



NEONATAL SEPSIS AND MENINGITIS CAUSED BY *Edwardsiella tarda* ISOLATES BELONGING TO THE SAME CLONE: A CASE REPORT

LEÃO R.S.^{1*}, SANTOS R.M.R.², ALBUQUERQUE A.L.M.C.², D'A. CARVALHO-ASSEF A.P.³ AND MARQUES E.A.¹

¹Departamento de Microbiologia, Imunologia e Parasitologia, Faculdade de Ciências Médicas, Universidade do Estado do Rio de Janeiro, Avenida 28 de Setembro, 87, fundos, 3º andar - Vila Isabel, Rio de Janeiro 20551-030, Brazil.

²Hospital Federal da Lagoa. Ministério da Saúde, R. Jardim Botânico, 501 - Jardim Botânico, Rio de Janeiro 22470-050, Brazil.

³Laboratório de Pesquisa em Infecção Hospitalar, Instituto Oswaldo Cruz, Av. Brasil, 4365 - Manguinhos - Rio de Janeiro 21040-360, Brazil.

*Corresponding Author: Email- robson.leao@uerj.br

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Abstract- *Edwardsiella tarda* is a member of the family *Enterobacteriaceae* and unusually causing human disease most often in gastroenteritis. *E. tarda* have rarely been associated with neonatal infections. Herein report a case of sepsis and meningitis caused by *E. tarda* isolates belonging to the same clone in preterm newborn infant, with a gestational age of 35 weeks. Maternal habits that could be correlated with the acquisition of this bacterium were investigated and pinpointed, such as: contact with marine environments, eating raw fish, immersion in a contaminated body of water and penetrating trauma from the colonized vector. All these factors were not observed. Histopathological examination of the placenta was performed and revealed consistent results with chorioamnionitis, which may suggest the acquisition of intrauterine infection. The newborn had a good treatment outcome at 21 days with cefepime and neurological involvement was not observed. In summary, in this report we describe the first case of neonatal meningitis by *E. tarda* in Latin America with possible intrauterine infection acquisition with no clear maternal risk factors associated.

Keywords- Neonatal sepsis, neonatal meningitis, *Edwardsiella tarda*

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Introduction

Edwardsiella tarda is a member of the family *Enterobacteriaceae* which can be found in aquatic environments and unusually causing human disease most often in gastroenteritis [1]. Other clinical syndromes associated with *E. tarda* are described, such as soft tissue infection, sepsis, hepatobiliary infections, meningitis, peritonitis, osteomyelitis, endocarditis, tubo-ovarian abscess and salpingitis [2-5].

The first report of meningitis and neonatal sepsis caused by *E. tarda* was described in 1968 [6], even so, there are few reports of neonatal sepsis and meningitis caused by *E. tarda* [7-9]. In this report we describe a case of meningitis and sepsis in a preterm newborn caused by *E. tarda* isolates which belong to one single PFGE clone.

Case Presentation

The patient is a female preterm newborn infant, with a gestational age of 35 weeks and a birth weight of 2110g who was born by spontaneous vaginal delivery, after 48h from the membrane's rupture. Apgar scores were 8/9 and patient was discharged after 2 days. Moments before labour, mother's vaginal culture was performed for *Streptococcus agalactiae*.

When the newborn was 10 days old, due to fever of 38,0°C and refusing breastfeeding, she returned to the hospital. Laboratory workup revealed WBC count of 5,700/mm³ (8% bands, 55% neutrophils, 27% lymphocytes, 10% monocytes). Spinal tap was performed and blood culture was collected on admission. Cerebrospinal fluid (CSF) white cell count was 7,000 mm³, red blood cell count was 623 mm³, and no microorganisms were seen on Gram stain.

Empiric intravenous antibiotic therapy was started with a combination of ampicillin (400mg/kg/d) and gentamicin (4mg/kg/d), administered twice and once daily respectively. CSF and blood culture showed *E. tarda* isolates. *E. tarda* was identified by the Vitek 2 Compact system using Gram-negative (GN) cards (ref no. 21341; bioMérieux) and confirmed by 16SrRNA gene sequencing using BLAST searches against the GenBank database. Using a disk diffusion test, according to CLSI (2013), both *E. tarda* isolates were susceptible to all antimicrobial agents tested, such as, ceftazidime, cefepime, cefotaxime, aztreonam, ciprofloxacin, piperacillin-tazobactam, amoxicillin-clavulanic acid, ampicillin-sulbactam, gentamicin, trimethoprim-sulfamethoxazole, chloramfenicol, imipenem and meropenem. Pulse Field Gel Electrophoresis was performed following digestion of intact genomic DNA with *Xba*I restriction enzyme (Roche Indianapolis IN USA) as previously described [10].

