An Outbreak of Type A Botulism Associated with a Commercial Cheese Sauce

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Background: Although botulism is rare, recognition of a possible case of this illness represents a public health emergency. To prevent more cases, prompt investigation must be done to determine whether illness is linked to a commercial product or restaurant. Botulism can masquerade as other illnesses, and seemingly unlikely foods can harbor botulinum toxin.

Objective: To confirm the diagnosis and determine the cause and extent of an outbreak of botulism associated with food served at a delicatessen.

Design: Retrospective cohort study of patrons of the delicatessen; laboratory analysis of food, serum samples, and stool samples; and traceback of implicated food.

Setting: Community in Georgia.

Participants: Patrons of the delicatessen.

Main Outcome Measures: Botulinum toxin in food, serum, or stool and Clostridium botulinum in food and stools.

Results: 8 of 52 patrons (15%) met the case definition for botulism. In 4 of the 8 patrons, an illness other than botulism was initially diagnosed. Five of the 8 were hospitalized, and 1 died. Stool cultures from 4 patrons yielded type A C. botulinum, and two serum samples contained botulinum toxin. All ill persons ate food from the delicatessen on 1 October 1993. Of the 22 persons who ate at the delicatessen that day, all 8 ill persons but none of the 14 well persons ate a potato stuffed with meat and cheese sauce. An open can of cheese sauce contained type A botulinum toxin and yielded C. botulinum on culture. Cheese sauce experimentally inoculated with C. botulinum spores became toxic after 8 days at a temperature of 22 °C (room temperature).

Conclusions: A commercial, canned cheese caused a botulism outbreak. This product readily becomes toxic when contaminated by C. botulinum spores and left at room temperature. Mild botulism caused by unusual vehicles may be misdiagnosed. Botulism should be included in the differential diagnosis of persons with signs or symptoms of acute cranial nerve dysfunction.

Botulism is a rare disease; between 1983 and 1992, an average of only 22 cases of food-borne botulism were reported to the Centers for Disease Control and Prevention each year (Unpublished data). Nevertheless, a reported case of food-borne botulism represents a public health emergency because many persons may be affected if the contaminated food is not identified. This is especially true of outbreaks linked to commercial products or restaurants. However, because few clinicians have ever seen a case of botulism, the diagnosis may be delayed or not even considered. Diagnosing botulism is a special challenge when patients present with mild symptoms and do not have a history of exposure to typical food vehicles, such as home-canned vegetables.

We describe an outbreak of botulism that was characterized by relatively mild symptoms and subtle physical findings. The outbreak was caused by a food vehicle that was initially considered to be unlikely. The investigation shows the importance of considering the diagnosis of botulism soon after patients present with acute cranial nerve dysfunction and of promptly reporting suspected cases to public health officials.

The Outbreak

On 4 October 1993, a 42-year-old woman (patient 1) visited her family physician in a small town in southern Georgia. She had had nausea, blurred vision, and loss of balance for 2 days. Results of physical examination were normal except for a possible sixth-nerve palsy. Labyrinthitis was diagnosed, and the patient was sent home. When her physician contacted her the next day, she was too weak to come to the telephone. Her husband reported that her speech was slurred and that she was having difficulty swallowing. He mentioned that their 21-year-old daughter (patient 2) also had nausea and difficulty swallowing. Both patients were referred to...
a neurologist, who recognized this unusual clustering of neurologic symptoms as possible botulism. The patients were admitted to a hospital, and public health officials were notified.

That same day, a 38-year-old woman with a history of hypertension (patient 3) was seen in the emergency department of the same hospital because of blurred vision, slurred speech, and weakness in her right arm. She was admitted to the medical ward with a diagnosis of transient ischemic attack. By coincidence, the family physician of patients 1 and 2 was also attending on the medical ward that night; he recognized that patient 3 might be another case of botulism. Patient 3 mentioned that her friend, patient 4, was having similar symptoms. Patient 4 was notified that her illness might also be botulism, and she too was hospitalized. Two days earlier, her new symptoms had been diagnosed as an allergic reaction to a tranquilizer. Patient 5 had visited an optometrist on 5 October with fatigue and blurred, double vision. She received a diagnosis of mild glaucoma and astigmatism and was given a prescription for eyeglasses. She presented to the emergency department on 7 October after hearing about the outbreak on the radio.

