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Case Report

A case of non-O1/non-O139 *Vibrio cholerae* septicemia and meningitis in a neonate

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SUMMARY

A case of septicemia with meningitis due to non-O1/non-O139 *Vibrio cholerae* in a neonate is reported. The genotype and phenotype of the isolate were examined in relation to the major virulence genes. The isolate was shown to be non-toxin but cytotoxin-producing, distinguished from the dominant clone of non-O1/non-O139 *V. cholerae* by multilocus sequence typing.

1. Introduction

Non-O1/non-O139 *Vibrio cholerae* are being recognized increasingly as invasive pathogens in bacteremia, particularly among patients in an immunosuppressed condition.[1] The presenting symptoms of bacteremia due to non-O1/non-O139 *V. cholerae* are well described. However, the genotype and phenotype of virulence factors that allow the strains to invade the bloodstream are not well elucidated. A case of sepsis with meningitis due to non-O1/non-O139 *V. cholerae* in a neonate is described herein, highlighting the pathogenicity of this strain.

2. Case report

An 11-day-old female infant with a 1-day history of low-grade fever, lethargy, and a refusal to feed was referred to the Qingdao Maternal and Child Health Care Hospital in July 2014. Neither vomiting nor diarrhea was present.

The initial physical examination revealed a weight of 2.95 kg, a pulse of 150 beats/min, and a temperature of 38.0 °C. The anterior fontanel was flat. There were no remarkable findings on physical examination, chest X-ray, or ultrasound of the abdomen. The initial laboratory test results revealed a white blood cell count (WBC) of 6.65 × 10^9/l (67.1% neutrophils) and a C-reactive protein (CRP) level of 88.9 mg/l. A cerebrospinal fluid (CSF) test showed a WBC of 18.06 × 10^9/l (89.0% neutrophils) and a protein level of 218.6 mg/dl. Blood and CSF cultures (bioMérieux, France) were collected before flucloxacillin and meropenem were administered intravenously.

The infant's condition deteriorated over the next 24 h, with the presentation of convulsions and the development of metabolic acidosis and intraventricular coagulopathy. The laboratory evaluation showed a WBC of 15.26 × 10^9/l (65% neutrophils) and a CRP level of 119.83 mg/l. Because of the generalized seizures and the continuing high temperature of 38.3 °C, the patient was transferred to Qingdao Municipal Hospital on the third day of admission.

After an incubation period of 12 h, both the blood and CSF cultures yielded curved Gram-negative rods. The organisms were suspected to be *V. cholerae*, as indicated by the Vitek 2 compact system (bioMérieux). This identification was confirmed by the Microbiology Laboratory of Shandong Provincial Center for Disease

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Control and Prevention by PCR test. The organisms showed no agglutination with the Vibrio O group 1 and group 139 antisera. An in vitro susceptibility test showed this strain to be sensitive to the penicillins, cephems, carbapenems, aminoglycosides, quinolones, and trimethoprim–sulfamethoxazole.

The patient was prescribed 450 mg of sulbenicillin and 198 mg of metronidazole administered intravenously per day, in addition to vitamin K1 and plasma to assist with the coagulation. A cerebral computed tomography (CT) scan performed on day 11 revealed a hemorrhagic focus in the bilateral frontal and temporal lobes, as well as multiple areas of low attenuation lesions (Figure 1). After 23 days of antibiotic therapy, the patient had survived, although with some neurological deficits, and was discharged home.

In assessing the pathogenic significance of the isolate from the patient, studies on the hemolytic, hemagglutination, protease, and cytotoxin activities of this strain were performed, as described previously, with some modifications.[2] The strain showed high hemolytic activity, moderate hemagglutination activity, high protease activity, and high cytotoxin activity.

In addition, PCR tests were performed to detect the genes related to the identification, virulence, and toxicity, as described previously.[2–4] The strain was found to be non-toxigenic, as it lacked the *ctx*A, *ctx*B, *tcp*A, and *tox*R genes. However, the strain carried other genes, such as *omp*W, *omp*U, *chx*A, *hly*A, *dth*, *rtx*C, *hap*, and *Prt*V, which may play crucial roles in the pathogenicity of this strain.

