Case Report

Infant botulism in Costa Rica: first report from Central America

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Abstract

Introduction: *Clostridium botulinum* is known to cause descending paralysis in infants throughout the world.

Methodology: The subject of this study was a three-month-old Costa Rican boy who was hospitalized because of poor suction and feeding, hypotonia, and constipation. Clinical history and physical examination findings suggested infant botulism. Samples were sent to the Winnipeg Public Health Laboratory, where *Clostridium botulinum* toxin A was identified by PCR and culture from the stools, making this the first report of infant botulism in Central America.

Conclusions: Although infant botulism is a known disease, the limitations in identifying it in Central America contributes to the misdiagnosis and under-reporting of this disease.

Key words: infant botulism; *Clostridium botulinum;* epidemiology; Costa Rica; Central America; Latin America

J Infect Dev Ctries 2014; 8(1):123-125. doi:10.3855/jidc.3594

(Received 27 March 2013 – Accepted 21 June 2013)

Introduction

Infant botulism (IB) is a neuroparalytic illness caused by the botulinum toxin of *Clostridium botulinum.* Its onset can be insidious or abrupt, with constipation usually being the first symptom noted by parents. Characteristically, IB presents as an acute, symmetrical, descending flaccid paralysis [1,2]. Flat facial expression, poor sucking and feeding, drooling, and floppiness are usually present at admission. Spinal muscular atrophy and metabolic disorders are the most common conditions mimicking IB [3]. Approximately 95% of cases of IB occur in infants younger than six months of age, as opposed to Guillain-Barre syndrome, which usually occurs in older children. Honey consumption as a risk factor for IB has been reported in as much as 60% of cases in Europe and outside the United States; however, an important percentage has not been associated with honey consumption. Microscopic dust is another source of spore ingestion [4,5]. Intravenous Botulism Immune Globulin (BIG-IV) has been shown to be a safe and effective treatment. Patients with IB who do not receive BIG-IV have been shown to have longer hospital and intensive care unit stays and more days of assisted mechanical ventilation [6]. In the absence of complications, full and complete recovery of strength and muscle tone is expected [1].

In Central America, no previous cases of IB have been published. We report the first case in a Costa Rican infant admitted to the only tertiary pediatric referral and teaching hospital in our country.

The Patient

A three-month-old boy was referred by his pediatrician to our hospital. He had a history of eight days of hypotonia, hypoactivity, irritability, and weak cry, and constipation four days prior. During the last two days, his parents noticed poor sucking, sleepiness, and hypoactivity, and difficulty breathing on the last day.

He was a full-term baby, whose mother had a normal pregnancy and delivery; he frequently visited an agricultural farm area. His birth weight was 3.6 kg (50th percentile), he was breast fed for the first month of his life, and he had been receiving formula since then. Newborn inborn metabolism errors were ruled

out. He had normal neurodevelopment until two months of age, when he began to fail to thrive; his milk formulas were then changed. Grape juice drops were given on his pacifier five days prior to the first symptoms, and there was no honey or corn syrup consumption history.

On admission, weight was 5.3 kg (10th percentile), length was 60 cm (25th percentile), weight/height was in the 10th percentile, temperature was 37.2°C, O_2 saturation was 87%, heart rate was 140 beats per minute, and respiratory rate was 22 breaths per minute. He looked moderately dehydrated, had cold extremities, slow capillary refill, difficulty breathing, lack of facial expression, and bilateral palpebral ptosis (Figure 1). He had a poor stimuli response, a weak cry, no gag reflex, normal symmetric bilateral osteotendinous reflexes with generalized hypotonia, descendent paralysis, and had mainly bulbar affection with facial diplegia and ophthalmoplegia. An infectious disease consultation suggested an IB diagnosis.

Hemoglobin was 11.4 g/dL, leukocytes were 20,300/mm^3 (71% neutrophils, 5% bands, 19% lymphocites, 5% monocytes), and platelets were 671,000/mm^3. C-reactive protein was 15 mg/dL, and blood gases, serum biochemistry, lactate, and ammonium were normal. Urinary metabolic screen and toxics were negative. His cerebral spinal fluid (CSF) was normal, and a bacterial culture was negative.

