

Elbow Septic Arthritis caused by *Klebsiella pneumoniae* in a Newborn - Case Report and Literature Review

Roxana Filip¹, Dana Georgeta Laura Murariu², Ramona Avramia³, Florin Filip^{1*}

1. Faculty of Medicine and Biological Sciences, Stefan cel Mare University of Suceava, Romania

2. Suceava Emergency County Hospital, Romania, Romania

3. Synevo Laboratory, Suceava County, Romania, Romania

Abstract

Septic arthritis is a rare condition in children, especially in neonates. Early recognition and proper treatment are required to avoid serious complications. We present the case of a male newborn diagnosed with septic arthritis of the right elbow who was treated with repeated joint aspiration and i.v. antibiotics (Amikacin and Meropenem). Blood culture and joint cultures were positive for *Klebsiella pneumoniae*. The final outcome was good, with no apparent local or systemic complications. General considerations regarding this rare condition, etiology and treatment options are also included in the paper.

Keywords: septic arthritis, elbow arthritis, newborn, aspiration, *K. pneumoniae*

Received: 21st March 2022; Accepted: 8th June 2022; Published: 19th June 2022

Introduction

Septic arthritis represents the bacterial infection of a joint; it may occur in isolation or related to a local osteomyelitis with secondary spreading to the adjacent joint (1). Its incidence is reported to be between 5-12 in 100.000 persons (2), and it can result in disabling complications, such as joint destruction or deformity, or even the patient's death (3). Septic arthritis in neonates is characterized by low incidence and lack of specific symptoms, which may seriously delay the timing of diagnosis (4,5). The classic presentation in children is a sick patient with fever,

swollen and painful joint, limited local range of motion. Weight bearing is severely limited if the lower limb is involved. Differential diagnosis includes several conditions, such as: osteomyelitis, viral arthritides, and juvenile rheumatoid arthritis, Lyme disease or sickle cell anemia (6). Serum WBC, CRP, and ESR levels can help to differentiate between transient hip synovitis from septic arthritis of the hip, although the laboratory data must be carefully analyzed (7). The serum WBC may be elevated above $10 \times 10^3/L$, but the sensitivity is only 42-90%; the sensitivity of ESR differs based on the cut-off value that is selected, with a sensitivity of 66% for 15 mm/

* **Corresponding author:** Florin Filip, Faculty of Medicine and Biological Sciences, Stefan cel Mare University of Suceava, Suceava, Romania. E-mail: florin.filip@usm.ro

hr to > than 90% for 30 mm/ hr. A CRP level of > 10 mg/ L also has a sensitivity approaching 90%. Procalcitonin has also been suggested for diagnosis purposes, but it requires further studies before routine use (8,9).

Synovial fluid represents the gold standard test for diagnosing septic arthritis. Synovial fluid culture is the single most important test and should be ordered in all patients from whom synovial fluid is collected (10). It will demonstrate bacterial growth in 80% of cases of non-gonococcal septic arthritis. Some biochemical markers of the synovial fluid, such as proteins, glucose, lactate and lactate dehydrogenase, are used for diagnostic purposes. Synovial lactate levels over 10 mmol/L have been suggested by several studies to have the best diagnostic accuracy of all synovial fluid markers in patients with septic arthritis. Blood cultures should also be obtained in patients with septic arthritis, as they can identify the etiology of infection in case the synovial fluid culture is negative. They will be positive in 1/3 of the patients, and 14% of the patients with negative synovial fluid cultures will have a positive blood culture.

The clinical management of suspect cases of septic arthritis is well defined at this time. If a child with acute symptoms has elevated CRP (>20 mg/L) or ESR (> 20 mm/hr) values, a joint aspiration is performed to identify a purulent aspirate and obtain a sample for biochemistry and bacteriology. Blood cultures are also obtained, as stated above. US may be used to detect joint swelling the guide the joint puncture. Plain X-ray is not very useful in diagnosis, but it may rule out fractures and detect joint swelling. MRI is difficult to perform in many institutions because it requires anesthesia in infants, but it is very useful to identify adjacent osteomyelitis or an abscess.

Treatment must be started immediately after obtaining samples of synovial fluid and blood culture. First-line antibiotics include Clindamycin

(or Vancomycin in case of resistance to Clindamycin) and first- generation cephalosporins. Penicillin monotherapy in large doses can be used in case of infection with *S. pyogenes* and *S. pneumoniae*. Penicillins and cephalosporins can also be used for cases with *K. kingae*. In most cases, antibiotics are given as a short, 2-4-day course, of i.v. therapy, after which they can be administered orally if the clinical appearance is good and the CRP levels are declining. The total duration of the treatment is 2-3 weeks, depending on the local involvement of the adjacent bone. Dexamethasone and non-steroidal anti-inflammatory drugs (NSAIDs) are also used for their symptomatic action.

