An Investigation of Family Clustering Botulism in Hsinchu City

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Abstract

On 14th February, 2008, two suspected botulism cases were notified by hospital, successively. The epidemiological investigation showed that the two cases lived together, (co-exposure). One of them developed typical neurological symptoms, including ptosis, diplopia, dysphasia, myasthenia on both proximal limbs, and respiratory muscle gravis. The case was admitted to the intensive care unit for mechanical ventilation. Anti-toxin of *Clostridium botulinum* was administered according to the clinical signs before laboratory diagnosis confirmed. The case recovered after 29 days of hospitalization. The other case developed dizziness, difficulty swallowing, ptosis, and mild proximal limbs weakness. This case received anti-toxin treatment before respiratory failure was shown. The case recovered after 5 days of hospitalization.

Serum and stool specimens were collected from patients for both

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toxin and culture testing for *Clostridium botulinum*. The serum from patients were both positive for toxin type A. There were no findings from all food samples.

According to the epidemiological results and both cases presented the same type of *C botulinum* toxin, this event was defined as a family cluster event caused by botulinum type A. By executing disease surveillance and prevention measures, there was no further case reported.

Keywords: *Clostridium botulinum*, food poisoning, foodborne botulism, antitoxin

Introduction

There are three main kinds of botulism: Intake of contaminated food will result in foodborne and intestinal forms; wound botulism is caused by the wound contamination. The pathogenesis of botulism is that the toxin of botulism will bind to the motor neuron synapses, and then the release of acetylcholine is stopped. Consequently, muscles will not be able to contract. Finally, the affected organs and systems will be dysfunctional. If the toxin affects the respiratory muscles, respiratory failure and even death may be the outcomes. Therefore, correct diagnosis and treatment and medical care of botulism must be done in time to avoid death.

On 14th February, 2008, Second Branch, CDC, received two suspected reports of botulism, successively. The initial investigation found that the two patients were sister, lived together, and they had developed similar neurological symptoms in a very short time, consequently. After medical examinations and differential diagnosis, a botulism cluster was highly suspected.

To investigate the possible cause of this cluster, CDC's Second

Branch, Seventh Branch and Epidemiological Field Training Program (FETP), and Health Bureau of Hsinchu City conducted an epidemiological survey on 15th February. The patients in the hospital were visited. At the same time, CDC medical officers communicated with the treating physicians. After ruling out the other different diagnoses, the treatment of anti-botulinum toxin was suggested. In addition, the side effects and the importance of administering in time were also mentioned. (Type A, B, and E. The instruction suggests 2 bottles each time via infusion drop. Patient's allergic reaction or fever response, including anaphylactoid/anaphylactic reaction, and pyretic reaction, should be observed closely. Serum sickness would occur 7 days after antitoxin injection, range from 5 to 24 days. Clinical physicians should note and treat the consequences.)

The purposes of this investigation included:

1. to conduct an epidemiological survey to find out other possible cases and the transmission route. Furthermore, the scale of the event could be evaluated.
2. to explore possible causes related to this event and to investigate the possible risk factors in order to avoid further epidemic events.
3. to understand the current clinical development of cases and provide recommendations to the physicians of preventive medicine.

The description of this epidemic event

On 14th February, 2008, Second Branch, CDC received a suspected botulism notification (Case 1) from Hsinchu General Hospital, Department of Health, Executive Yuan, R.O.C. (Hsin Chu hospital). The hospital also asked for the method of sampling and antitoxin treatment.

The officials of CDC discussed the situation of the case with the clinical doctor in charge. The doctor said Case 1 had developed dizzy and blurred vision. Then diplopia, general weakness, and unsteady gait occurred before she went to see a doctor. Because of the above symptoms, she went to the emergency department of Hsin Chu hospital to seek for doctor's advice and examinations. She was hospitalized for treatment, consequently. On the second day of hospitalization, she developed ptosis. Then swallow difficulty, severer ptosis and mild myasthenia on proximal limbs were observed on the third day after hospitalization. She accepted associated neurological and laboratory examinations. Her blood and cerebral spinal fluid were tested. However, the cause was still unknown. Her condition was worse at the fourth day after hospitalization. She was still conscious but respiratory failure was observed. After ruled out other possible diseases, doctors suspected that she had suffered botulism, according to the development of typical botulism symptoms. Then, she was transferred into the intensive care unit (ICU) and accepted mechanical ventilation. At the same time, she was reported as a suspected botulism case.

