Salmonella Meningitis: a rare case in a 3-month-old infant without evident neurological sequelae

Salmonella Meningitis: um caso raro em uma criança de 3 meses de idade sem seqüelas neurológicas evidentes

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ABSTRACT

We report here the case of a 3-month-old child with an unusual case of Salmonella spp. meningitis. The disease consisted of typical features of prostration, irritability, persistent fever, and seizure. The incubation time was relatively long for non-typhoids (04 days), but, it was relatively short for typhoid strains, whose incubation takes 7 to 14 days. Intravenous ceftriaxone was started on admission. Additional measures were taken due to hemodynamic instability and status epilepticus, requiring volume expansion, continuous infusion of vasoactive amines and intravenous midazolam, and mechanical ventilation. It generally has a poor prognosis in babies with high rates of acute neurological complications (75%) and mortality (13%). However, this case was resolved without evident neurological sequelae. Periodic assessment of cognitive growth and development is essential in this patient.
Keywords: Salmonella, infant, Meningitis.

RESUMO
Relatamos aqui o caso de uma criança de 3 meses de idade com um caso incomum de meningite Salmonella spp. A doença consistia em características típicas de prostração, irritabilidade, febre persistente e convulsões. O tempo de incubação foi relativamente longo para as cepas não tifoídes (04 dias), mas, foi relativamente curto para as cepas tifoídes, cuja incubação leva de 7 a 14 dias. A ceftriaxona intravenosa foi iniciada na admissão. Medidas adicionais foram tomadas devido à instabilidade hemodinâmica e estado epiléptico, exigindo expansão de volume, infusão contínua de aminas vasoativas e midazolam intravenosa, e ventilação mecânica. Geralmente tem um prognóstico ruim em bebês com altas taxas de complicações neurológicas agudas (75%) e mortalidade (13%). Entretanto, este caso foi resolvido sem seqüelas neurológicas evidentes. A avaliação periódica do crescimento e desenvolvimento cognitivo é essencial para este paciente.

Palavras-chave: Salmonela, lactente, Meningite.

1 INTRODUCTION
Salmonella spp. are enterobacteria with approximately 2,500 serotypes whose infections are commonly categorized as typhoid salmonellosis (Salmonella enterica serovar Typhi and Salmonella enterica serovar Paratyphi) and non-typhoidal. 1,2

Non-typhoid salmonellosis usually causes self-limited, non-bloody acute gastroenteritis, despite being a cause of dysentery, which lasts four to seven days. 2,3-5 Diarrhea and abdominal cramps can be accompanied by fever, chills, myalgia, and headache. Typhoid strains, however, prevent the intestinal immune response and cause severe localized or systemic infections more commonly than other serovars. 3,4 Hematogenous dissemination and consequent bacteremia and extra-gastrointestinal involvement occur in 5% to 10% of infections, both during and after the acute condition, with meninges being the sites most rarely affected. 1,6,7

Bacterial meningitis due to Salmonella is uncommon in developed countries, according to a survey of cases in England and Wales from 1975 to 1991, in which this genus of bacteria was responsible for 0.9% (n = 18) and 0.02% (n = 55) of occurrences in neonates and the other age groups, respectively. 8

Ramos, Feferbaum, Manissadjian and Vaz (1992)9 described Salmonella
spp. as the etiological agent of 9.2% of cases of purulent meningitis in neonates (n = 109) admitted to the intensive care unit of the Hospital das Clínicas, University of São Paulo School of Medicine (São Paulo, São Paulo state, Brazil) between 1977 and 1987.

Bryan, Silva, Tavares, Rocha, and Scheid (1990) reviewed admissions to isolation fever hospital in Salvador city (Bahia state, Brazil), between 1973 and 1982, of which 6,751 (27.0%) were due to meningitis, and of these 4,100 (61.0%) of definite or probable bacterial etiology. Members of the Enterobacteriaceae caused 149 cases (3.6%) of total meningitis, being Salmonella spp. responsible for 44.0% of these infections. Salmonella meningitis occurred almost exclusively children under 2 years.10

It is most frequently diagnosed in infants under one year of age, especially those under the age of three months, from emerging and underdeveloped countries and with a tropical climate. It generally has a poor prognosis in babies and young children with high rates of acute (75%) and late neurological complications (71%) and mortality (13%). Survival without neurological sequelae can be expected if the disease is diagnosed and treated early. The possibility of relapse after apparent recovery should be considered. 10-15

2 CASE REPORT

A 3-month-old babe, weight 5,800Kg (12.8 pounds), mixed race, daughter of a primiparous woman with gestational diabetes and father with systemic arterial hypertension, induced labor, forceps delivery, 1-min Apgar score: 7 and 5-min Apgar score: 9, breastfeeding with bottle feeding using formula milk. Received the Bacille Calmette-Guérin (BCG) vaccine, Hepatitis B vaccine, inactivated poliovirus vaccine (IPV), Pneumococcal conjugate vaccine (PCV10), Rotavirus vaccine, and Meningococcal vaccine.

