



Case Report

Foodborne Botulism in the First Trimester of Gestation

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Abstract

Objective: Botulism is a rare paralytic disease, causes a spectrum of illness from mild cranial nerve paralysis to acute respiratory failure. Botulism has not been associated with any direct adverse effect on the foetus, however only 2 of 17 published cases to date describes botulism during the first trimester of pregnancy. **Case report:** We present a case of a foodborne botulism in a 29-year-old woman at 11 weeks of gestation. The clinical signs included nausea, vomiting, headache, disturbances of accommodation, double vision and dry mouth. Botulinum toxin B was detected, therapy with equine botulinum antitoxin was successful. Ultrasound at 12 weeks of gestation revealed a normal foetus development. Woman was discharged 24 days after the onset of illness with mild blurred vision. At 42 weeks of gestation, she spontaneously delivered a healthy 3,650 g boy; his growth and development was normal. **Conclusion:** Botulism during the first trimester of pregnancy resulted in full recovery of the mother and spontaneous delivery of child without any developmental sequel.

Keywords: Botulism; Pregnancy; Trimester; Toxin B; Antitoxin

Abbreviations: IU: International Unit; kDa: Molecular weight in Dalton unit

Introduction

Botulism is a rare serious paralytic illness caused by a nerve toxin of anaerobic bacterium *Clostridium botulinum* [1,2]. There are seven types of botulism toxin designated by the letters A to G, only types the A, B, E and F cause illness in humans [3]. There are three principal categories of botulism: foodborne, infant and wound botulism [1]. Initial clinical signs of foodborne botulism include nausea, dry mouth and diarrhoea followed by a descending symmetrical paralysis with blurred vision, diplopia, ptosis, pupillary dilation, slurred speech, facial weakness and respiratory failure [2]. Interestingly sensation and reflexes are preserved [1,3]. Treatment of botulism is aimed at early diagnosis, stopping the progression of weakness by administration of botulinum antitoxin, preventing complication with good supportive care and mechanical ventilation in some patients [3]. Case fatality rate decreases from

60% (1960s) to around 5-15% today [1,2]. In pregnancy, botulism is a rare disease and when diagnosed, it has not been associated with any direct adverse effect on the foetus [1,4-9]. The reason for this may be large molecular weight of botulinum toxin (150 to 165 kDa), which prevents its passage through placental barrier [2,10]. Nevertheless, there are indirect risks of damage to the foetus that may come from maternal hypoxemia, mechanical ventilation and complication during intensive care [1]. Over the 45-year period (1961-2007) botulism has been diagnosed in the Czech Republic only in 113 cases [11]. Only four deaths in adults were reported. Out of 113 botulism cases, 111 were of foodborne origin while infant botulism was diagnosed only in two children. Wound botulism was not reported at all. A major source of infection was home made tins, occasionally also tinned fruit or commercially tinned meat [11]. To our knowledge botulism during pregnancy has not been reported in the Czech Republic.

Case report

A 29-year-old woman, at 11 weeks of gestation, celebrated with other 13 persons at a garden party. Twenty four hours later she developed nausea and vomiting. Later on within next day,

other clinical signs appeared including headache, disturbances of accommodation, double vision and dry mouth. During her illness she was not febrile. Sixth day after the party, she was hospitalized at the local neurology department. Primary diagnosis was a blockade of atlantooccipital joint with irritation of cervical sympathetic nerves. Screening toxicology test for drug poisoning and lumbar puncture for neuroinfection were all negative. However, in view of her deterioration (double vision and ptosis) and a reported case of illness with similar symptoms of other woman attending the same party, botulism was suspected. Active surveillance of party participants found two additional women with moderate clinical signs of botulism including blurred vision and dysphagia. Fermented cucumbers were indicated as a probable source of botulinum toxin. Unfortunately this was not confirmed by toxicology examination because there was no food available from the party anymore. Blood samples were collected for botulinum toxin analysis from our woman at tenth day after the garden party and from three non-pregnant women at tenth or eleventh day. Blood sample from pregnant woman was positive for botulinum toxin by a mouse bioassay, in which a patient's serum (with or without antiserum) was injected intraperitoneally into mice that were subsequently observed for symptoms [1,2]. At eleventh day after party, first mouse bioassay with polyvalent antiserum against toxin A, B or E proved botulism, second mouse bioassay with monovalent antiserum confirmed botulinum toxin B. Botulinum toxin was not detected at three non-pregnant women. Anaerobic cultures of stool of all four women did not reveal *Clostridium botulinum*.