In the following epidemiological survey, Case 1's sister had neurological symptoms at the first stage. Mild progress of disease was observed. According to the suggestions by medical officers of CDC, Case 1's sister, who was noted as Case 2, needed hospitalization immediately. She was treated as a suspected case and then reported.

On the notifying day, CDC dispatched 4 bottles of antitoxin to the hospital. CDC also suggested collecting serum and samples from patients' gastrointestinal tracts, such as feces and vomit firstly; then, the antitoxin was administered consequently.

Materials and Methods

The subjects of investigation

The subjects of investigation in this event were the suspected botulism cases, the possible cases, and the people having the co-exposure history within the patient's incubation period.

The definition of a suspected botulism case is that person has developed typical neurological syndrome of botulism, such as double vision, blurred vision, swallow difficulty, medullary-type paralysis, and symmetrical neurological paralysis.

The definition of a possible case is that the case fits the definition of suspected botulism case and has epidemiological linkage. For example, the possible case is the person who has eaten home-made cans within 48 hours.

The definition of contact is the person has the co-exposure history in the suspected or confirm case's incubation period. According to the definition, family, neighbors, and friends of the suspected cases are all contacts. They will be asked for the presence of neurological symptoms.

The definition of confirm case is that case fits the definition of suspected case and is laboratory confirmed, or suspected case has eaten the same foods which consumed by the confirm case.

The investigation period

Patient with foodborne botulism usually develops neurological symptoms within 12 to 36 hours after eating foods (the duration is defined as the incubation period). However, the symptoms can be seen after few days as well.

The investigation of risk factors

There are three types of botulism according to its transmission routes and infection types. Both foodborne and intestinal botulism result from eating contaminated food. Wound botulism is caused by wound contamination. Hence, two things, the suspected foods and the situation of wound contamination, were explored.

Firstly, in the issue of investigating the suspected foods, the foods that the two cases ate together were noted as the suspected foods. The food processing method, the storage method and whether the food was heated were all checked.

Clostridium botulinum is an obligate anaerobic spore-forming bacterium. The spores of *Clostridium botulinum* are not destroyed during food processing, if foods are not processed well; such as incomplete sterilized cans, inadequate cooking, or unsealed containers with inadequate preservation or without refrigeration. Finally, the undestroyed spores, which can survive in an anaerobic condition, sprout, produce toxin, then cause botulism. Because of the above reasons, the investigators asked the cases to recall their dietary history within a week before onset of the symptoms. Possible foods related to foodborne botulism, which have been mentioned in articles, were special discussed. Pickle foods, can foods, especially those are home-made were asked and listed.

In order to clarify the possibility of getting toxin by wound contamination, the two patients were asked for experience of wounds contaminated by botulism.

Sampling methods and laboratory examinations

Human samples

Serum and stool specimens of the two patients were collected. The protocol followed the 'Manual of sampling method related to samples of epidemic prevention and control, CDC, Taiwan'. Serum specimens were collected before being administered antitoxin. Specimens were kept in 4℃ and then sent to CDC's laboratory for examinations.

The tests include toxicity and neutralization assays (animal test) of botulinum toxins type A, B, and E and culture for *Clostridium botulinum*.

Food samples

The suspected foods, which were listed according to the cases' dietary history, were collected by Health Bureau. The leftover foods, the opened and un-opened foods were all sampled. Case 1 only could communicate by pen and paper because of unable to speak. The common foods consumed were described by Case 2.

The suspected foods were sent to Bureau of Food and Drug Analysis, Taiwan (BFDA) for examinations. Tests of pH values, the botulism toxin, and culture of *Clostridium botulinum* were all performed.

Results

The subjects of investigation

The contact of Case 1 in her incubation period was her sister. They had symptoms such as ptosis, and unable to speak from 8th February. The difference was Case 1's course of disease progressed faster and much severe. She went to hospital for treatment on 11th February. On 14th February, she presented respiratory muscle gravis and was transferred into

ICU for mechanical ventilation care. Case 2's symptoms were mild and her course of disease developed slower.

According to the information, the people under the same exposure were 2; no other people involved.

The development of the course of disease

Case 1

Case 1 was non-aboriginal, divorced, 51-year-old female. She did not live with her children. At 12:00 pm, the 8th February, which was the 38th hour after co-exposure, she developed symptoms such as ptosis, unable to speak, and diplopia. She went to the hospital's emergency room seeking for treatment. The symptoms had not been improved till 11th February; the date she decided to seek doctor's advice again. The tentative diagnosis was myasthenia gravis suspected. She was hospitalized for further diagnoses. On 12th February, she presented myasthenia gravis on both proximal limbs. On 13th February, swallow difficulty, and choking at eating were observed. Nasogastric tube was installed. Tachypnea was observed on 14th February; then the course of disease progressed quickly. She was transferred into ICU for mechanical ventilation on the same day. She was still conscious and could communicate by pen and paper. The hospital reported she was a botulism suspected case on 14th February.

