ISSN 0971-9032
Curr Pediatr Res 2023; 27 (11):2078-2080 www.currentpediatrics.com

Concerning laboratory diagnostics for primary spinal infections in pediatric population.

Giacomo De Marco, Oscar Vazquez, Blaise Cochard, Silvia Valisena, Christina Steiger, Romain Dayer, Dimitri Ceroni*

Department of Pediatric, Orthopedics Geneva University Hospital, Switzerland

Received: *04 December, 2023, Manuscript No. AAJCP-23-121948;* **Editor assigned:** *06 December, 2023, Pre QC No. AAJCP-23-121948 (PQ);* **Reviewed:** *20 December, 2023, QC No. AAJCP-23-121948;* **Revised:** *27 December, 2023, Manuscript No. AAJCP-23-121948(R);* **Published:** *03 January, 2024, DOI:10.35841/0971-9032.27.11.2078-2080.*

Accepted on 15th December, 2023

Description

Spinal Infections (SI) include a large variety of conditions that may affect the vertebral body, the intervertebral disk, the adjacent paraspinal tissues, and even the content of the medullary canal. In the pediatric population, SI is rarely restricted to one compartment, since they have the natural tendency to spread, targeting therefore several structures of the vertebral column [1]. In order to fully understand any spinal infection, it remains fundamental to identify the causative pathogen and to know the recipient characteristics' according to patient's age, immunization status and medical history. Given the heterogeneity of this condition, a classification based on patient's age helps the clinician to differentiate between 3 main clinical forms of pediatric SI [2-9].

The neonate form affects infants less than 6 months old and represents the most severe and rare manifestation of the disease [2,4]. Prematurity accounts for the most important risk factor in this specific age group moreover in patients with a long Intensive Care Unit (ICU) history and several invasive procedures [10]. *Staphylococcus aureus* and gram negative bacteria are the most relevant pathogens responsible for SI in this group, often presenting with septicemia and multiple infectious foci [11].

The infantile form concerns children from 6 to 48 months old, representing up to 80% of all cases of pediatric spondylodiscitis. Often the disease appears when the weak immunity system of the child takes over the maternally inherited immunity. Some studies in this age group have suggested that *Kingella kingae (K. kingae)* is the prevalent microorganism responsible for spinal infections [2-4,6].

Finally, the form of PSI affecting children above 4 years old, is more prone to affect vertebral bodies causing osteomyelitis due to *S. aureus*, often leading to high fever and rapid degeneration of patient's general status [8,9].

Laboratory tests in SI often provide non-specific information, since they are usually normal or slightly elevated [2-4,12-14]. Increase in WBC count above 12,000 per mm3 is rare, accounting only for 35%-40% of all cases, in addition to that 60%-65% of the patients with SI have been reported to have normal or near-normal CRP levels [2-4,13,15].

ESR (abnormal values in >80% cases) and Platelet Count (abnormal values in 50%-60% of cases appear to be the most sensitive and reliable markers of inflammation in this specific group of patients according to most recent literature [2-4,6-16]. Caution is then required when interpreting blood tests results as these parameters can vary according to the causative germ and patient's age.

Obtaining bacteriological samples in SI could be even more challenging as opposite to others osteoarticular infections such as septic arthritis. Blood cultures in pediatric SI are characterized by a high percentage of negative results, ranging from 88%-100% [12-14,17,18]. This high rate of negative blood cultures could be explained by the high frequency of PSI in children under 4 years old. It is in-fact recognized that in this age group, infections seem to be mainly caused by *K. kingae*, a *fastidious bacillu*s difficult to isolate in blood [3,19,20-25]. In addition to that, biopsy and/or needle aspiration are still matter of debate when talking about pathogen isolation in the pediatric population. Indication for invasive procedures, is currently not well established and even considered heretical by most of the authors [2,3,7]. Even though some authors evoke the obtention of a spinal specimen by closed percutaneous or open surgical biopsy, a critical review of the literature shows that the success rates for a needle aspiration and/or an open biopsy to identify causative organisms ranges from 0%-63% in pediatric spondylodiscitis [2,6,18,26-28]. Here again, cultures could stay silent because of the involvement of *K. kingae* in 80% of SI among patients between 6 months and 4 years of age.