Surgery is a crucial part of the clinical management in children with septic arthritis. Repeated joint aspirations are recommended, and open arthrotomy is only reserved for cases which do not respond to this treatment. Another surgical option is arthroscopy, which can be used in older children with knee, hip or shoulder arthritis.

We present a case of elbow septic arthritis in a 12-day-old neonate which was properly diagnosed and treated.

The informed consent was obtained from the subject and the protocol has been approved by the Ethics Committee of the Suceava Emergency County Hospital, 8/15.03.2022.

Case presentation

A 2-week-old newborn male admitted to the Neonatal Intensive Care Unit (NICU) of our hospital developed progressive right arm swelling and decreased elbow range of motion (ROM) starting on the 12th day of life. His personal history was significant for twin pregnancy and prematurity (gestational age – 33 weeks). His birth weight was 1810 gr and his Apgar scores were 7 and 9 at 1 and 5 minutes, respectively. He had moderate respiratory distress after birth, with a few episodes of dyspnea and cyanosis, for

which he was admitted to NICU for appropriate treatment. He received mask-delivered O₂, Ampicillin, Miophyllin and i.v. hydration with good clinical response. Local right arm symptoms developed over 3-4 days, but he had no fever and the clinical condition was good. A sepsis work out performed and he received Ceftriaxone empirically. Chest X-ray was negative for pulmonary lesions; right arm X-ray also showed no apparent bone lesions.

Urine culture was negative, as well as the results of a CSF (cerebrospinal fluid) aspiration sample. While the WBC level was normal, the CRP level on the 4th day of local symptoms was 0.677 mg/dL (normal value < 0.5 mg/dL) - see Table 1, row 1. With the suspicion of arthritis or osteomyelitis, a surgical consultation was required. On local examination, he was found to have apparent right elbow pain and swelling, with increase local temperature. Clinical examination raised the suspicion of elbow arthritis; informed consent was obtained from the family and elbow aspiration under local anesthesia was performed. No other radiological studies (US or MRI) were performed, given the likely diagnosis of arthritis and the need for rapid diagnosis. Green pus in amount of 4-5 mL was obtained and sent for complete microbiological examination (microscopy, culture and sensitivity testing). Blood cultures were also taken the same day. Based on the clinical appearance (joint pain and swelling, upper arm pseudo-paralysis), elevated CRP levels and appearance of joint aspirate (pus), a diagnosis of septic arthritis of the elbow was confirmed. The patient was started on Amikacin 5 mg/kg BID

and Meropenem 40 mg/kg TID. Two days later, a second right elbow aspiration was performed because local swelling and pain persisted and the CRP level had increased to 3.399 mg/dL (see Table 1, row 2). Another 1 mL of pus was obtained and sent again for analysis. Both pus cultures as well as blood culture were positive for EsβLA (+) *K. pneumoniae* – as etiological agent. Identification was done by classical microbiological methods (culture on selective media; identification by multitest media) and sensitivity testing by disk diffusion method (Bauer Kirby) according to CLSI. It was sensitive to: Amikacin, Amoxicillin/ Clavulanic Acid, Chloramphenicol, Ciprofloxacin, Ertapenem, Gentamicin, Meropenem, Piperacillin/ Tazobactam; resistant to: Ceftazidime, Ceftriaxone, Cefuroxime, Kanamycin, Ticarcillin. Resistance phenotype was the same for both *K. pneumoniae* strains - from blood culture and joint aspirate. Afterwards, the clinical course was favorable, with gradual decrease of local inflammatory changes. A third aspiration was again performed after 3 days, but failed to produce a significant amount of pus or local secretion, which was considered to represent local healing of the inflammatory process. Lab values also showed near-normal levels - see Table 1, row 3. The patient was able to resume active movements and ROM gradually returned to normal. He received Amikacin 5 mg/kg BID and Meropenem 40 mg/kg TID for 14 days, followed by Ampicillin/ Sulbactam 100 mg/kg/day for another 8 days. He was discharged 3 weeks after the onset of the acute episode in good health condition. Laboratory inflammation

Table 1. Laboratory data

Date of test	CRP (mg/dL)	WBC (x 10 ³ /μL)	PMNeu (%)
11th July 2021	0.677	16.08	59.3
13th July 2021	3.399	8.98	64.3
15th July 2021	1.088	10.65	46.1
19th July 2021	0.61	9.63	35.9
24th July 2021	0.046	9.73	32.6
1st August 2021	0.007	9.13	33.2

markers (CRP, WBC and Neu%) were normal (Table 1- rows 3-6), and a second blood culture drawn before discharge was negative. At 1- and 3-month visit he was doing well with no residual changes and normal ROM for the right elbow.