Case 1 was hospitalized between 11th February and 10th March; she was on mechanical ventilation for 23 of the 29 days hospitalized. The antitoxin was administered on 14th February, the 7th day after onset of symptoms and the 4th day of hospitalization. The mechanical ventilation was discharged on 7th March, which was the 22nd day after being administered antitoxin. She was discharged from the hospital on 10th March.

She recovered soundly and was able to go back to her usual activities, except some tiredness and muscle weakness were still presented.

Case 2

Case 2 was divorced, 50-year-old female. She was Case 1's sister. They lived together. She developed ptosis, diplopia on 8th February as well. She did not seek doctor's advice because only mild symptoms presented. On 14th February, the symptoms still presented; neither worse nor improved. She saw that her sister's course of disease progressed severer and then she felt worry. She complained that she had suffered from the similar symptoms for a few days. She told doctors that she had the similar symptoms, which her sister had in the first few days. She was accepted into the hospital on 14th February. The doctor reported the case to CDC on the same day.

In order to prevent respiratory muscle paralysis, she was given the antitoxin on 16th February. The treatment was stopped because significant allergic reaction during the course of treatment. The development of neurological symptoms was observed closely. Luckily, after 5 days of observation in hospital, she did not develop any new symptoms. She was discharged from the hospital on 19th February. Her eyelid ptosis did not recover fully then.

The courses of disease for Case 1 and 2 and their medical treatments were described in Figure 1 by order.

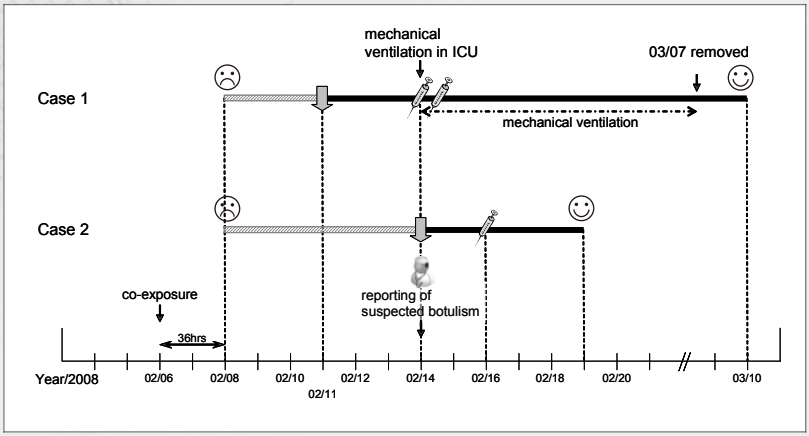

Figure 1: Clinical progression of the 2 cases from the family clustering.

illustration：

- onset of symptom
- hospitalization
- injecting antitoxin
- discharge
- antitoxin
- the period during diagnosis
- the period of hospitalization

Case 1 and Case 2 had the same food exposure history on 6th Feb. After 36 hours of the incubation period, they had developed symptoms since 8th Feb. Case 1 had significant and fast progress of clinical signs. 23 out of 29 day of hospitalization, she needed mechanical ventilation to help breathe. Case 2 had mild symptoms and was discharged after 5 days of hospitalization.

Case 1 had been treated by antitoxin since 14th Feb. Two bottles was administered. One dose was used for Case 2 on 16th Feb. The treatment was stop because of allergic reaction.

The investigation results of risk factors

The investigation results of the suspected foods

The two people had very different dietary habits, when the dietary history of co-exposure before a week of symptoms onset was reviewed. The only meal they ate together happened at 23:00, 6th February, which was the 36th hour before the symptoms onset. The food they ate together were mock minced pork (gluten), mustard leaves, boiled peanuts, and mock pig stomach (gluten). Case 2 said she ate a few. In addition, the common food they were used to eat was pickled vegetables, according to

the statement.

There were 5 suspected foods in this investigation: mock minced pork, mock pig stomach, pickled white gourds, pickled cucumbers, and pickled gingers. Only mock pig stomach was made and labeled by a legal food manufacturer. The others were all home-made without label, which were put in room temperature. In addition, the expiration date was unclear. The 5 suspected foods can be eaten without heating. For the above reasons stated, during the manufacturing process, if it has been contaminated by spores of *Clostridium botulinum*, such as unsuccessful sterilization or toxin has existence, the people eat the food would suffer from the toxin. Table 1 showed the results of examinations, which was done by BFDA.

