Archives de Pédiatrie xxx (2018) xxx–xxx

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Short communication

Infant botulism: Two case reports and electroneuromyogram findings

J. Bernardor [a], J. Neveu [a,*], H. Haas [a], G. Pitelet [a], M.-R. Popoff [b], C. Mazuet [b], E. Bérard [c], C. Boulay [d], B. Chabrol [d]

[a] *Hôpitaux pédiatriques de Nice CHU, Lenval, 57, avenue de la Californie, 06200 Nice, France*
[b] *Unité des bactéries anaérobies et toxines, Institut Pasteur, 25, rue du Dr-Roux, 75724 Paris cedex 15, France*
[c] *Hôpital de l'Archet, CHU de Nice, 151, route de St-Antoine, 06200 Nice, France*
[d] *Service de neuropédiatrie, hôpital La Timone-Enfants, AP–HM, 264, rue St-Pierre, 13385 Marseille cedex 5, France*

ARTICLE INFO

Article history:
Received 6 March 2018
Accepted 20 May 2018
Available online xxx

Keywords:
Botulism
Infant
Electromyography
Botulinum toxin

ABSTRACT

Botulism is an uncommon severe neuromuscular disorder. We report two recent cases of confirmed infant botulism diagnosed in an 11-week and a 5-month-old infant along with electroneuromyogram (ENMG) findings. Then, we discuss the EMG features of infant botulism. In severe forms of infant botulism, presence of these features might help decide to use botulinum immune globulin. To our knowledge, case 1 is the first case reported in France based on confirmed dust contamination.

1. Introduction

Botulism is an uncommon progressive severe neuromuscular disorder caused by the neurotoxin of *Clostridium botulinum*, which blocks the release of acetylcholine at neuronal endings, resulting in flaccid paralysis. Of the seven subtypes of *C. botulinum*, four (A, B, E, F) are responsible for human botulism [1]. We report two recent cases of infant botulism in France, one caused by dust contamination and we present electroneuromyogram (ENMG) findings.

2. Observations

2.1. Observation No. 1

A 5-month-old male infant was the second child of unrelated parents, born normotrophic at term with no pre-, peri-, or postnatal medical history or neurodevelopmental delay. He was exclusively breastfed until the week prior to hospitalization, when dietary diversification was begun with industrial mashed fruits. He had presented rapidly progressing symptoms over the last 4 days:

- acute hypotonia with loss of head control;
- feeding difficulties;
- constipation, and oliguria.

Clinical examination showed a lethargic child with global hypotonia, bilateral ptosis, and areflexic semimydriasis, no pyramidal syndrome and normal deep tendon reflexes. He presented no fever or organomegaly, and his cranial perimeter was normal.

Complete blood count, blood electrolytes, ammonemia, creatine kinase (CK), cerebrospinal fluid (CSF) protein levels and cytology were normal. Blood and urine toxicology screens in the child and his mother were negative. Plasma and urine amino acid and urine organic acid profiles were normal. Electroencephalography and cerebral magnetic resonance imaging (MRI) with gadolinium injection showed no anomaly. Antiacetylcholine receptor antibodies were negative.

During the following days, the symptoms remained stable. The clinical course was marked by aspiration pneumonia due to suction difficulties, successfully treated with antibiotics and nasogastric feeding.

Motor nerve conduction studies performed 10 days after the onset of symptoms showed compound muscle action potentials (CMAP) with reduced amplitudes on the right ulnar and median (motor and sensitive) nerves. Repetitive motor nerve stimulation

* Corresponding author.
E-mail address: J.Neveu[a]neveu.julien@gmail.com (J. Neveu).

https://doi.org/10.1016/j.arcped.2018.05.002
0929-693X/

(RMNS) at 3 Hz showed no decrement, but was only performed in one nerve–muscle pair (right ulnar nerve–abductor digiti minimi). Needle electromyogram (EMG) was not performed.

Investigations of stool samples by the National Reference Center for botulism resulted in isolation of *Clostridium botulinum* type B and detection of botulinum toxin B, confirming the diagnosis of infant botulism. *C. botulinum* B was also detected in three soil samples from a building site close to the family home by enrichment cultures, polymerase chain reaction (PCR) detection, and mouse bioassay, whereas maternal milk, honey consumed recently by the mother and industrial baby food samples returned negative.

Human botulism immune globulin was not administered because of the spontaneously favorable evolution prior to diagnosis confirmation. The patient was discharged home after 4 weeks. Hypotonia gradually improved over the following month and the last clinical examination at age 8 months was normal.

2.2. Observation No. 2

An 11-week-old female infant was hospitalized for acute hypotonia and feeding difficulties. She was the first child of unrelated parents, born normotrophic at term with no pre-, peri-, or postnatal medical history or neurodevelopmental delay. She had been exclusively breastfed since birth apart from a single bottle of artificial milk around 10 weeks of age. She presented with global hypotonia, progressively worsening for 6–7 days, with a fluctuating pattern during the day. Hypotonia was associated with discomfort, repeated episodes of unexplained crying, and feeding difficulties with weight loss (5% of body weight). She had a history of constipation with the last stools 1 week before. Clinical examination revealed segmentary and peripheral hypotonia with reduced extremity movements, bilateral reactive mydriasis, fluctuating bilateral ptosis, normal ocular pursuit, bilaterally present and normal deep tendon reflexes. She had considerable asthenia but awareness was not impaired. There was no fever before or after the onset of symptoms. There were no signs of respiratory distress. Her cranial perimeter was normal.