None of the patients had eaten any home-canned foods. However, on 1 October, all of them had eaten food from a delicatessen that had re-opened on 23 September after having been closed for 6 months because of the owner’s family obligations. Local health officials closed the delicatessen on 6 October and seized leftover foods.

Methods

Clinical and Epidemiologic Investigation

Hypothesis-generating interviews were done with the hospitalized patients and the owner of the delicatessen. Each step in the preparation and storage of foods was reviewed. After a standardized questionnaire that addressed food histories and symptoms was developed, investigators attempted to interview (either by telephone or in person) all persons who had eaten food from the delicatessen in the 6 days it was open between 23 September and 2 October 1993. For the purposes of the investigation, a case of botulism was defined as dysphagia, dysphonia, dysarthria, or diplopia that developed after 23 September in any person who had eaten food purchased at the delicatessen.

A press release was issued to identify patrons of the delicatessen. The press release asked all persons who had eaten at the delicatessen to call the local health department. The owner and patrons of the delicatessen were asked to name other patrons, and businesses in the neighborhood around the delicatessen were surveyed as to whether workers had eaten food from the delicatessen.

In an attempt to find additional cases, 50 physicians in the area were called and asked whether they had seen any patients since 23 September who reported blurred or double vision, dry mouth, difficulty swallowing, change in voice, or muscle weakness. To identify any cases that may have been mistakenly diagnosed as other conditions, physicians were also asked if they had recently seen any patients with a diagnosis of stroke, transient ischemic attack, the Guillain-Barré syndrome, or myasthenia gravis. Logs from the emergency department of the local hospital were reviewed for these symptoms and diagnoses.

All hospitalized patients were examined by the same neurologist, and their hospital and outpatient records were reviewed. No neurologic examination was done on three persons who met the case definition for botulism but did not seek medical attention. These patients were identified by their responses to the standard questionnaire.

The delicatessen was inspected by officials of the Georgia Department of Agriculture. Officials of the Food and Drug Administration inspected the canning facility and searched for unused cans of the same batch of cheese sauce.

Laboratory Investigation

Samples of food taken from the delicatessen were assayed for botulinum toxin and were cultured for Clostridium botulinum as described elsewhere (1). All persons who ate the implicated food were asked to submit serum and stool specimens. Gastric aspirate specimens were obtained from two hospitalized patients. Serum, stool, and gastric aspirate specimens were assayed for C. botulinum toxin, and stool specimens were cultured for C. botulinum.

Inoculation experiments were done in the Food and Drug Administration botulism laboratory to determine the time and temperature needed for C. botulinum to grow and for toxin to be produced in the implicated brand of cheese sauce. Spores harvested from cultures of the outbreak strain of C. botulinum were heat-shocked at 80 °C for 10 minutes and then diluted with sterile water to a concentration of 10^4 spores/mL. Twenty g of the cheese sauce was then added to sterile test tubes that contained 0.1 mL of inoculum; the final concentration was 10^3 spores/20 g of cheese. The tubes were incubated at 22°C and 5°C; they were then assayed for toxin on day 8 and every 3 to 4 days for 2 months. Toxin testing was also done before incubation to ensure that no toxin was transferred with the inoculum. Toxin was measured in mouse minimum lethal doses using the mouse bioassay (2).
Results

Epidemiologic Findings

The delicatessen first opened in August 1992 and then closed for 6 months from March to September 1993. It reopened on 23 September 1993, serving lunch 3 days a week (Thursday through Saturday). Food was served at the delicatessen from 23 to 25 September and from 30 September to 2 October (Figure 1). Routine inspections of the delicatessen done on 30 September and after the outbreak showed no violations of state standards for retail food sale establishments.

Fifty-two persons who ate food from the delicatessen in the 6 days it was open between 23 September and 2 October 1993 were identified and interviewed. Eight (15%) met the case definition for botulism. Their ages ranged from 20 to 48 years; 6 were women. No additional cases were identified through the review of emergency department logs or the physician survey. The owner of the delicatessen estimated that she served about 20 meals each day. Many of the patrons were friends of the owner or members of the owner's family and had eaten there more than once.