Cases also pointed out they bought foods from a shop behind a temple in Miaoli City. Second Branch, CDC worked with the food safety section, Health Bureau, Miaoli County to check the foods on 20th February. In total, 402 homemade canned foods were sealed up on government orders. The pickled cucumbers and pickled white gourds were sampled and sent to BFDA for examination. The other foods were sealed up.

The investigation result of possible wound infections

The two cases had no wound and then, it was hard to be contaminated by botulism, after the investigation.

Table 1. The suspected co-exposure food and the test result

		①mock minced pork 600g/can	②mock pig stomach vacuum packed	③pickled white gourd 600g/can	④pickled cucumbers 600g/can	⑤pickled gingers 600g/can
Status of eating	Case 1	+	+	+	+	+
	Case 2	+	+	+	+	+
Label	Label	−	+	−	−	−
	shelf life	−	+	−	−	−
Storage and Cooking	Refrigeration	+	−	−	−	−
	Require cooking	−	−	−	−	−
	Place of sampling	Patient's home	market	Patient's home	Patient's home	Patient's home
test and results	pH value	6.5	6.5	5.5	6.0	3.5
	Botulinum toxin in foods	Not detected	Not detected	Not detected	Not detected	Not detected
	C. botulinum	Negative	Negative	Negative	Negative	Negative

Explanation: 1. The co-exposure foods suspected were listed on this table, in which ① and ③ to ⑤ were collected from patient's house. ② was bought from the same place where the patient bought the sample, because no leftover foods left. 2. the source of examination: BFDA.

Results of laboratory examinations

Two serum samples, 2 fecal samples, and 1 nasogastric tube lavage from Case 1 were collected and examined. The results showed that botulinum type A was detected from both cases'. The food samples, including two samples from Miaoli City, were all botulinum toxin negative, according to the reports from BFDA. The culture of *C botulinum* was negative as well (Table 1).

Prevention policy

To prevent further cases from occurring by eating the suspected foods while the investigation was on-going, CDC informed four health bureaus (Taoyuan County, Hsinchu County, Hsinchu City, and Miaoli County) to strengthen surveillance the possible botulism cases from 21st February,

2008. In the event of suspected cases, investigation should include detailed dietary histories, especially ask about the suspected foods identified in this event. The purpose was to prevent big outbreak by surveillance. Luckily, no any further case was reported.

Discussion and Conclusion

According to the transmission routes of botulism, foodborne and wound infections are the two main types. The foodborne transmission type can be divided into eating the toxin or eating the spore (the intestinal type). Because Case 1 and Case 2 did not have wound, getting infection by wound can be ruled out firstly. Hence, foodborne type, especially via eating the co-exposure foods was highly suspected.

Botulism of foodborne type is rarely reported as a reason of food poisoning. There are about 250 food poisoning outbreaks every year in Taiwan. The cause related to botulism was less than 1 case a year [1]. According to the disease reporting information database system, CDC, there were 3, 6, 13 reported cases from 2005 to 2007, respectively. The confirmed cases in the three years were 1, 2, and 7, respectively [2]. The causes of foodborne botulism were mainly related to home-made cans and traditional salted meat [3-6]. The biggest outbreak of botulism in Taiwan was recorded in September 1986. Workers in a printing plant in Changhua County ate caned home-made pickled peanuts, which were made by a non-licensed family factory. There were 9 confirmed cases and then 2 people died [3].

The cause was assumed as foodborne botulism after careful consideration. Thus, the foods ate by the two cases were investigated.

Because the cases lived in a cluster housing department and no cluster outbreak was reported, the factor related to water supply contamination was ruled out. From the recalled dietary history, they did not drink tomato juice or vegetable juice. The fifth suspected food in Table 1 was acidic and the first to the fourth food were mildly acidic. Only the second food was vacuum-packed, which was made by a food factory. The other foods were home-made cans. These foods were sampled according to the methods published in previous reports. Cases all stated that the foods were kept in room temperature and did not cook before they ate them. Thus, these foods were highly suspected as the causes.

There were 2 people suffering in this event. Their serum specimens, and fecal samples, and foods eaten by the two cases together were examined to test for botulinum toxin type A, B or E. The results showed that the sera from the two cases were botulinum toxin type A positive. On the contrast, the results of the food samples were all negative.