DNA fragment patterns were analysed using BioNumerics version 6.6 (Applied Maths, St. Marten-Latem, Belgium) and clusters were defined using the Dice coefficient of similarity. UPGMA dendrograms were drawn with a position tolerance of 1.00% and optimization of 1.00%. Both *E. tarda* isolates belonged to the same clone.

Antibiotic therapy was changed to intravenous cefepime (100mg/kg/d), due to the better penetration in the central nervous system, which was maintained for 21 days. Ampicillin was not tested by disk diffusion test, thus the antibiotic therapy with this antimicrobial was suspended. As the newborn was readmitted to the hospital, a histopathologic examination of the placenta was performed. Transcranial doppler ultrasonography (transfontanel) was normal and the newborn had a good evolution during de hospitalization hence respiratory support was not necessary. On the third day of hospitalization a new collection of CSF and blood culture was conducted and both of them were negative. She was discharged after 27 days of hospitalization.

Discussion

Bacterial meningitis in the newborn is a major challenge to neonatologists due to its high mortality rate and later complications, mainly neurologic, the late ones may even compromise the newborn's future life quality [11]. The incidence is described as 0.25-6.1 per 1000 live births (developed countries 0.3; Asia 0.48-2.4; Africa and South Africa 0.81-6.1) [12]. In neonates (children younger than 28 days), the most common causative organisms of bacterial meningitis are *Streptococcus agalactiae* (Group B streptococcus), *Escherichia coli*, *S. pneumoniae* and *Listeria monocytogenes* [11,13].

There are scarcities of data on neonatal sepsis and meningitis in Brazilian publications. Data from 2010 showed that the incidence of meningitis was 0.6% and the mortality was 27%. These data, from 22 cases, also demonstrated that from all microorganisms isolated, 59% were Gram-negative bacteria, 36% Gram-positive bacteria and 5% were fungi [14].

E. tarda is a typical marine gram-negative pathogen that affects mostly catfish and thus is an important issue in aquaculture affecting fish markets and this commodity's economy. Extraintestinal human infections by these bacteria are rare, especially neonatal sepsis and meningitis [5,6,15].

Our patient presented a severe sepsis that was confirmed by microbiological tests. *E. tarda* was isolated from blood and CSF, with both isolates belonging to the same clone by PFGE analysis. Considering the epidemiology of human infections caused by *E. tarda*, maternal habits that could be correlated with the acquisition of this bacterium were investigated and pinpointed, such as: contact with marine environments, eating raw fish, immersion in a contaminated body of water and penetrating trauma from the colonized vector [2, 9]. All these factors were not observed, although a possible vertical transmission could not be excluded. The epidemiological data was also collected for the newborn at readmission with the same negative findings.

Histopathological examination of the placenta was performed and revealed consistent results with chorioamnionitis, which may suggest the acquisition of intrauterine infection by *E. tarda*. No other cause could be correlated to the infection. Scientific studies showed that membrane rupture lasting more than 18 hours will increase the probability of infection by commensal microorganisms [15,16]. In this case report mother's membrane had a rupture lasting 48h before delivery which could suggest a causative origin for the infection.

tion.

The vaginal swab from the mother, obtained during delivery, showed no evidence of *E. tarda*, although in the hospital laboratory the microbiological culture media used is selective to *Streptococcus agalactiae* (group B *Streptococci*) hence inhibiting the growth of *E. tarda*.

Clinical diagnostic of meningitis in the neonate is difficult with no more specific signs than fever, diarrhea, vomiting, poor feeding and respiratory distress, these factors can compromise treatment leading to neurologic sequelae, such as, cerebral palsy, epilepsy, mental retardation and hydrocephalus [11,14]. Despite the difficulty of diagnosis, in the clinical case described in this report, the patient had a good treatment outcome at 21 days with cefepime and neurological involvement was not observed. Grave neurological outcome manifested as microcephaly, late cerebrate, developmental delay, and spastic quadriplegias have been described after meningitis caused by *E. tarda* [10,17]. In summary, in this report we describe the first case of neonatal meningitis by *E. tarda* in Latin America with possible intrauterine infection acquisition with no clear maternal risk factors associated.

Competing Interests: The authors declare that they have no competing interests.

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