Although the specific serotype of this isolate was not determined, multilocus sequence typing (MLST) was performed to identify its gene sequence type. Three new alleles of *gyr*B, *mdh*, and *met*E were submitted to the MLST database and designated as 60, 57, and 101, respectively. This strain was assigned a novel sequence type (ST188) (http://pubmlst.org/vcholerae/).

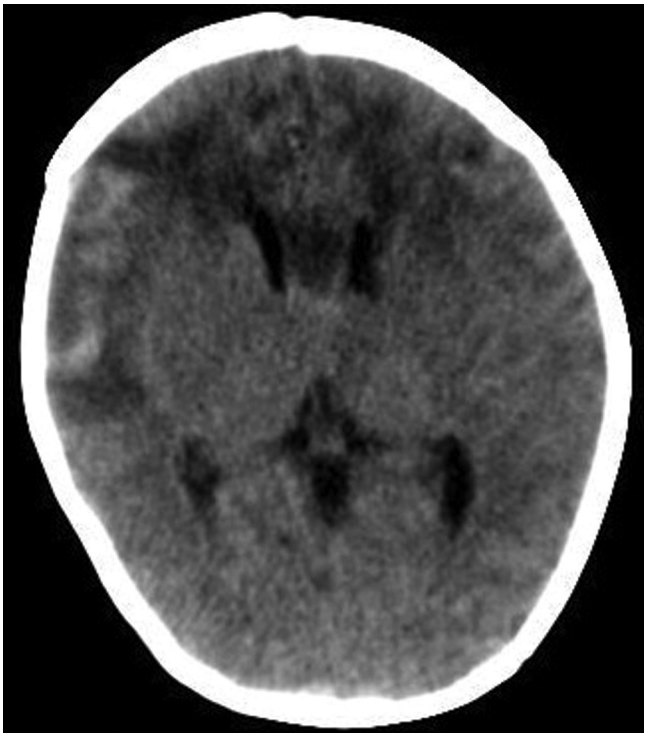

Figure 1. Cerebral CT scan of the patient 22 days after admission demonstrating a hemorrhagic focus in the bilateral frontal and temporal lobes, along with symmetric low attenuation lesions in the bilateral frontal lobes.

3. Discussion

Septicemia caused by non-O1/non-O139 *V. cholerae* is a rare but life-threatening condition, particularly in infants. To the best of our knowledge, there have been only six reports of infants who have developed septicemia due to non-O1/non-O139 *V. cholerae*. From these reports and the present case, it appears that in infancy, septicemia due to non-O1/non-O139 *V. cholerae* is associated with a very high rate of meningitis (6 of 7). Meanwhile, the prognosis of the disease is poor; two patients have died and three patients have survived with neurological sequelae. According to the previous literature, most of the organisms have been sensitive to the third-generation cephalosporins, piperacillin/tazobactam, fluoroquinolones, and tetracyclines. Early diagnosis, timely antibiotic therapy, and an adequate duration of treatment may improve the prognosis.

Infections with non-O1/non-O139 *V. cholerae* typically arise from water sources. Our patient was delivered uneventfully by cesarean section, and the perinatal acquisition of the organism from the vaginal or fecal flora was therefore unlikely. The acquisition of the organism was most likely through contaminated food and paraphernalia.

Interestingly, diarrhea was absent in all of the infant patients. The MLST results demonstrated that this isolate was distinguished from the dominant clone *V. cholerae* that has been reported. The pathogenicity-related genotype traits and the phenotypic tests showed the high pathogenicity of the isolate. *hly*A and *rtx*C act by dismantling the host tissue barriers and enabling the strains to survive the innate immune system.[5] Factors such as *hap*, *Prt*V, and *chx*A primarily have associations with extraintestinal rather than enterotoxic infections,[4] which may explain the absence of gastrointestinal symptoms in our patient. These various putative accessory virulence factors may have played synergistic roles in the invasion of the bloodstream and the seeding of the meninges.[2]

In this report, the pathogenicity and invasiveness of nontoxigenic *V. cholerae* are highlighted. Non-O1/non-O139 *Vibrio cholerae* should be added to the differential diagnosis of neonatal septicemia and meningitis.

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Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijid.2015.05.004.

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