According to the symptoms of the two suspected cases and the results of examinations, the two cases fitted the definition of botulism stated above and then they were considered as confirm cases. Based on the clinical signs, epidemiological relationship among people, time, and place, and the same type of botulism was detected from the two patients, this event was defined as a family cluster event caused by botulinum type A.

The culprit in this cluster is not found, because the patients could not provide complete information, or the other suspected foods are not known. Nevertheless, health bureaus in counties and cities had implemented measures to prevent further outbreaks, such as sealed the foods having the same batch numbers. In addition, the Health Bureaus in charge also helped

to improve their food production processes.

There are some factors related to unable to find the causal foods in this investigation. Firstly, it was the sixth day after onset of symptoms when the case was reported. The patient might be too uncomfortable to recall the dietary history in the incubation period. The leftover foods might have been cleaned out as well. The above assumptions might result in unable to sample comprehensively. These are the factors causing unable to identify the causal foods finally.

The severity and progress of the two cases' courses of disease were very different. The severity of clinical symptoms of botulism may vary. Type of toxin, the amount exposed and the length of the incubation period, time to diagnosis, time to antitoxin treatment, and the clinical presentation all affect prognoses. Higher mortality is associated with respiratory muscle paralysis [7,8]. In addition, the duration of hospitalization or in ICU, the use of mechanical ventilation, and the recovery time will affect the prognosis as well. Case 2 insisted that she ate little daily. Thus, the intake amount was assumed as a factor associated with the severity of the outcome.

Administering antitoxin treatment in time can help stop the development of neural paralysis, and it is the only treatment method to retard the progress of botulism [9]. Early administering antitoxin to neutralize the free botulinum toxin in patients can reduce the efficacy of the toxin binding with motor neuron synapses; the binding can block the release of acetylcholine And finally muscles cannot contract and the organs or systems will be dysfunctional. Case 1 was administered antitoxin on the 6^{th} days after the onset of symptoms. Her condition and

symptoms had become stable gradually. Case 2 showed mild symptoms. However, early antitoxin treatment in time can avoid respiratory failure. Although it resulted in allergic reaction eventually and then the treatment terminated, Case 2 stop to develop new symptoms and then she was discharged from the hospital earlier.

The symptoms of botulism are very similar to neurological muscular diseases and phosphorous poisoning and it is hard to differentiate from these diseases. Doctors in the areas or countries, where the incidence is very low, may not be familiar with the diagnosis, clinical signs, the course, and the care method of the disease. In addition, they may not have enough clinical experience about botulism. Then, they may postpone making an exact diagnosis. Moreover, the delay of sample collection, and lack of laboratory data are also the factors being unable to make the correct diagnosis [7-9]. Although the incidence rate is low in Taiwan, the confirmed cases have gradually increased recently [2]. When clinical doctors discover patients presenting double vision, blurred vision, medullary type paralysis and symmetry paralysis, they should ascertain their patients do suffer from botulism or not. The doctors should investigate patient's epidemiological and dietary histories as well. The people having the co-exposure history should be found as well. Those are helpful to find any other suspected cases in order to make correct diagnosis and find the potential possible cases to prevent a large scale outbreak. To identify the possible causal factor and the type of botulism, the clinical physicians not only should report the case to the health department in charge but also send the samples of the suspected cases' blood, stool, vomit and any suspected food for examinations, if they have

found suspected cases. However, the most important thing is to get samples before administering antitoxin. If people have similar symptoms, they should go to see doctors immediately and provide food history. The leftover food should be kept for investigation. This might serve to benefit the investigation and possible food recall.

The storage, the supply management, the emergency transport and the clinical suggestions of antitoxin are the key factors related to whether the patients can be administered the antitoxin in the early stage of the course of disease. Taiwan CDC has the trivalent botulinum antitoxin, which contains type of A, B, and E. However, because the antitoxin is hard to get, it still belongs to the group of special medicines. Thus, it is necessary for clinical physicians to discuss cases' conditions with the officials or preventive medical doctors of CDC, when they reported the cases. It is beneficial to exclude related different diagnoses. Early administering antitoxin can avoid the development of the course of botulism but good and sufficient supportive medical care is even more important to those patients who have respiratory failure. Moreover, that can avoid the death due to the respiratory failure [2].

Botulism toxin is one of the most toxic substances and trace of toxin can result in death. The mortality rate of botulism is the highest among all bacterial foodborne poisoning. Although the spores of *Clostridium botulinum* is heat-resistant and can only be destroyed by high-pressure sterilization, its toxin is heat-labile. Cooking at 100℃ for 10 minutes, the toxin can be destroyed. Thus, heat food fully is the best method for prevention.

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