Nowadays, the advent of Nucleic Acid Amplification Assays (NAAAs) has made spectacular progresses to detect pathogens on samples, and continues to improve both in terms of efficiency and specificity [28-30]. The crucial contribution of these diagnostic tools has drastically improved the treatment of infectious diseases in children, as is already the case in adult SI. Despite this, indication for biopsy and/or needle aspiration in pediatric population remains rare and should be reserved only in case of medical treatment failure.

However, the improvement of NAAAs can promote identification of causative pathogens by their indirect recognition without recurring to invasive investigations. On that point, it has already been proven that an oropharyngeal swab Polymerase Chain Reaction (PCR) test could detect the *K. kingae* Repeats in ToXin (RTX) gene in almost 90% of the toddlers with confirmed spondylodiscitis [3]. This strong evidence comes from previous studies suggesting that *K. kingae* DNA can be found in the oropharynx of children with

osteoarticular infections. Thus indicating that a pharyngeal swab could prove *K. kingae* as responsible for spinal infections in a specific pediatric population ranging from 6 months to 4 years old when found positive in oral cultures [3,4].

Moreover recent advances in Next Generation Sequencing (NGS) resulted in the advent of very efficient methods to identify microorganisms. Metagenomic NGS (mNGS) is based on high-performance DNA sequencing technologies; this new technique can arbitrarily amplify and detect all the pathogens present in a clinical sample. This new technology, already being used in clinical practice, could be established indirectly on plasma samples (Plasma mNGS) in a recent future as many authors advocate. When mNGS is performed in plasma (known as "liquid biopsy"), the method detects not only pathogens in the bloodstream but also those responsible for focal infections. On that point, an interesting multicenter study performed mNGS in plasma and detected *K. kingae* in 10 young children (median age: 16.5 months, range: 10–23 months) with spondylodiscitis [31]. The blood cultures were negative in all patients, but the detection of *K. kingae* by mNGS in plasma could establish the diagnosis without biopsy. These promising results make mNGS a novel and promising versatile tool expected to drastically change bacteriological investigations in a near future especially in pediatric SI.

