

## Case Report

# Clinical manifestation and treatment of botulism in two pregnant women: Case report

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## Abstract

The current paper reports two pregnant patients with botulism were infected during a botulism outbreak. They were a 26-year-old Gravida 2 Para 1, 24 weeks and a primigravida 29-year-old, 27 weeks women. The first one suffered from ptosis, blurred vision, chewing muscles weakness, dysphagia and urinary incontinence a few days after eating local yogurt. Moreover, the second one was intubated due to dyspnea, dysphonia, muscles weakness and decreased O<sub>2</sub> saturation, 20 hours after ingestion of local yogurt. Both of them were treated by trivalent antitoxin every 8 h for 2 days. They were discharged at the 5<sup>th</sup> and 25<sup>th</sup> days in well condition, respectively. There was no problem with their pregnancy until they were followed up. In conclusion, in pregnant patients with botulism, treatment should be started as soon as possible and the earlier treatment will reduce the risk of complications.

**Keyword:** Botulinum antitoxin, Disease outbreaks, Food-borne botulism, Pregnancy

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## INTRODUCTION

Botulism is a rare neuroparalytic illness caused by botulinum neurotoxin (BoNT). BoNT is produced by bacterium *Clostridium botulinum* and is the most potent known toxin. BoNT affects acetylcholine-dependent synapses in the peripheral neurons; however, the central nervous system is not involved.<sup>[1]</sup> The most common form of botulism is food-borne botulism which is usually caused by eating the BoNT contaminated food the form mentioned is usually found in homemade food.

The gastrointestinal manifestations are the initial symptoms that are followed by neurologic symptoms, cranial neuropathies and descending weakness, usually after 12–24 h.<sup>[2]</sup> However, there is no fever, sensory, or consciousness problems.<sup>[1]</sup>

There are a few case reports on botulism in pregnant women and the current paper reports two pregnant patients with botulism and their management that were infected during a botulism outbreak.

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## CASES REPORTS

### Case 1

A 26-year-old pregnant woman, Gravida 2 Para 1, was referred to Imam-Reza toxicology center in Mashhad [Table 1]. Her gestational age was 24 weeks and 2 days. Her chief complaint was weakness. The patient's symptoms started a few days after eating local yogurt. After 2 days urinary incontinence was added. At the time of admission, she was alert with normal vital signs; however, she suffered from ptosis, blurred vision. She had dysphagia and complained about weakness in chewing muscles. She had a little trouble getting up off the ground.

On physical examination, she had bilateral ptosis, dysphonia, hoarseness, and weakness of jaw muscles. Her gag reflex was reduced. The upper and lower extremities had normal muscle power. Other neurological examination, such as deep tendon reflexes and walking on the heels and toes, were normal. There was no problem in the range of motion of her joints. Her electromyogram was normal; however, the findings of the nerve conduction velocity test are compatible with neuromuscular junction disorders with no evidence of electro-diagnostic signs of peripheral polyneuropathy or inflammatory myopathy and others neuropathic and myopathy process in both lower limbs.

Obstetric ultrasound reported a live fetus with normal fetal heart rate (FHR = 142), cephalic presentation with anterior placenta and normal amniotic fluid with gestational age of 25 weeks + 4 days. Her urinalysis was normal, and her urine culture was negative. The laboratory data at admission are summarized in Table 2.

The patient was admitted with a clinically diagnosis of botulism and received one vial of trivalent antitoxin on close observation every 8 h for 2 days. While monitoring her vital signs, she was treated by regular intravenous fluid and electrolytes and also received laxative.

On the 2<sup>nd</sup> day of admission, ptosis and weakness of the jaw muscles were decreased. She had a normal level of consciousness with normal vital signs. Her reduced gag reflex became normal, so oral nutrition was started. Her symptoms improved over time. Urinary incontinence improved during hospitalization, but her urgency and frequency persisted. She did not consent to perform urodynamic tests.

She was discharged in good condition on the 5<sup>th</sup> day with normal muscle force and without any evidence of ptosis, dysphonia, and hoarseness. Unfortunately, we missed her follow-up, and we have no information about the outcome of her pregnancy; however, her fetus was in good condition when she was discharged.

### Case 2

A primigravida 29-year-old woman, whom gestational age was 27 weeks and 4 days, was referred to Imam-Reza toxicology center from the secondary care hospital. She complained of abdominal pain, nausea, and vomiting about 12 hours after ingesting local yogurt. About 8 hours later, she felt dyspnea, dysphonia, vertigo, and dysphagia. On physical examination, she had ptosis in both eyes and dilated pupils and absent gag reflex. The facial muscles forces were decreased. Her muscular forces were 4/5. The patient was admitted to the local hospital [Table 1]. Because of dyspnea and decreased O<sub>2</sub> saturation, she was intubated