According to the mother’s report, the patient started fever on September 24th, 2019. She was taken to an Emergency Care Unit (ECU) in Belo Horizonte city, Minas Gerais state, Brazil, where laboratory tests were performed, and a urinary tract infection was diagnosed. Cephalexin orally was started on September 26th. After four days, she returned to this unit due to diarrhea, and the antibiotic was switched to Amoxicillin.
The child evolved with gradual prostration, irritability, hypoxia, and oliguria, and persistent fever. On October, 2nd, she suffered a sudden ventilatory and fixed stare followed by tonic-clonic movements. She was taken again to a ECU in which, on admission, she had a fever (axillary temperature (AT): 37.8 °C / 100.0 °F), tachycardia (heart rate (HR): 200 beats/minute), and seizure. He was then referred to the Odilon Behrens Hospital, in Belo Horizonte and medicated with intravenous (IV) Metamizole and Midazolam. Cranial computerized tomography (CCT) of this day showed dilated lateral ventricles, and the cerebrospinal fluid (CSF) exam has revealed: cloudy aspect, white blood cell leucocytes (WBC): 5.430, polymorphonuclear leukocyte (PMN): 81%, monocytes: 19%, glucose 1mg/dL, protein 1032 mg/dL, lactate dehydrogenase (LDH): 11.7 mg/dL, and gram without staining bacteria. Then Ceftriaxone IV 100mg/Kg/day was started on this date.

On October 3rd, she had intermittent and frequent spasms in the upper limbs in the morning and, despite the administration of Phenobarbital IV (10mg / Kg at 06: 00h pm and 10mg / Kg at 08:00 pm) and Phenytoin IV (15mg / Kg as 11:00 pm and 5mg / Kg at 07:00 are), evolved to status epilepticus and hemodynamic instability, requiring volemic expansion, continuous infusion of vasoactive amines and Midazolam IV (gradual increase to 7.5 ug / Kg/minute), and mechanical ventilation. Started in this same day Topiramate IV 1.7mg / Kg once a day. Phenobarbital IV was maintained at 2.5 mg/kg twice a day. The blood and CSF culture revealed a posteriori Salmonella spp. The transfontanelle ultrasound of the next day detected the only ventriculomegaly, according to previous CCT.

She maintained about two feverish peaks (AT 38.0 °C / 100.4 °F) daily until October 7th and afebrile from the following day. She was extubated on October 8th, after five days at the Pediatric Intensive Care Center. Midazolam was suspended two days and Phenytoin three days after the last seizure (October 10th), and Dexamethasone IV was administered during these days. The blood count of the October 6th showed: erythrocytes 3.81 million / mm3, hemoglobin 10.7 g / dL, hematocrit 32.5%, WBC 14310 / mm3 (segmented neutrophils: 54.0%, lymphocytes 35.0%, monocytes 5.0%, eosinophils 3.0%), Platelets: 635,900 / mm3. The Polymerase chain reaction (PCR) was 89 mg / dL. CSF exam on October 08th revealed clean aspect, WBC: 64, PMN: 0%, monocytes: 100%, erythrocytes: 03, glucose 11 mg / dL, protein 199 mg / dL, LDH: 4.2 mg / dL, gram
without staining bacteria, and CSF culture negative.

Admitted to the pediatric ward on the 13th day of hospitalization (October 14th) hemodynamically stable, breathing in room air, acyanotic, (oxygen saturation 98%), eupneic (42 respiratory incursions per minute), afebrile (AT 36.4 ° C / 97.5 ° F), hydrated, reactive to clinical examination, usual diuresis, and defecation, good acceptance of the diet by nasoenteral probe.

On the 17th day of antibiotics (October 19th), the CSF exam showed aspect limpid, WBC: 174, PMN: 6.0%, monocytes: 94%, erythrocytes: 02, glucose 26 mg / dL, protein 145 mg / dL, LDH: 1.7 mg / dL, gram without staining bacteria, and CSF culture negative. CSF exam of the October 28th (day 26 of antibiotic therapy) revealed hemorrhagic aspect, WBC: 106, PMN: 5.0%, monocytes: 95%, erythrocytes: 7260, glucose 30 mg / dL, protein 120 mg / dL, LDH: 1.8 mg / dL, and gram without staining bacteria.