One day before confirmation of botulism, our woman was transferred to the Department of Infectious Diseases. The initial clinical evaluation revealed blurred vision, mydriasis, ptosis and dysphagia with no signs of respiratory muscle fatigue. At this time trivalent equine botulism antitoxin for intramuscular use (Antitoxinum botulinicum polyvalent A+B+E, Biomed, Poland) was administered. Two additional doses of antitoxin were given during two subsequent days. Each dose contained 5000 IU of antitoxin A, 5000 IU of antitoxin B and 1000 IU of antitoxin E. In the first day, application of antitoxin in a regimen of desensitization was complicated with headache, pallor, pruritus and short time of dyspnoea. For this reason hydrocortison 200 mg and bisulepinum one mg were administered intravenously with application of an oxygen mask. Within a few minutes the woman fully recovered. Hydrocortison 100 mg and bisulepinum one mg intravenously were followed prior each dose of antitoxin, no other complications were observed. Our woman was not administered any antibiotics. Clinical features improved quickly. Dysphagia vanished one day after the last dose of antitoxin, ptosis persisted for one week, only blurred vision improved gradually. During the first three days of hospitalization woman was able to tolerate only liquid diet, therefore a partial intravenous nutrition was instituted

for five days. The woman suffered from constipation having the first stool after six days. The diagnosis of botulism was supported with electrophysiological study with repetitive muscle stimulation, which showed augmentation of potential (increment of 60% in the 50-Hz rate) seen in botulism and Eaton-Lambert myasthenic syndrome [2,3]. The progress of pregnancy, despite the clinical signs of botulism, appeared normal. Obstetrics ultrasound at 12 weeks of gestation revealed a normal foetus development. Reassurance also came from a genetic specialist stating that probability of damage to the foetus is very low because of large botulinum toxin molecules are not able to pass through the placenta and because of a foetus at 12 weeks of pregnancy had not mature synapses (target for botulinum toxin). Our woman decided for her pregnancy to continue. She was discharged 24 days after the onset of illness free of any clinical signs except for the mild blurred vision. Follow-up neurological examination at eight weeks after poisoning revealed only a residual ocular fatigue. At 42 weeks of gestation woman spontaneously delivered a healthy 3,650 g boy. The child was breast-fed for 10 months. Three-month check-up did not reveal any abnormalities in neurological development with the exception of mild plagiocephalia. Telephone communications with parents confirmed child's normal growth and development until this five years of age.

Discussion

Outbreak of foodborne botulism in two or more persons is usually caused by contaminated foods [3]. In general, clinical diagnosis of botulism is often difficult to make. Clinicians should be vigilant for symptoms of botulism including initial ocular signs, descending flaccid paralysis, bulbar signs and subsequently respiratory failure [3].

It is well established that botulism is frequently misdiagnosed because of its similar clinical findings with other neuromuscular diseases, neuroinfections and intoxications [1,2,7]. This was also true in our case where a suspicion of botulism came relatively late and first clinical signs were misdiagnosed for the cervical abnormality. Published literature on botulism during pregnancy is very rare. For example, Robin, et al. reported a case of foodborne botulism in 24-year-old woman at 16 weeks of gestation. She was treated with two doses of trivalent antitoxin and later on delivered a healthy boy at 42 weeks of gestation [5]. Another study described 37-year-old woman with foodborne botulism at 23 weeks of gestation. She was almost completely paralysed. Only visible motions were foetal movements. Despite an antitoxin treatment, she required mechanical ventilation for two months. However, her healthy baby was spontaneously delivered in term [4]. Morrison et al. reported case of wound botulism in 23-year-old heroin-abusing woman at 36 weeks of gestation [1]. This woman underwent urgent caesarean section followed by antitoxin treatment and mechanical ventilation. Her new-born daughter required treatment

for a respiratory tract infection and drug withdrawal; however no specific treatment was necessary with respect to the maternal botulism. St. Clair, et al. reported a case of botulism in 32-year-old woman at 34 weeks of gestation [6]. After successful trivalent antitoxin therapy, she suffered from partial placental abruption. She delivered prematurely at 34 weeks of gestation a male infant without evidence of botulism and without detectable toxin in serum four hours after birth. Premature infant suffered from aspiration pneumonia and probable intraventricular haemorrhage. As a result, the baby was blind, with developmental retardation and hydrocephalus at a 20 month. Cengiz, et al. described another case of mild botulism in 20-year-old pregnant woman [7]. These authors however have not provided information about progress of gravidity, delivery or infant follow-up. In general, foodborne or wound botulism is not known to cause any direct adverse effect on the pregnancy or the foetus [1,4-6]. Only 2 of 17 published cases in literature to date describes clinical signs of botulism during the first trimester of pregnancy [8]. We report third foodborne botulism in the first trimester of gestation. Several reports also describe either incidental or therapeutic administration of botulinum toxin A for cosmetic purpose, headaches, dystonia and spasticity in women in early stages of pregnancy [10,12,13]. In these studies only two women suffered a miscarriage while another woman had a therapeutic abortion [10,13]. The rest of pregnancies went to full term and there were no foetal malformations. Based on published literature so far, botulism toxin A appears to be relatively safe not only for mother and but also for a foetus [10]. Treatment of botulism is identical for all patients including pregnant women. In the Czech Republic where human or pentavalent botulinum antitoxins are not available, only equine botulinum antitoxin is used for the treatment of botulism [2]. Pregnancy is not a contraindication for treatment with equine antitoxin however hypersensitivity rates vary between 9% and 20% [1,2]. Mild hypersensitivity associated with such therapy in our woman was well managed and short lived. We would like to conclude that botulism during the first trimester of pregnancy resulted in full recovery of the mother and spontaneous delivery of child in full term without any developmental sequel.

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