IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Case Report

Myocarditis and Meningitis during Early Sepsis in a Neonate with *Streptococcus pseudopneumoniae*: A Case Report

Yazdan Ghandi[1*], Vahab Ghanbari sheldareh[2], Saeed Alinejad[3], Danial Habibi[4]

1. Amirkabir Hospital, School of Medicine, Department of Pediatrics, Pediatric Cardiology, Arak University of Medical Sciences, Arak, Iran
2. Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran
3. Department of Neonatology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran
4. Department of Biostatistics, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran

ABSTRACT

Although myocarditis is uncommon in neonates, a wide variety of infectious pathogens can result in myocarditis, including viruses, bacteria, rickettsia, fungi, and protozoa. Viruses are most often the infectious disease found to cause acute myocarditis. On the other hand, bacterial myocarditis (BM) is an unusual cause of infectious myocarditis. BM is commonly seen in the context of sepsis or as part of a bacterial syndrome.

Streptococcus pseudopneumoniae has mostly been isolated from the respiratory tract specimens. This infection is not prevalent in neonates. In this case report, a 5-day-old male neonate was admitted with the signs of fever, jaundice, and poor feeding. Moreover, he was lethargic and hypotonic with reduced neonatal reflexes and obvious tachycardia.

Clinical and physical examinations were performed in addition to chest X-rays, echocardiography, cerebrospinal fluid (CSF) analysis, and other laboratory tests. The final diagnosis was confirmed as myocarditis and meningitis. The patient was treated with antibiotics and intravenous immunoglobulin (IVIG).

On the sixth day of hospitalization, fever of the neonate fever resolved. On the 24th day, the CSF analysis was normal and the CSF, as well as blood culture were negative. The patient was discharged on the 30th day in good general and physical condition. The subsequent echocardiography performed four months' post-hospitalization was normal.

Keywords: Early sepsis, Meningitis, Myocarditis, Neonate, *Streptococcus pseudopneumoniae*

Introduction

Streptococcus pseudopneumoniae was described in 2004 as a new human pathogen acknowledged in several clinical infections, which were typically associated with the respiratory tract (1). *S. pseudopneumoniae* is Gram-positive cocci, which lacks pneumococcal capsule. This bacterium is bile-insoluble and optochin-resistant when incubated in 5% carbon dioxide (CO_2). However, it is optochin-susceptible when incubated under ambient conditions containing O_2 (1).

S. pseudopneumoniae is most commonly isolated from the respiratory specimens and is associated with chronic obstructive pulmonary disease, as well as aspiration pneumonia, suggesting it as a border between being commensal and pathogenic. Among the viridansgroup streptococci (VGS), *S. pseudopneumoniae* is phenotypically and genetically similar to *Streptococcus pneumoniae*, *Streptococcus mitis*, and *Streptococcus oralis* (2).

S. pseudopneumoniae has possibly originated from *S. pneumoniae* following a complex evolution of recombination events. Although it is unusual in neonates, has been identified as colonized among children and respiratory samples (3, 4). Antimicrobial susceptibility profile of *S. pseudopneumoniae* indicates a higher level of resistance, compared to the other VGSs (5, 6). Antimicrobial resistance is clearly documented for *S. pseudopneumoniae* and it is significantly more

* *Corresponding author:* Yazdan Ghandi, Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran. Tel: 09123833712; Email: y.ghandi@arakmu.ac.ir

Please cite this paper as:
Ghandi Y, Ghanbari Sheldareh V, Alinejad S, Habibi D. Myocarditis and Meningitis During Early Sepsis in a Neonate with *Streptococcus pseudopneumoniae*: A Case Report. Iranian Journal of Neonatology. 2018 Sep: 9(3). DOI: 10.22038/ijn.2018.30299.1414

resistant than *S. pneumoniae* (3, 6). The present report describes a rare case of meningitis and myocarditis caused by *S. pseudopneumoniae* and treated with antibiotics and IVIG.

Case report

A 5-day-old male neonate was admitted with fever and jaundice that developed one day prior to hospital admission and was accompanied by poor feeding. His mother had a history of hypothyroidism treated with levothyroxine before and during pregnancy. The patient had no abnormal birth history and was kept at home for approximately four days after birth.

At the time of admission, the neonate had jaundice and was lethargic. Moreover, he was hypotonic with reduced neonatal reflexes and body temperature of approximately 39 °C. The primary vital signs were as follows: blood pressure 68/35, pulse rate 180, respiratory rate 55, and body temperature 39 °C. Other clinical and physical examination findings were found to be normal, except the obvious tachycardia. Laboratory tests reported white blood cells (WBC) 4500/µl, neutrophils 59%, lymphocytes 39%, and negative C-reactive protein (CRP). The TORCH titer was screened in order to rule out infections. Treatment was initiated by administering empirical parenteral antibiotics with ampicillin and cefotaxime to consider early-onset neonatal sepsis. A lumbar puncture was performed on the second day of hospitalization.