Ceftriaxone IV was suspense on October 31th (29 days). However, due to the CSF exam of the November 04th (clear aspect, WBC: 90, PMN: 15.0%, monocytes: 85%, erythrocytes: 0, glucose 32 mg / dL, protein 83 mg / dL, LDH: 1, 6 mg / dL, and gram without staining bacteria, and CSF culture negative), it was decided to start Trimethoprim / sulfamethoxazole (TMP / SMX) 50mg / Kg / day.

CSF exam on November 14th (day 09 antibiotic therapy) revealed a clear aspect, WBC: 26, PMN: 2.0%, monocytes: 98%, erythrocytes: 08, glucose 37 mg / dL, protein 76 mg / dL, LDH: 1, 8 mg / dL, and gram without staining bacteria. CSF culture was negative. The therapy was maintained until 14 days, as instructed by the Hospital Infection Control Committee (HICC).

On November, 19th, the child had clinical and hemodynamic stability, afebrile since October 08th, without recurrence of seizures since October 10th, smiling, preserved appetite, diuresis, and defecation usual, without apparent neurological changes.

3 CONCLUSION

Hospital Municipal Odilon Behrens (HMOB) is a referral and teaching public hospital located in Belo Horizonte city (Minas Gerais state, Brazil) that provides around 480 clinical and traumatological urgency and emergency care per day and has 321 hospital beds, being 46 of these neonatal and pediatric intensive care.
Few national studies, whether descriptive or analytical, have been published to date on Salmonella meningitis. Carneiro, Patrício, Jain, Rodrigues, and Fracalanzza (2018) reported a case of meningitis caused by Salmonella enterica serotype Panama in a 4-month-old male newborn in Brazil. This child had a history of fever for more than five days and diarrhea, similar to what happened with our report, whose onset of hyperthermia preceded eight days and diarrhea by two days the staring and tonic-clonic movements. CSF exam of their report showed more intense pleocytosis (11.9 × 10^3 cells/mm^3 versus 5.43x10^3 cells/mm3), lower concentration of proteins (440mg/dL versus 1.032 mg/dL), an equal concentration of glucose (1mg/dL). Gram staining of the CSF was positive for gram-negative bacilli, while in this report it was negative.

Salmonella spp. are of the fecal-oral route that occurs as a result of poor hand hygiene, after handling, for example, domestic animals, especially birds and reptiles (non-typhoid), or ingesting contaminated water and food (typhoid and non-typhoid). In the case of infants, contamination is also due to the careless preparation of infant formula or neglect of breastfeeding care, which favors the transmission of fecal particles from contact hosts of the pathogen. Carneiro, Patrício, Jain, Rodrigues, and Fracalanzza (2018) have incriminated in their meningitis case report maternal milk as the source of S. Panama. However, the mother denied contact of her and other family members with animals at home or symptoms suggestive of gastrointestinal infection in them and reports adequate hygiene habits to breastfeed and food preparation. The hypothesis of nosocomial infection has thus become the most plausible.

This microorganism is capable of colonizing equipment and intravenous fluids used in pediatric beds. This source of contamination is even cited by Ramos, Feferbaum, Manissadjian, and Vaz (1992) as likely responsible for a considerable portion of the ten cases of bacterial meningitis caused by Salmonella spp. of your study.

The incubation time, however, was relatively long to non-typhoid strains (September 24th, 2019: emergency medical care - September 28th, 2019: return to the hospital due to diarrhea) as the initial symptoms of gastroenteritis usually appear from 12-48 hours after contagion. On the other hand, this interval was...
relatively short to the typhoid strains, whose incubation takes 7 to 14 days.20

The benign clinical evolution must probably be related to the early initiation of antibiotic therapy and reinforces the importance of empirical treatment (Ceftriaxone) in the face of clinical and laboratory conditions suggestive of bacterial meningitis. Late neurological complications are expected in about 70% of cases.15 Therefore, periodic assessment of cognitive growth and development is essential in these patients.

This case represents a rare occurrence of gastrointestinal infection (presumed) by Salmonella sp. complicated by bacteremia and, consequently, acute meningitis, resolving without evident neurological sequelae, approached in a tertiary referral hospital in a Brazilian metropolis. The main limitation of this report was the no typing of the Salmonella sp., due to the technical limitations of the institution's laboratory, which compromised the reasoning about the origin of the infection and clinical evolution.

**DISCLOSURE STATEMENT**

No potential conflict of interest was reported by the authors.
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