**Table 1: Summarized the clinical manifestation and course pregnant patients with botulism**

|                                      | Case 1  | Case 2  |
|--------------------------------------|---|---|
| Age (years)                          | 26  | 29  |
| Gravidity(G) and parity(P)           | G2 P1   | Primigravida  |
| Gestational age                      | 24 weeks and 2 days   | 27 weeks and 4 days   |
| Chief complaint                      | Weakness  | Weakness  |
| Incubation period                    | A few days  | 12 hours  |
| Initial symptoms                     | Normal vital signs; bilateral ptosis; blurred vision; dysphagia; weakness in chewing muscles; dysphonia; hoarseness; reduced gag reflex and normal other neurological exams | Initial Gastrointestinal manifestation followed by dysphonia; vertigo; dysphagia; bilateral ptosis; dilated pupils; absent gag reflex; 4/5 muscular forces; dyspnea and decreased blood O <sub>2</sub> saturation |
| Lab tests                            | Normal  | Normal  |
| Fetal solography                     | Normal fetus  | Normal fetus  |
| Anti-toxin                           | 1 vial of trivalent antitoxin every 8 h for 2 days (total=6 vials)  | 2 vials of trivalent antitoxin followed by 1 vial every 12 h up to 2 days (total=6 vials)   |
| Other therapies                      | Conservative treatment  | Intubation and mechanically ventilation for 14 days   |
| Start of recovery                    | At the second day   | At the fifth day  |
| Total time of hospitalization (days) | 5   | 25  |
| Discharge condition                  | Normal muscle forces, without any other symptom except urgency and frequency  | Normal muscle forces without any other symptom  |
| Outcome of pregnancy                 | Missed follow-up  | Missed follow-up  |

**Table 2: Summarized the laboratory results of two pregnant patients with botulism at admission**

| Lab test (unite)                     | Results of case 1 | Results of case 2 |
|--------------------------------------|-------------------|-------------------|
| White blood cells (×1000)            | 13500             | 14100             |
| Neutrophils (%)                      | 75.9              | 88                |
| Lymphocytes (%)                      | 17.7              | 10.2              |
| Hemoglobin (mg/dL)                   | 11.8              | 11.5              |
| Hematocrit (%)                       | 36.3              | 32.2              |
| Platelets (×1000)                    | 218               | 193               |
| Urea (mg/dL)                         | 17                | 21                |
| Creatinine (mg/dL)                   | 0.5               | 0.5               |
| Creatine phosphokinase               | 123               | 203               |
| Prothrombin time (s)                 | 12                | 12.5              |
| Partial thromboplastin time (s)      | 29.8              | 30                |
| International normalized ratio (INR) | 1                 | 1.05              |
| Calcium (mg/dL)                      | 10.2              | 8.5               |
| Magnesium (mg/dL)                    | 2.1               | 1.8               |
| Sodium (mEq/L)                       | 139               | 141               |
| Potassium (mEq/L)                    | 3.8               | 3.8               |
| Total bilirubin (mg/dL)              | 1.1               | 1.3               |
| Direct bilirubin (mg/dL)             | 0.4               | 0.6               |
| Aspartate aminotransferase (U/L)     | 18                | 23                |
| Alanine aminotransferase (U/L)       | 52                | 33                |
| Alkaline phosphatase (U/L)           | 353               | 264               |
| PH                                   | 7.44              | 7.41              |
| PCO <sub>2</sub> (mm Hg)             | 36.4              | 33.5              |
| Bicarbonate (mEq/L)                  | 25.1              | 28.6              |

and then referred to our hospital (Tertiary Hospital). Her laboratory data at admission are summarized in Table 2.

On arrival at toxicology center, she had been intubated and had normal vital signs. She was admitted to the poisoning intensive care unit. She was breathing with mechanical ventilator aide and the ventilator setting included: Synchronized intermittent mandatory ventilation mode with tidal volume = 420 ml, respiratory rate = 12 cycle/min, Fio<sub>2</sub> = 60%, positive end-expiratory pressure (PEEP) = 5 cm H<sub>2</sub>O, and inspiration/expression ratio = 1/2.

At first, because of the clinical diagnosis of botulism, she received two vials of 1:10 diluted trivalent antitoxin in normal saline intravenously and then one vial every 12 h for 2 days.

Her vital signs were monitored, and she was treated by regular intravenous fluid and electrolytes, anticoagulant, and laxative. Ptosis and pupils size became normal after 5–6 days, and her respiratory failure gradually improved. Hence, after 10 days, her spontaneous breathing was supported by the ventilator with pressure support ventilation = 10 cm H<sub>2</sub>O and PEEP = 5 cm H<sub>2</sub>O. Symptoms of neuromuscular weakness gradually improved in the patient and she was extubated after 14 days. Her gag reflex improved gradually, and oral nutrition was started after 20 days.

The all obstetric ultrasounds reported living fetus with normal FHR, cephalic presentation, anterior placenta, normal amniotic fluid, and no abnormality.

She was discharged in well condition with normal muscle force and without any evidence of dysphagia, dysphonia, vertigo, and dyspnea after 25 days. Unfortunately, we missed her follow-up, and we have no information about the outcome of her pregnancy; however, her fetus was in good condition when she was discharged.