Blood electrolytes, ammonemia, CK, CSF protein level and cytology were within the normal range. Blood and urine toxicology screens were negative. Blood, urine and CSF cultures were sterile. Electroencephalography revealed no paroxystic anomaly or signs of encephalopathy. Cerebral MRI with gadolinium injection and spectroscopy showed no anomaly. Complete blood count revealed aregenerative, normocytic, moderate anemia (hemoglobin 9.5 g/dL, mean corpuscular volume 84 fL, reticulocyte count 31×10^9/L), with discrete signs of megaloblastosis on peripheral blood film. A low level of vitamin B_{12} was measured (198 pmol/L, normal $>$ 197 pmol/L) with elevated methylmalonic acid in serum (1.5 μmol/L, normal $<$ 0.4 μmol/L), homocysteine 15 μmol/L (normal $<$ 14 μmol/L) and folic acid 17.6 nmol/L (normal $>$ 3.9 nmol/L), but these results could not explain the severity of the symptoms.

The symptoms remained stable during the following days.

An electroneuromyogram performed 12 days after onset of symptoms showed CMAP of reduced amplitudes on the right ulnar nerve. CMAP amplitudes on the right tibial nerve were at the lower limit of normal. Motor nerve conduction velocities were normal. Sensitive nerve conduction velocities were not studied. RMNS at 3 Hz obtained only one decrement (Fig. 1A) in six different muscle–nerve couples studied (right peroneal nerve–tibialis anterior, right ulnar nerve–abductor digiti minimi, right and left spinal nerve–trapezius, right and left axillary nerve–deltoideus). Needle EMG in the right tibialis anterior and left deltoideus revealed abnormal spontaneous activities (fibrillation potentials, double and triple discharges) at rest (Fig. 1B) and short-duration, low-amplitude, polyphasic motor unit potentials (MUP) during voluntary muscular contraction (Fig. 1C); these data were consistent with the functional denervation produced by impaired acetylcholine release.

Investigations of stool samples by the National Reference Center for botulism resulted in isolation of *Clostridium botulinum* type B and detection of botulinum toxin B, confirming the diagnosis of infant botulism. Dust from the family house was also evaluated for botulism but returned negative. Maternal and artificial milk were not tested.

The clinical course was spontaneously favorable, with progressive normalization of intestinal transit within a few days, oral feeding within 2 weeks and hypotonia within a month. Human botulism immune globulin was not administered because of the spontaneously favorable evolution prior to diagnosis confirmation. Biological anomalies related to vitamin B_{12} deficiency were corrected after 3 days of oral supplementation. The patient was discharged home after 12 days of hospitalization. At last follow-up at age 5 months, the clinical examination was normal.

3. Discussion

Infant botulism, first described in 1976, is caused by ingestion of *C. botulinum* spores from contaminated food (e.g., honey, infant formula) [2] or dust particles, which multiply and produce botulinum toxin in the immature digestive tract of newborns and infants under 6 months and are released into the bloodstream [3]. One hundred new cases are diagnosed every year in the U.S. [4]. In Europe, only three cases of infant botulism with an identified source of contamination have been reported, one in Finland from contaminated soil in 2005 [5] and two in the UK from contaminated water from tanks housing pet terrapins in 2015 [6]. Fifteen cases of infant botulism were reported between 2004 and 2017 in France, with no identified source of contamination [7,8]. It has been suggested that exposure to dust or soil from active construction sites may also increase the risk of contracting botulism, e.g., by living near a construction site, like our case 1 [9]. Clinical manifestations include feeding difficulties, severe acute hypotonia, constipation, ptosis and respiratory failure by diaphragmatic paralysis in severe forms [10]. In all probability, infant botulism is underdiagnosed in Europe, first because of its wide clinical spectrum with differential diagnoses such as myasthenia gravis, acute inflammatory demyelinating polyneuropathy, or inborn errors of metabolism, as in our case 2 where vitamin B_{12} deficiency of unknown etiology was first diagnosed. Infant botulism has also been reported in cases of sudden infant death syndrome [5]. In a case of recent progressive hypotonia, botulism must be sought.

As reported by Gutierrez et al., electrodiagnostic tests in cases of infant botulism suspicion could be helpful. It should include motor and sensory nerve conduction velocity in at least one arm and one leg, 2-Hz nerve stimulation to two distal muscles and needle EMG with sufficient sampling. The search for tetanic and post-tetanic facilitation to assess a presynaptic block is also mentioned, but was not performed in our cases, and we believe it is unnecessarily painful. The best way to assess the presence of a presynaptic block would be to search for an increment (100% or more) of CMAP after 20–30 s of maximum voluntary contraction, but this is impossible to perform in infants. Diagnosis can be suspected based on electrodiagnostic features, including CMAP of decreased amplitude in at least two muscle groups, as shown in our cases. Needle EMG can reveal abnormal spontaneous activities (fibrillation, positive waves) and short-duration, low-amplitude motor unit potentials, but the latency for these findings can be longer than 1 week. These findings can at first suggest myopathic abnormalities, but in the case of infant botulism are due to functional denervation of muscle

Please cite this article in press as: Bernardor J, et al. Infant botulism: Two case reports and electroneuromyogram findings. Archives de Pédiatrie (2018), https://doi.org/10.1016/j.arcped.2018.05.002