Case Report

Early Onset Neonatal Sepsis Due to *Salmonella enterica* Serovar 4,5,12:i:-: A Case Report with Literature Review

Kannikar Vongbhavit MD*, Salocha Itdhi-amornkulchai MD*,
Jantana Panburana MD*, Olarn Prommalikit MD*

** Department of Pediatrics, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand*

The authors report a case of a 36-week male infant born via spontaneous vaginal delivery who developed Salmonella sepsis at HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, Nakhon Nayok, Thailand. He was born to a mother without identifiable risk factors. On day 3, he developed fever, tachycardia, lethargy, poor feeding and diarrhea prompting a sepsis evaluation. Blood and stool cultures were positive for S. enterica serovar 4,5,12:i:-. Therefore, Salmonella infection should be considered in the differential diagnosis of early onset neonatal sepsis (EOS) particularly in endemic areas.

Keywords: *Salmonella enterica, Early onset neonatal sepsis, Salmonella infection*

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The term early onset neonatal sepsis (EOS) is used to describe systemic bacterial infection documented by a positive blood culture in the first 7 days of life. Most common pathogens are usually from bacterial colonization in the maternal vagina including group B *Streptococcus* (GBS), *Escherichia coli* and other gram negative bacteria[1]. The World Health Organization estimates that 1 million deaths per year are due to neonatal sepsis and that 42% of these deaths occur in the first week of life[2]. Although there are numerous reports of non-typhoidal salmonella causing neonatal sepsis, *Salmonella enterica* serovar 4, 5, 12: i:- has so far not been shown to be a causative pathogen in EOS. The authors report a case of *S. enterica* serovar 4, 5, 12: i:- bacteremia in a 3-day old infant.

Case history

A 2,250-gram-male infant was born vaginally with Apgar scores of 7 and 9 at 1 minute and 5 minutes, respectively at HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, Nakhon Nayok, Thailand. His mother was 17 years old with 36 weeks of gestation and had no recent history of fever, diarrhea, or rupture of membrane. She also received ampicillin 2 grams intravenously prior to delivery for GBS prophylaxis due to gestational age less than 37 weeks. He was admitted at postnatal ward with his mother. He was transferred to neonatal intensive care unit (NICU) on the third day of life because he developed fever (37.8°C), tachycardia, lethargy, poor feeding and frequent stools. Complete blood count showed haemoglobin level of 12.6 g/dL, white blood cell count of 2,210 cells/mm^3 (50% neutrophils, no immature neutrophils and 31% lymphocytes) and platelets count of 173,000 cells/mm^3. Cerebrospinal fluid (CSF) revealed white blood cell of 2 cells/mm^3, red blood cell of 85 cells/mm^3, protein of 154 mg/dL, glucose of 87 mg/dL (blood sugar 102 mg/dL). Stool examination showed loose yellowish-green color with white blood cell of 30-50 cells/HPF. Intravenous cefotaxime (50 mg/kg every 12 hours) and cloxacillin (25 mg/kg every 12 hours) were given as empirical antibiotics. Three days after treatment, he still had temperature instability, lethargy, and frequent stools. Antibiotic regimen was switched to meropenem. Blood and stool cultures were identified as *Salmonella* group B on day-of-life ten which was resistant to ampicillin and susceptible to cefotaxime, ceftriaxone, ceftazidime, cefepime, ciprofloxacin, co-trimoxazole and meropenam. The minimum inhibitory concentration (MIC) of cefotaxime was not performed.

Correspondence to:
Vongbhavit K, Department of Pediatrics, Faculty of Medicine, Srinakharinwirot University, 62 Moo 7, Ongkharak, Nakhon Nayok, 26120 Thailand.
Phone: +66+89-6670504, Fax: +66-37-395085
E-mail: vkannikar@gmail.com

CSF culture resulted negative. *Salmonella* serotyping was examined at the National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand. It was identified as *S. enterica* serovar 4, 5, 12: i:-. His mother's stool culture was reported *Salmonella* serovar Give. Blood and stool cultures were repeated after effective antimicrobial therapy and the result revealed negative for pathogenic organisms. Meropenem was given for 14 days.

Discussion

Salmonella is a genus of gram-negative bacilli with approximately 2,600 serotypes, most disease is caused by serotypes Typhimurium and Enteritidis[3]. Salmonellosis is the most common cause of invasive bacterial disease among young infants and the immunosuppressed[3,4] in developing countries in Africa and Asia, including Thailand[5]. *S. enterica* serovar 4, 5, 12: i:- is a serotype antigenically similar to serotype Typhimurium but lacking second-phase flagellar antigens. This serovar is increasingly in human disease and larger outbreaks reported from European countries and the United States. This strain was isolated from pigs, pork and humans. Pork and its products contaminated with this serovar were identified as sources for human *Salmonella* infections[6,7]. However, it has so far not been shown to be a causative pathogen in EOS. Other serotypes of *S. enterica* were reported as cause of EOS and clinical presentations of these serotypes are variable ranging from asymptomatic to severe sepsis and death. A review of EOS due to *S. enterica* had ten published reports (Table I). In the summarized reports[8-17], signs and symptoms include feeding intolerance, respiratory distress, fever, hypothermia, bilious vomiting, seizure and lower limb ischemia. Clinically, the pictures of salmonellosis were like that of any other EOS. Severe localized infections outside the gastrointestinal tract including

Table 1. Clinical presentation of early onset neonatal sepsis due to *Salmonella enterica*