## DISCUSSION

Botulism manifests as descending motor neuropathy with sparing sensory pathways and consciousness. Botulism can have an incubation period of 12 hours to a few days, which was observed in our patient.<sup>[3]</sup> Cranial neuropathies include blurred vision, nystagmus, diplopia, ptosis, dysarthria, dysphagia, dysphonia and hoarseness, and weakness of the facial muscles.<sup>[2]</sup> Descending weaknesses include weakness of the trunk and then lower extremities. Other common symptoms include: constipation, urinary retention due to the involvement of smooth muscles.<sup>[1,4]</sup> Both patients showed descending motor neuropathy which is the typical pattern for botulism.

Respiratory failure requiring intubation may last for a long period.<sup>[1,2]</sup> It occurs due to diaphragm paralysis, respiratory muscles weakness, upper airway involvement or all of them.<sup>[1,2]</sup> Antidote therapy neutralizes the circulatory BoNT and it could not reverse the paralyzed neurons; hence, recovery of paralyzed diaphragm and respiratory muscles function may be time-consuming.<sup>[5]</sup> The second case had been intubated and mechanically ventilated for 14 days.

Diagnostic evaluations should not postpone treatment for food-borne botulism. The treatment of patients suspected with botulism includes antitoxin, respiratory support and nasogastric tube-based nutritional support to reduce the risk of aspiration.<sup>[6]</sup> Symptoms of botulism in pregnancy are similar to those of not pregnant patients, so the sooner treatment begins, the better for patient's prognosis.<sup>[7]</sup> In our both cases antitoxin treatment was started promptly. In the first case, the muscle weakness improved after 5 days and she was discharged. However, the second case was intubated and ventilated despite of antitoxin therapy. After 14 days respiratory status was improved and she was extubated and discharged a few days later. O'Horo *et al.* meta-analyzed of 61 papers and concluded that immediate antitoxin therapy and intensive care are essential for the optimal outcome.<sup>[8]</sup>

The first case suffered from urinary incontinency, she had normal urinary tests, and the force of lower extremities was normal. She had no frank paralysis of trunk muscles. Her symptoms improved over time and she was discharged in good condition on the 5<sup>th</sup> day. In botulism, downward muscle weakness extends to the trunk and extremities and also smooth muscle paralysis induces bowel habit problem, constipation, and urinary retention.<sup>[9]</sup> There are some documents on effective treatment of neurological bladder by BoNT A.<sup>[9]</sup>

The second case had dyspnea and was intubated because of respiratory failure. Chatham-Stephens *et al.* published a systematic review and described the clinical features of botulism.<sup>[7]</sup> According to their report, female sex, ptosis, and type E had greater odds of presenting with respiratory distress. Our second case had all of these risk factors. Chatham-Stephens *et al.* also concluded that 40% of patients with symptoms of dyspnea, respiratory distress, or respiratory failure on admission required intubation.<sup>[7]</sup> This systematic review reported that 30% of patients had 1–2 signs of cranial nerve involvement at the time of referral and 30% had 3–4 signs of cranial nerve involvement and 30% had >5 signs of cranial nerve involvement.<sup>[7]</sup> Both cases in our study had >5 signs of cranial nerve involvements. Gottlieb *et al.*, in 2007, also reported that 15% of their patients were hospitalized near 1 month, and 25% of them required intubation.<sup>[10]</sup>

It seems that the BoNT and antitoxin have low teratogenic effect. A systematic review published in 2016 reported that 2.7% of 137 pregnant patients who were treated by BoNT A, on a botulinum toxin A, during pregnancy had fetal complications in a follow-up study, that was no different with the general population.<sup>[11]</sup> However, Badell *et al.* reported that preterm labor occurred in 35% of cases of botulism in pregnant women treated by antitoxin. None of these cases have had any neurological complications in the fetus.<sup>[12]</sup> On the other hand, there have been no reports of adverse effects of botulism antitoxin in pregnancy; therefore, promptly administration of the antitoxin will improve the prognosis.<sup>[13]</sup>

It seems that botulism intoxicated pregnant patients have a higher risk of intubation than general. Badell *et al.* systematically reviewed 17 pregnant patients suffered from botulism.<sup>[12]</sup> They found that more than half of them required ventilator support. However, Chatham-Stephens *et al.* reviewed >200 papers that reported just 400 patient and found that a 38% (154/402) intubation as general.<sup>[7]</sup> This difference may be related to the reduction of respiratory muscle strength, the maximal

inspiratory and expiratory pressures and peak expiratory flow rate in pregnancy.<sup>[14,15]</sup> Moreover, the female sex is a risk factor of intubation.<sup>[7]</sup> One of our patients was intubated and mechanically ventilated a long time.

In conclusion, in pregnant patients with botulism, treatment should be started as soon as possible and the early treatment will reduce the risk of complications.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Conflicts of interest

There are no conflicts of interest.

### Authors' contribution

Ataee, Z. and Moshiri, M. visited and managed the patients. Ataee, Z. wrote the first draft of manuscript and Moshiri, M. finalized it and is correspond.

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