References

1. Hadjipavlou AG, Mader JT, Necessary JT, et al. Hematogenous pyogenic spinal infections and their surgical management. Spine 2000;25(13):1668-1679.
2. Dayer R, Alzahrani MM, Saran N, et al. Spinal infections in children: A multicentre retrospective study. Bone Joint J 2018;100(4):542-548.
3. Chargui M, Krzysztofiak A, Bernaschi P, et al. Presumptive bacteriological diagnosis of spondylodiscitis in infants less than 4 years by detecting *K. kingae* DNA in their oropharynx: Data from a preliminar two centers study. Front Pediatr 2022;10:1046254.
4. Ceroni D, Belaieff W, Kanavaki A, et al. Possible association of *Kingella kingae* with infantile spondylodiscitis. Pediatr Infect Dis J 2013;32(11):1296-8.
5. Bonfiglio M, Lange TA, Kim YM. Pyogenic vertebral osteomyelitis: Disk space infections. Clin Orthop Relat Res 1973;96:234-47.
6. Garron E, Viehweger E, Launay F, et al. Nontuberculous spondylodiscitis in children. J Pediatr Orthop 2002;22(3): 321-328.
7. Menelaus MB. Discitis. an inflammation affecting the intervertebral discs in children. J Bone Joint Surg Br févr 1964;46:16-23.
8. Dayer R, De Marco G, Vazquez O, et al. Laboratory diagnostics for primary spinal infections in pediatric and adult populations: A narrative review. N Am Spine Soc J 2023;16:100270.
9. Ceroni D, Chargui M, De Marco G, et al. Better Comprehension of Primary Pyogenic Spinal Infections. Pediatr Infect Dis J 2023;42(1):e39-40.
10. Van Dalen IV, Heeg M. Neonatal infectious spondylitis of the cervical spine presenting with quadriplegia: A case report. Spine 2000;25(11):1450-2.
11. Principi N, Esposito S. Infectious discitis and spondylodiscitis in children. Int J Mol Sci 2016;17(4):539.
12. Early SD, Kay RM, Tolo VT. Childhood diskitis. J Am Acad Orthop Surg 2003;11(6):413-20.
13. Fernandez M, Carrol CL, Baker CJ. Discitis and vertebral osteomyelitis in children: An 18-year review. Pediatrics 2000;105(6):1299-304.
14. Spencer SJ, Wilson NI. Childhood discitis in a regional children's hospital. J Pediatr Orthop B 2012;21(3):264-8.
15. De Moraes Barros Fucs PM, Meves R, Yamada HH. Spinal infections in children: A review. Int Orthop 2012;36:387-95.
16. Gouliouris T, Aliyu SH, Brown NM. Spondylodiscitis: Update on diagnosis and management. J Antimicrob Chemother 2010;65(suppl_3):iii11-24.
17. Brown R, Hussain M. Discitis in young children. J Bone Joint Surg Br 2001;83(1):106-11.
18. Ventura N, Gonzalez E, Terricabras L. Intervertebral discitis in children: A review of 12 cases. Int Orthop 1996;20:32-4.
19. Juchler C, Spyropoulou V, Wagner N, et al. The contemporary bacteriologic epidemiology of osteoarticular infections in children in Switzerland. J Pediatr 2018;194:190-6.
20. Ceroni D, Cherkaoui A, Ferey S, et al. *Kingella kingae* osteoarticular infections in young children: Clinical features and contribution of a new specific real-time PCR assay to the diagnosis. J Pediatr Orthop 2010;30(3):301-4.
21. Samara E, Spyropoulou V, Tabard-Fougère A, et al. *Kingella kingae* and osteoarticular infections. Pediatrics 2019;144(6).
22. Coulin B, DeMarco G, Vazquez O, et al. Osteoarticular Infections in Children: Accurately Distinguishing between MSSA and *Kingella kingae.* Microorganisms 2022;11(1): 11.
23. Coulin B, Demarco G, Spyropoulou V, et al. Osteoarticular infection in children: An update on the epidemiological, clinical, and biological features of *Kingella kingae.* Bone Joint J 2021;103(3):578-83.
24. Dubnov-Raz G, Ephros M, Garty BZ, et al. Invasive pediatric *Kingella kingae* infections: A nationwide collaborative study. Pediatr Infect Dis J 2010;29(7):639-43.
25. Dubnov-Raz G, Scheuerman O, Chodick G, et al. Invasive *Kingella kingae* infections in children: Clinical and laboratory characteristics. Pediatrics 2008;122(6):1305-9.
26. Ryöppy S, Jaaskelainen J, Rapola J, et al. Nonspecific diskitis in children. Clin Orthop Relat Res 1993; 297:95-9.
27. Enoch DA, Cargill JS, Laing R, et al. Value of CT-guided biopsy in the diagnosis of septic discitis. J Clin Pathol 2008;61(6):750-3.
28. Sehn JK, Gilula LA. Percutaneous needle biopsy in diagnosis and identification of causative organisms in cases

of suspected vertebral osteomyelitis. Eur J Radiol 2012;81(5):940-6.

29. DeMarco G, Chargui M, Coulin B, et al. *Kingella kingae* osteoarticular infections approached through the prism of the pediatric orthopedist. Microorganisms 2021;10(1):25.
30. Ceroni D, Dayer R, Steiger C. Are we approaching the end of pediatric culture-negative osteoarticular infections?. Future Microbiol 2019;14(11):917-9.
31. Yagupsky P. The Past, Present, and Future of *Kingella kingae* Detection in Pediatric Osteoarthritis. Diagnostics 2022;12(12):2932.

***Corresponding to**

Dimitri Ceroni

Department of Pediatric Orthopedics,

Geneva University Hospital, Switzerland

E-mail: dimitri.ceroni@hcuge.ch