Discussion

Elbow arthritis in newborn is a rare condition (1-3). Early diagnosis is mandatory in order to avoid permanent dysfunction or deformity. Various maneuvers performed around birth (umbilical vein catheterization, femoral artery blood sampling, etc.) represent risk factors, and infection with *Staphylococcus aureus* is seen most frequently. However, characteristic signs and symptoms often lack in small children, which can obscure the diagnosis. Generally, it manifests as a septic condition with fever, poor oral intake, irritability, etc. Local symptoms develop later and may contribute to the failure of proper diagnosis and treatment. It was suggested that careful clinical examinations and the use of various radiological techniques, including US, MRI, and arthrography, may help to obtain an early diagnosis. In our case, clinical examination raised the suspicion of elbow arthritis, which was confirmed by joint aspiration, culture and sensitivity testing of the pus.

Traditionally, surgery and antibiotics have been considered the mainstay of treatment (10, 11). Surgical drainage was recommended in most patients with septic arthritis. Advantages include: - drainage of pus with decrease in local joint pressure, which can further decrease the risk of complications such as avascular necrosis (AVN) of the bone or growth disturbances as a result of permanent cartilage damage; - pus or joint secretion sampling for histological and microbiological studies (12,13). However, several studies have also shown good results without surgery in children with septic arthritis. *Frederiksen et al.* reported a number of 25 neonates with septic

arthritis treated without surgery, of whom 66% recovered without sequelae (11). *Li et al.* (14) published their results with delayed treatment of septic arthritis in 52 cases, and found no differences between patients who had surgery and patients without surgery in terms of complications or outcome. Further data are required to clarify this issue, but for us it looks appropriate to drain a joint with obvious collection (pus) inside.

In what concerns the etiology of septic arthritis in neonates, the study performed by *Li et al.* on 52 cases identified *S. aureus* and *Klebsiella spp.* to be the most commonly involved pathogens (14). According to a study published by *Cohen et al.*, the knee was the most common joint involved in neonatal arthritis, followed by hip, ankle, shoulder, and elbow joints (15). The pathogens involved in neonatal arthritis include *Klebsiella pneumoniae*, *Kingella kingae*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae* (16-19). The same study concluded that surgery is complementary to antibiotics in the management of arthritis and not complementary resource antibiotics, postulating that the joint must be washed and the pus has to be drained. In our study, *K. pneumoniae* was identified in all cultures (2 aspirate samples and blood culture).

Finally, it has to be mentioned that *Paakkonen* introduced a simplified diagnosis and treatment protocol for neonatal arthritis (6); according to this, the presence of clinical signs and symptoms (fever, local pain, and swelling, etc.) suggestive for septic arthritis and pathological lab data (WBC, CRP, ESR) should allow the surgeon to perform joint puncture and aspiration and prescribe empiric antibiotic coverage until bacterial identification and sensitivity testing become available. We found this approach to be appropriate for our case, where we had a high index of clinical suspicion confirmed by increased CRP levels. Close clinical and laboratory data monitoring prompted a second aspiration procedure,

after which the clinical course was favorable and the final outcome was very good.

Conclusions

Septic arthritis of the elbow should be promptly recognized based on a high index of clinical suspicion and the appropriate use of laboratory and radiology information. We consider that surgery is an essential part of the treatment protocol, besides antibiotics. Medium- and long-term follow-up is required in order to rule-out the appearance of local or systemic complications.

Abbreviations

NICU: neonatal intensive care unit
 ROM: range of motion
 O₂: medical oxygen
 CSF: cerebrospinal fluid
 WBC: white blood count
 CRP: C reactive protein
 US: ultrasound
 MRI: Magnetic resonance imaging
 BID: every 12 hours
 TID: every 8 hours
 EsβLA: extended spectrum beta lactamase
 CLSI: Clinical Laboratory Standard Institute
 AVN: avascular necrosis
 NEU: Neutrophiles
 ESR: erythrocyte sedimentation rate
 NSAID: non-steroidal anti-inflammatory drugs

Acknowledgements

We are much indebted to dr. A. Petrescu who analyzed the X-ray picture.

Authors' contribution

Conceptualization: RF, FF; Conception, execution, design and interpretation: RF, FF; laboratory data acquisition: RA, RF; clinical data acquisition: DGLM, FF; writing, reviewing the

manuscript: RF, FF. All authors have approved the final version of the manuscript.

Conflict of interest

None to declare.