Eight (36%) of 22 persons who ate food from the delicatessen on Friday, 1 October, met the case definition compared with none of the 30 who ate the food only on other days. Among the 22 persons who ate food from the delicatessen on 1 October, all 8 ill persons but none of 14 well persons had eaten a barbecue stuffed potato. Six other persons had eaten barbecue stuffed potatoes before 1 October but remained well. The owner did not recall selling any stuffed potatoes on 2 October.

Table 1. Symptoms Reported by Eight Persons with Botulism

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Persons with Symptom, n</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurologic</strong></td>
<td></td>
</tr>
<tr>
<td>Dry mouth</td>
<td>7</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>6</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>6</td>
</tr>
<tr>
<td>Dysphonia</td>
<td>6</td>
</tr>
<tr>
<td>Weakness in an extremity</td>
<td>5</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>5</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5</td>
</tr>
<tr>
<td>Diplopia</td>
<td>3</td>
</tr>
<tr>
<td>Paresthesias</td>
<td>2</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5</td>
</tr>
<tr>
<td>Constipation</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3</td>
</tr>
<tr>
<td><strong>General</strong></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>5</td>
</tr>
<tr>
<td>Sore throat</td>
<td>2</td>
</tr>
</tbody>
</table>

Clinical Findings and Laboratory Confirmation of Botulism

The illnesses ranged from mild to severe. Most patients had few, subtle objective neurologic findings despite having many symptoms characteristic of botulism. Symptoms developed a median of 2.5 days after exposure (range, 1 to 6 days). All ill persons had 3 or more symptoms consistent with botulism (median, 8.5 symptoms; range, 3 to 14 symptoms) and, by definition, at least 1 symptom that suggested a cranial nerve abnormality. The most common symptoms were dry mouth, difficulty speaking and swallowing, and change in voice quality (Table 1). All ill persons had neurologic and gastrointestinal symptoms. Three persons had illnesses so mild that they did not seek medical care. Five persons were hospitalized in an intensive care unit after botulism was suspected; in four of these persons, an illness other than botulism was initially diagnosed (Table 2).

Patient 3, the most severely affected, developed complete bilateral ptosis, markedly dysarthric speech, weakness of the tongue and palate, arm and leg weakness, and respiratory failure. She died of a pulmonary embolism after being supported by mechanical ventilation for 18 days. Patient 1 was noticeably dysarthric and required nasogastric intubation because of difficulty swallowing. Patients 2, 4, and 5 had few objective findings other than mild ptosis and slightly reduced arm strength. Patients 1, 3, and 5 received trivalent botulism antitoxin. All four surviving hospitalized patients gradually recovered. At follow-up visits 6 months later, the results of neurologic examinations of these four patients were normal.

Laboratory studies confirmed the diagnosis of botulism in four patients (Table 2). Scrum samples from the two most severely ill patients contained...
low levels of botulinum toxin. Although the mice that were injected with the patients’ serum did not die, they showed typical signs of botulism when given a double dose (0.8 mL) of serum. Stool cultures from the first four hospitalized patients yielded C. botulinum that produced type A toxin. Stool cultures from the remaining four persons with botulism were obtained more than 5 days after the onset of illness and were negative for C. botulinum. Botulinum toxin was not detected conclusively in any stool samples. An extract of a stool sample from patient 5 caused death in some of the injected mice. The pattern of death and survival was incomplete but did suggest the presence of type A toxin. However, because the stool cultures from this patient did not yield toxigenic organisms, this result was questionable. No toxin was detected in gastric aspirates obtained from two patients.

Preparation and Source of Food

The potatoes were purchased at a local supermarket and then washed and placed in a refrigerator. When a patron ordered a barbecue stuffed potato, a raw potato was wrapped in a paper napkin and cooked in a microwave oven for 6 to 8 minutes. When steaming hot and soft, the potato was sliced open; margarine, hot barbecued pork, barbecue sauce, cheese sauce, and pickles were added. Each of these items except the cheese sauce was also served with other menu items. The cheese sauce was dispensed from 2-ounce plastic cups, which were filled each business day from a 6-pound, 11-ounce bulk can. The words “Refrigerate After Opening” were written in fine print (letters 2 mm in height) on the label. The owner stated that the plastic cups and the bulk can were stored in a refrigerated delicatessen case. The temperature of the case at the time of the investigation was 2.8 °C (37 °F).