A chest radiograph documented a right upper lobe atelectasis. Due to his worsening condition and respiratory failure, he was intubated and transferred to the Pediatric Intensive Care Unit (PICU). Brain ultrasound and electroencephalogram (EEG) were normal. A head computerized tomography (CT) scan showed fronto-temporo-parietal atrophy. On neurology consultation, rhomboencephalitis and Miller Fischer syndrome were also considered. A neurography and repetitive nerve stimulation did not evidence a significant decrease in amplitude of the fourth potential nor post-tetanic potentiation.

The patient required PICU management for 21 days, and remained ventilated for 17 days. He received intravenous clindamycin, cefotaxime, gentamicin, and acyclovir for 12 days; the antibiotic therapy was given because he had aspiration pneumonia on admission, and acyclovir was given because he was thought to have encephalitis when the diagnosis of IB had not yet been confirmed. No BIG-IV was given, as it is not available in Costa Rica. The patient recovered completely by 10 months of age and has no permanent sequelae.

Figure 1: Infant Botulism in Costa Rica: first report from Central America

Stool samples were submitted to the Winnipeg Public Health Laboratory and tested for *C. botulinum*. DNA was extracted with a Qiagen QIAamp DNA Stool Mini Kit. This extract was used as a template for the Centers for Disease Control Laboratory Response Network's real-time PCR assay for the detection of *C. botulinum* toxin gene targets A-G. DNA extracted from this sample was positive for *C. botulinum* toxin type A. For the mouse bioassay, four injection groups of two mice each were used and observations were taken at two hours and four hours post-injection. Mice injected with EBD11-002 and positive control preparations displayed symptoms consistent with botulism poisoning. Mice injected with antisera-treated samples displayed no symptoms of botulism poisoning. The culture for *C. botulinum* was positive in the stools but negative in the milk formulas and honey samples. Thus, two months later, IB was confirmed.

Discussion

This case illustrates the importance of promptly considering the diagnosis of IB. Treatment with BIG-IV should be started right away, without waiting for confirmation tests.

Worldwide epidemiology of IB was described recently [5]. In that report, 524 IB cases from 25 countries in Asia, Australia, Europe, North America, and South America were found. Despite large populations in the countries of Latin America, cases were reported only from Argentina (366), Chile (3), Venezuela (1), and Mexico (1). Subsequently, other South American countries have reported IB cases in

the English literature [7], but there are none from Central America or the Caribbean. In Costa Rica, the first reports of *C. botulinum* in soils were in 1993 [8,9], and in a small study of 64 honey samples, no identification of the organism was made [10]. In Argentina, the most frequent serotype associated with infant botulism is serotype A, which is similar to the most common serotype in Europe, but not the United States [11], and which is the same serotype that was found in the patient described in this study.

Although we could not prove the infecting source in this patient, warning labels about the risk of honey consumption and IB should be placed on honey bottles in Costa Rica during packaging, as warning labels are not currently uniform or widespread. Also, increasing disease awareness among physicians should be a priority. It is possible that this patient ingested the spores from the dust at the agricultural farm he frequently visited. The neurological recovery of this patient in the hospital was similar to the recovery of the patients reported by Underwood *et al.* [6], with a prolonged period of assisted mechanical ventilation, PICU, and hospital stay. The recovery after discharge in this patient was slow; as described in the literature, recovery can take weeks to months [12]. We cannot rule out that there have been more patients with IB in our country in whom the diagnosis was not suspected and therefore not tested for. It is concerning that even though IB is a disease of public heath importance worldwide, physicians in Costa Rica and Central America have the misperception that it is not a problem in our region, given there are no cases reported in the literature until this case. Therefore, as in other countries, IB should be included among the national compulsory report registries. Cooperation alliances should be encouraged throughout Latin America to make diagnosis and prompt treatment available, to improve reporting, and to prevent eventual outbreaks.

Acknowledgements

Elena Campos, MQc. Centro Nacional de Referencia en Bacteriología, INCIENSA; Tres Ríos, Costa Rica.

Cindi R. Corbett, PhD. Bioforensics Assay Development and Diagnostics Section, Science Technology and Core Services Division; Microbial Immunity Section, National Microbiology Laboratory Public Health Agency of Canada.

The sample processing was done with the contribution of Canada´s National Public Health Laboratory.

The samples transport was done with the contribution of the National Public Health Laboratory in Costa Rica.

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Conflict of interests: No conflict of interests is declared.