The CSF test indicated that WBC count was elevated with the results of neutrophils 26%, lymphocytes 74%, protein > 300 mg/dl, and glucose 9 mg/dl. In addition, the CSF smear revealed paired Gram-positive cocci, which is rare. The CSF and blood cultures were positive for *S. pseudopneumoniae* sensitive to ampicillin, cefotaxime, vancomycin, erythromycin, azithromycin, and penicillin. The patient received ampicillin, cefotaxime, and vancomycin for three weeks. Furthermore, the result of evaluation for immunodeficiency was negative.

The chest X-ray (CXR) showed a cardiothoracic ratio > 0.6% on the anteroposterior (AP) view. Electrocardiography revealed low QRS voltages and ST depressions on anterior leads, in addition to nonspecific ST and T-wave changes on other leads, suggesting acute ischemia. Echocardiography performed due to high fever and tachycardia indicated an ejection fraction (EF) of 40%, moderate mitral regurgitation (MR), mild tricuspid regurgitation (TR) (PG=30 mmHg), E/A ratio of 2.89, and moderate left ventricular enlargement. Furthermore, decreased systolic LV function (EF=40%) was distinguished.

The concentration of troponin I was found to be 769 ng/ml. The final diagnosis was myocarditis and meningitis during the early sepsis in this neonate. Antibiotic therapy was performed for meningitis, and we administered IVIG at the dose of 500 mg/kg with a 6-hour infusion rate based on the probable diagnosis. On the sixth day of hospitalization, the fever resolved. The TORCH test was negative, and troponin I level diminished to 20.8 ng/ml. The lumbar puncture showed WBCs as 600/µl (neutrophil 10%, lymphocyte 90%), glucose 25 mg/dl, protein 163 mg/dl, as well as negative blood and CSF cultures. CXR was indicative of a CT ratio less than 55% that was in the normal range.

On day 24 of hospitalization, the fever resolved completely, the third lumbar puncture analysis was normal, in addition to negative CSF and blood cultures results. Moreover, physical examination and repeated echocardiography findings were normal. After 30 days of proper treatment, the patient was discharged from the hospital in good general and physical conditions. The echocardiography carried out four months after discharge was normal.

Discussion

Myocarditis is an uncommon problem in the neonates. An immune response is induced in myocardial infection, which results in myocardial edema. Subsequently, the systolic and diastolic functions are disturbed in myocardial infection. The outcome is very poor because newborns have immature myocardium that has limited ways of adaptation in an acute phase. During the acute phase, sinus tachycardia and gallop on auscultation are the most common presentations. The echocardiogram revealed reduced ventricular function. Oxygen, diuretics, and inotropic agents are useful in treating heart failure. The role of immunosuppressive therapy and IVIG are not yet clearly established.

A wide variety of infectious pathogens can result in myocarditis, including viruses, bacteria, rickettsia, fungi, and protozoa. Viruses are most often the infectious disease found to cause acute myocarditis and Coxsackievirus B is the most prevalent one in this regard. Coxsackievirus B is known as an enterovirus. Other viruses were also found to be associated with myocarditis, such as parvovirus B19, human Herpes Virus 6, influenza virus, and rubella virus. Viral studies

are useful diagnostically for discovering the pathogens. Bacterial myocarditis (BM) is an unusual cause of infectious myocarditis, which is commonly seen in the context of sepsis or as a part of bacterial syndrome.

S. pseudopneumoniae has likely originated from *S. pneumonia* following a complex series of recombination events (1, 2). *S. pseudopneumoniae* pathogenicity was clearly demonstrated in a murine model, in which intraperitoneal injection of *S. pseudopneumoniae* resulted in 100% mortality (7). Recently, molecular mapping of tonsillar crypt microbiota in healthy adults and children and those with recurrent tonsillitis demonstrated the presence of *S. pseudopneumoniae* in all samples (8). This microbe has been recognized in many respiratory-associated clinical infections, while has occasionally been demonstrated in sterile body sites (9). It was recently shown in blood of two patients without neither clinical information provided nor clinical significance discussed (9).

Keith et al. described *S. pseudopneumoniae* and association of this bacterium with history of chronic obstructive pulmonary disease (COPD) or exacerbated COPD (9). This retrospective case-control study compared patients with *S. pseudopneumoniae* in their sputum with the matched controls. They observed statistically significant relationship between the presence of this agent with COPD history and exacerbated COPD. This finding was not confirmed in a recent French study (3); however, a relationship with respiratory tract infection was demonstrated.

Laurens et al. (3) retrospectively analyzed the clinical and antimicrobial susceptibility profiles of 140 *S. pseudopneumoniae* isolates. Respiratory tract samples were the source for almost all the isolates and most isolates were from patients with underlying diseases.

Pneumonia was documented in 38 patients (27.1%) in whom aspiration pneumonia was the most prevalent presentation and all required intensive care unit admission [N=20 (53%)]. No isolates were isolated from blood cultures. This finding further supports *S. pseudopneumoniae* as a respiratory tract colonizer or as a mild opportunistic pathogen involved in pneumonia and bronchitis, most commonly isolated with other potential pathogens. Interestingly, no mixed infections due to *S.pneumoniae* or *S. pseudopneumoniae* were observed.

