving a favorable outcome in children and even more so in neonates with SA.<sup>8</sup> Delayed diagnosis can lead serious sequelae which may result in lifelong disability for the affected individuals.

Blood examination is a valid instrument for the diagnosis. Complete blood count with differential, C-reactive protein (CRP) and blood culture are mandatory. CRP is described by Levine *et al.* as the better independent predictor of SA, they analyzed a population of 39 patients with SA (mean age 4.6 years old) to determine the test characteristics of CRP in the diagnosis of septic arthritis and concluded that in comparison to ESR, CRP is a better independent predictor of disease. CRP is a better negative predictor than a positive predictor of disease. Indeed, if the CRP is <1.0 mg/dL, the probability that the patient does not have septic arthritis is 87%.<sup>9</sup> The mean age of Levine's study population is bigger than neonatal age so we aren't sure that CRP alone have the same predictive value and others study are necessary. In our case CRP was 13.3 mg/L according with Levine's evidence.

Diagnosis is made also by imaging studies and arthrocentesis. Ultrasound is a noninvasive and sensitive instrument to diagnose hip effusion, and it is a common imaging modality for a pediatric population and particularly in the neonatal age.<sup>10</sup> Ultrasound is a noninvasive, rapid and no-radiation test, confronting with MRI, it not requires general anesthesia or sedation. Laine *et al.* in a population of 33 pediatric patients, 26 with a diagnosis of SA alone and 6 with SA and osteomyelitis (OM), demonstrated that once a hip effusion is confirmed on ultrasonography, septic arthritis does not need advanced imaging (MRI) before arthrotomy and debridement.<sup>10</sup>

The evaluation of characteristics of joint fluid and culture examination is necessary in all suspected cases of SA of hip in neonates. It is useful to define the infective agents and to start an effective treatment. Moss *et al.* postulated that compatible with a joint effusion, with the indication to aspiration, was the presence of fluid adjacent to the entire length of the femoral neck measuring at least 5 mm in width. The authors described a population of 26 volunteers aged 20-37 years. We think that when there is a hip effusion associated with limitation of movement, swelling and warmth in a neonatal age patient the cut-off to the aspiration cannot be 5 mm like an adult population. In our case the effusion was 3.4 mm so we think that in a pediatric population when there is an evident effusion also smaller than 5 mm a joint aspiration is necessary, not

only for the diagnostic testing but also to reduce intra-articular pressure and decrease probability of epiphyseal ischemia.

Data about the culture results in neonatal septic arthritis in the literature are limited and not homogeneous. Sreenivas *et al.* in their case series observed that the most common microbiological agents were *Klebsiella pneumoniae* in 9/29 cases and no growth in 11/29. Analyzing data of Li *et al.*, in their review of 52 neonatal cases of septic arthritis they cultivated from pus or local tissue *Staphylococcus aureus* in 10 patients, *Klebsiella pneumoniae* in 3, and *Klebsiella oxytoca* in 1 child. In our case we isolated *Staphylococcus epidermidis* by articular fluid and group B Streptococcus by urine culture both sensible to the antibiotic therapy prescribed. We think that these data are related to the limitations and difficulties in the joint fluid aspiration and in general in microbiological culture in this population.

About the treatment in the literature there are many evidence and guidelines that invite to use antibiotic therapy for a long time, 25-29 days in the US,<sup>11</sup> 4-6 weeks in South America,<sup>12</sup> 31 days in Australia<sup>13</sup>, 3 weeks in UK,<sup>14</sup> 5 weeks in Iran.<sup>16</sup> Pääkkönen M and Peltola H. in a review in 2011 analyzing prospective randomized trials showed most cases of OM, SA and OM+SA healed with a total course of 3 weeks (OM, OM+SA) or 2 weeks (SA) of an appropriate antibiotic.<sup>16</sup> In particular in a prospective, randomized trial in 2009 they demonstrated in a population of 130 children that large doses of well-absorbed antimicrobials for <2 weeks and only 1 joint aspiration were sufficient for treatment of childhood septic arthritis, if there were good clinical response and C-reactive protein level normalized shortly after initiation of treatment. Relatively to the joint, antibiotics have a good penetrance, 1 hour after infusion the synovial concentration is similar to serum concentration.

## Conclusions

Our case demonstrated that also in the neonatal age the short therapy is efficacy for the treatment of SA when there is only one joint involved. The joint aspiration is mandatory when there is effusion on ultrasound examination, with a difference <5 mm compared with the contralateral. Further studies are necessary to indicate in pediatric population a cut-off in mm of amount of effusion that establish as mandatory the joint aspiration, this cut-off may be stratified for age and body size.

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