No.	Salmonella species	Day of life	Sex	Gestational age	Signs and symptoms	Maternal history
1[8]	*S. typhi*	1	Female	Term	Asymptomatic (sepsis screening)	Fever, diarrhea
	S. typhi	1	Female	Term	Respiratory distress	Fever, chill
	S. typhi	1	Female	Term	Respiratory distress, multifocal convulsion	Fever
	S. typhi	2	Male	Term	Feeding intolerance	Normal
	S. paratyphi A	5	Male	28 weeks	Sluggish, sclerema, jaundice	Normal
2[9]	*S. paratyphi A*	5	Male	Term	Sluggish, feeding intolerance	Hypo-thyroidism $GDMA_1$
3[10]	*S. paratyphi A**	2	Male	35 weeks	Respiratory distress, abdominal distension	Fever, diarrhea
4[11]	*S. paratyphi B*	3	Male	N/A	Left lower limb ischemia	N/A
5[12]	*S. paratyphi B*	6	Female	Term	Fever, bloody diarrhea, vomiting	Normal
6[13]	*S. weltevreden*	5	Male	N/A	Hypothermia	Normal
	S. weltevreden	3	Female	N/A	Hypothermia, feeding intolerance	Normal
7[14]	*S. enteritidis**	2	Female	Term	Abdominal distension, bilious vomiting, bloody stool	Fever, diarrhea
8[15]	*S. berta**	3	Male	Term	Lethargy, poor perfusion, seizure	Diarrhea
9[16]	*S. montevideo*	2	Male	34 weeks	Hypoglycemia, apnea, seizure	Fever, diarrhea
10[17]	*S. agona*	6	Male	Term	Fever, diarrhea poor feeding	Normal

* died; N/A = not available; $GDMA_1$ = Gestational Diabetes Mellitus type 1

endovascular infections[11,14] and meningitis[8,15-17] can occur. Three babies in five whose mothers had history of diarrhea prior to delivery died[10,14,15]. There are no data to guide pediatricians in the care of infants born to mothers with diarrhea. Management of salmonellosis with antibiotics is not indicated in cases of non-invasive gastroenteritis because this can prolong colonization[4]. Treatment for *Salmonella* infection is recommended in infants younger than 3 months of age or patients who have chronic gastrointestinal diseases, malignancies, hemoglobinopathies, and/or HIV infection[3,4,18]. The antimicrobial resistant profiles of serovar 4, 5, 12: i:- showed a marked increase in the drugs resistance to ampicillin, streptomycin, sulfonamides and tetracyclines in several countries[19]. A recent survey of antimicrobial susceptibilities against *Salmonella* serovar among patients and asymptomatic carriers between 2001 and 2006 in central Thailand also pointed to a relatively high rate of antimicrobial resistance, especially among invasive serovar, to various antibiotics particularly third-generation cephalosporins[5]. Clinicians should consider *S. enterica* as a possible cause of fulminant sepsis in neonates and the increasing prevalence of drugs resistant *Salmonella* has been of concern. The patients may die before the availability of susceptibility results. Thus, appropriate empirical antibiotic should be given in severe cases especially if maternal history of fever and diarrhea are present prior to the specific antibiotic susceptibility is determined by culture and sensitivity assays. In the presented case, the isolate was reported susceptible to cefotaxime by disk diffusion method, but his condition did not improve and may have been a case of in vivo resistance. His mother's stool was reported *Salmonella* serovar Give. This serovar is an enteric serotype frequently isolated from ruminants and causes enteric infections[20]. Acquisition of EOS occurs either by vertical transmission from the mother or by horizontal transmission in the exogenous sources. Vertical transmission may be due to transplacental spread or infection by the feco-oral route during passing through the lower birth canal and infection from an exogenous source may occur from milk supplemented with contaminated water in endemic areas. The source of this infection could not be ascertained despite infection surveillance activity to the health care personal, the family members and environment including the labor room, postnatal ward and NICU. No other neonates in the NICU were affected. We cannot draw a conclusion of whether the patient contracted the infection by vertical transmission, feco-oral route or environmental transmission through contaminated top feeds or via breast milk.

Conclusion

Salmonella infection should be considered in the differential diagnosis of EOS particularly in endemic areas especially if the maternal history with fever and diarrhea are present prior to delivery.

What is already known on this topic ?

Salmonella infection can cause EOS with manifestations similar to sepsis caused by other bacteria. Clinicians should be aware of the invasive nature of this pathogen which could cause serious complications.

What this study adds ?

The decision to choose an empirical antibiotic is very important. Prompt recognition of risk factors in mother and adequate treatment of neonate is mandatory for a successful outcome.

Potential conflicts of interest

None.

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การติดเชื้อในกระแสเลือดจาก Salmonella enterica serovar 4, 5, 12: i:- ในระยะต้นของทารกแรกเกิด: รายงานผู้ป่วยและทบทวนวรรณกรรม

กรรณิการ์ วงศ์ภาวิทย์, สโรชา อิทธิอมรกุลชัย, จันทนา พันธ์บูรณะ, โอพาร พรหมาลิขิต

ผู้นิพนธ์นำเสนอเคสผู้ป่วยทารกเพศชายอายุครรภ์ 36 สัปดาห์ คลอดปกติที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี มหาวิทยาลัยศรีนครินทรวิโรฒ จังหวัดนครนายก ประเทศไทย มารดาไม่มีปัจจัยเสี่ยงขณะตั้งครรภ์ อายุ 3 วัน ทารกมีไข้ หัวใจเต้นเร็ว ซึม รับนมไม่ได้ และท้องเสีย ทำการตรวจเลือดและเพาะเชื้อในเลือดและอุจจาระ ผลการเพาะเชื้อในเลือดและอุจจาระพบเชื้อ S. enterica serovar 4, 5, 12: i:- ดังนั้นการติดเชื้อ Salmonella ในกระแสโลหิตระยะต้น ควรพิจารณาในการวินิจฉัยแยกโรคในพื้นที่ที่มีเชื้อนี้ประจำถิ่นอยู่