Keith et al. (9) made a similar observation, where ten patients were classified as mixed infections. *S. pseudopneumoniae* was clearly the predominant isolated organism. Variable incidences of *S. pseudopneumoniae* have been reported in respiratory tract specimens ranging from one *S. pseudopneumoniae* isolate in 120 pneumococcal isolates (7) to 12 per 100 pneumococcal isolates (3). This variability might reflect the method used to identify the species. Until recently, *S. pseudopneumoniae* was mostly isolated from respiratory tract specimens.

Rolo et al. showed that *S. pseudopneumoniae* could grow in blood culture, which indicates the potency of this agent to cause invasive infections (10). Most of the 61 analyzed *S. pseudopneumoniae* isolates belonged to the respiratory tract samples. However, eight isolates were from sterile sites, two of which belonged blood. This was the first description of *S. pseudopneumoniae* isolation from blood culture. Nonetheless, significance of this isolation has not yet been determined as no clinical information was available.

To date, rarely reports have been published regarding myocarditis and meningitis in neonates due to infection with this organism. Our report demonstrates that *S. pseudopneumoniae* can potentially cause invasive infections, such as early sepsis in neonates.

Rolo et al. found that among disease isolates classified as atypical pneumococci, nearly half (46.2%) were *S. pseudopneumoniae* and only a quarter were pneumococci (17.4 and 8.3% were capsulated and non-typeable, respectively). In addition, 9.8% were *S. mitis* and the remainders were unidentified non-pneumococci (10). Arbique et al. consistent with other studies, showed that *S. pseudopneumoniae* is of low clonality. Furthermore, antimicrobial resistance has well been investigated in this species (1).

Our study highlights the clinical role of *S. pseudopneumoniae* and non-typeable pneumococci as they can lead to invasive disease and high antimicrobial resistance rates, which is greatly concerning. In conclusion, this report described a rare case of neonatal meningitis and myocarditis, in addition to the role of *S. pseudopneumoniae* as a probable cause of early sepsis in a neonate. Therefore, it is important to consider *S. pseudopneumoniae* infections as possible causes of early sepsis in neonates.

Acknowledgments

We would like to thank all the staff of the Neonatal Intensive Unit Care in Amir Kabir Hospital for their kind cooperation with

collecting the required data throughout the project.

Conflicts of interests

The authors of this study declare no conflicts of interests.

References

1. Arbique JC, Poyart C, Trieu-Cuot P, Quesne G, Maria da Glória SC, Steigerwalt AG, et al. Accuracy of phenotypic and genotypic testing for identification of streptococcus pneumoniae and description of streptococcus pseudopneumoniae sp. nov. J Clin Microbiol. 2004; 42(10):4686-96.
2. Sistek V, Boissinot M, Boudreau DK, Huletsky A, Picard FJ, Bergeron MG. Development of a real-time PCR assay for the specific detection and identification of Streptococcus pseudopneumoniae using the recA gene. Clin Microbiol Infect. 2012; 18(11):1089-96.
3. Laurens C, Michon AL, Marchandin H, Bayette J, Didelot MN, Jean-Pierre H. Clinical and antimicrobial susceptibility data of 140 Streptococcus pseudopneumoniae isolates in France. Antimicrob Agents Chemother. 2012; 56:4504-7.
4. Simões AS, Sá-Leão R, Eleveld MJ, Tavares DA, Carriço JA, Bootsma HJ, et al. Highly penicillin-resistant multidrug-resistant pneumococcus-like strains colonizing children in Oeiras, Portugal: genomic characteristics and implications for surveillance. J Clin Microbiol 2010; 48(1): 238-46.
5. Keith ER, Murdoch DR. Antimicrobial susceptibility profile of Streptococcus pseudopneumoniae isolated from sputum. Antimicrob Agents Chemother. 2008; 52(8):2998.
6. Mohammadi JS, Dhanashree B. Streptococcus pseudopneumoniae: an emerging respiratory tract pathogen. Indian J Med Res. 2012; 136(5):877-80.
7. Harf-Monteil C, Granello C, Le Brun C, Monteil H, Riegel P. Incidence and pathogenic effect of Streptococcus pseudopneumoniae. J Clin Microbiol. 2006; 44(6):2240-1.
8. Jensen A, Fagö-Olsen H, Sørensen CH, Kilian M. Molecular mapping to species level of the tonsillar crypt microbiota associated with health and recurrent tonsillitis. PLoS One. 2013; 8(2):e56428.
9. Keith ER, Podmore RG, Anderson TP, Murdoch DR. Characteristics of Streptococcus pseudopneumoniae isolated from purulent sputum samples. J Clin Microbiol. 2006; 44(3):923-7.
10. Rolo D, Simoes AS, Domenech A, Fenoll A, Linares J, de Lencastre H, et al. Disease isolates of Streptococcus pseudopneumoniae and non-typeable S. pneumoniae presumptively identified as atypical S. pneumoniae in Spain. PLoS One. 2013; 8(2):e57047.