References

1. Offiah AC. Acute osteomyelitis, septic arthritis and dis-citis: differences between neonates and older children. *Eur J Radiol.* 2006 Nov;60(2):221-32. DOI: 10.1016/j.ejrad.2006.07.016
2. García-Arias M, Balsa A, Mola EM. Septic arthritis. *Best Pract Res Clin Rheumatol.* 2011 Jun;25(3):407-21. DOI: 10.1016/j.berh.2011.02.001
3. Agarwal A, Aggarwal AN. Bone and Joint Infections in Children: Septic Arthritis. *Indian J Pediatr.* 2016 Aug;83(8):825-33. DOI: 10.1007/s12098-015-1816-1
4. Castellazzi L, Mantero M, Esposito S. Update on the Management of Pediatric Acute Osteomyelitis and Septic Arthritis. *Int J Mol Sci.* 2016 Jun 1;17(6):855. DOI: 10.3390/ijms17060855
5. Halder D, Seng QB, Malik AS, Choo KE. Neonatal septic arthritis. *Southeast Asian J Trop Med Public Health.* 1996 Sep;27(3):600-5.
6. Paakkonen M. Septic arthritis in children: diagnosis and treatment. *Pediatr Health Med Therap.* 2017;8:65-8. DOI: 10.2147/PHMT.S115429
7. Sultan J, Hughes PJ. Septic arthritis or transient synovitis of the hip in children: the value of clinical prediction algorithms. *J Bone Joint Surg Br.* 2010 Sep;92(9):1289-93. DOI: 10.1302/0301-620X.92B9.24286
8. Faesch S, Cojocaru B, Hennequin C, Pannier S, Glorion C, Lacour B, Chéron G. Can procalcitonin measurement help the diagnosis of osteomyelitis and septic arthritis? A prospective trial. *Ital J Pediatr.* 2009 Nov 4;35(1):33. DOI: 10.1186/1824-7288-35-33
9. Maharajan K, Patro DK, Menon J, Hariharan AP, Parija SC, Poduval M, Thimmaiah S. Serum Procalcitonin is a sensitive and specific marker in the diagnosis of septic arthritis and acute osteomyelitis. *J Orthop Surg Res.* 2013 Jul 4;8:19. DOI: 10.1186/1749-799X-8-19
10. Swan A, Amer H, Dieppe P. The value of synovial fluid assays in the diagnosis of joint disease: a literature survey. *Ann Rheum Dis.* 2002 Jun;61(6):493-8. DOI: 10.1136/ard.61.6.493

11. Frederiksen B, Christiansen P, Knudsen FU. Acute osteomyelitis and septic arthritis in the neonate, risk factors and outcome. *Eur J Pediatr*. 1993 Jul;152(7):577-80. DOI: 10.1007/BF01954084
12. Ceroni D, Kampouroglou G, Valaikaite R, Anderson della Llana R, Salvo D. Osteoarticular infections in young children: what has changed over the last years? *Swiss Med Wkly*. 2014 Jun 12;144:w13971. DOI: 10.4414/smw.2014.13971
13. Pääkkönen M, Peltola H. Management of a child with suspected acute septic arthritis. *Arch Dis Child*. 2012 Mar;97(3):287-92. DOI: 10.1136/archdis-child-2011-300462
14. Li Y, Zhou Q, Liu Y, Chen W, Li J, Yuan Z, Yong B, Xu H. Delayed treatment of septic arthritis in the neonate: A review of 52 cases. *Medicine (Baltimore)*. 2016 Dec;95(51):e5682. DOI: 10.1097/MD.00000000000005682
15. Cohen E, Katz T, Rahamim E, Bulkowstein S, Weisel Y, Leibovitz R, Fruchtman Y, Leibovitz E. Septic arthritis in children: Updated epidemiologic, microbiologic, clinical and therapeutic correlations. *Pediatr Neonatol*. 2020 Jun;61(3):325-330. DOI: 10.1016/j.pedneo.2020.02.006
16. Nigussie B, Eifa A, Tagesse B, Ketema W. A Neonatal Hip Septic Arthritis Caused by *Klebsiella pneumoniae* at Hawassa University Comprehensive Specialized Hospital Neonatal Unit, Hawassa, Sidama, Ethiopia. *Int Med Case Rep J*. 2021 Jul 13;14:471-474. DOI: 10.2147/IMCRJ.S321935
17. Le Quellec S, Gaillot O, Chotel F, Freydière AM, Laurent F, Vandenesch F, Doléans-Jordheim A. Septic arthritis caused by noncapsulated *Haemophilus influenzae*. *J Clin Microbiol*. 2013 Jun;51(6):1970-2. DOI: 10.1128/JCM.03377-12
18. Pavlik DF, Johnston JJ, Eldredge JD, Dehority W. Non-Type b *Haemophilus influenzae* Septic Arthritis in Children. *J Pediatric Infect Dis Soc*. 2017 Sep 1;6(3):e134-e139.
19. Peltola H, Kallio MJ, Unkila-Kallio L. Reduced incidence of septic arthritis in children by *Haemophilus influenzae* type-b vaccination. Implications for treatment. *J Bone Joint Surg Br*. 1998 May;80(3):471-3. DOI: 10.1302/0301-620X.80B3.0800471