The implicated can of cheese sauce was manufactured on 11 August 1992, more than 1 year before the outbreak. Officials from the Food and Drug Administration inspected the cheese-canning facility and found no evidence that the product had been inadequately sterilized. The cheese had been heated to a temperature of 135.5 °C (276 °F) for at least 11.7 seconds and then aseptically canned. On 11 August 1992, 2484 cans of this cheese sauce were produced and distributed to a wholesale food chain. The owner of the delicatessen stated that her husband had purchased the implicated can of cheese sauce the week before the delicatessen reopened and that she had opened the can on 23 September 1993. The can was reportedly not swollen or damaged, and the cheese did not appear to be spoiled. Purchase records from the owner's charge account at the wholesale food store showed that the most recent possible date of purchase was 10 December 1992.

Laboratory Investigation of Cheese Sauce

Only two other cans bearing the same lot number as the implicated can of cheese could be located. One of these tested negative for botulinum toxin. The other showed no signs of swelling after being incubated for 14 days at 35 °C. Cheese sauce left over from the implicated can contained at least 400 mouse minimum lethal doses of type A botulinum toxin per gram. Cultures of the cheese sauce yielded type A C. botulinum. Cultures of the surfaces of raw potatoes from the delicatessen yielded type A C. botulinum, as did cultures of the cutting board on which the potatoes were prepared and of the delicatessen case in which the cheese was stored. The pH of the cheese sauce was 5.8. The water activity (A_w), a measure of the amount of available moisture in the cheese, was 0.96. (A_w = P/P_0, where P = vapor pressure of the food and P_0 = vapor pressure of pure water.)

The inoculation studies showed growth of C. botulinum and toxin production in the cheese sauce at 22 °C (room temperature). On day 8, toxin was detected at 20 or more mouse minimum lethal doses per gram of cheese. Growth and toxin production increased during incubation until day 15 and reached a peak toxin level of at least 20,000 mouse minimum lethal doses per gram. The cheese became toxic without showing overt signs of spoilage. Inoculated tubes of cheese sauce incubated at 5 °C showed no growth or toxin production after 120 days. However, when these tubes were transferred to higher temperatures, growth and toxin production occurred in 5 days at 35 °C and in 15 days at 22 °C.

Discussion

Thermally processed, aseptically canned commercial cheese sauce contaminated with type A C. bot-
*Clostridium botulinum* caused an outbreak of botulism that affected eight persons, one of whom died. It is not surprising that laboratory studies could confirm the diagnosis of botulism in only half the cases. Because of the delays in presentation and clinical diagnosis, early serum and stool specimens were obtained from only the first four hospitalized patients. Toxin is detected in only 13% to 28% of serum samples collected more than 2 days after ingestion of botulinum toxin (3). Stool cultures remain positive longer than do results of serum toxin assays; even so, only approximately 36% of stool cultures obtained more than 3 days after ingestion of the toxin yield type A *C. botulinum* (3). Electromyography with rapid repetitive stimulation might have confirmed the diagnosis in the mildly symptomatic patients from whom specimens were collected several days after the contaminated food was ingested (4). However, this test was not available at the hospitals to which the patients were admitted.

In general, the severity of botulism correlates with the amount of botulinum toxin ingested (5). The range of severity of illness seen in this outbreak may have resulted from unequal distribution of toxin in the cheese sauce or from partial inactivation of the toxin by heat from the potatoes. Patients may also have had different susceptibilities to toxin (5). Had the outbreak gone undetected and the cheese sauce been served again the following week, the concentration of toxin in the cheese sauce probably would have been higher; consequently, additional and more severe cases would have occurred.

Most outbreaks of botulism are associated with home-canned foods, especially vegetables and fish (6). Cheese and other dairy products are rarely vehicles for botulism; they account for fewer than 1% of the botulism outbreaks reported in the United States since 1899 (7). The only other case of botulism associated with processed cheese was reported in 1951 (8). To our knowledge, this is the first reported outbreak of botulism associated with cheese that had been thermally processed to destroy botulinum spores. An outbreak of botulism caused by a commercially processed food such as this, even though it rarely occurs, is of special public health importance because of the potential for many persons to become ill.

The manner in which the cheese sauce became contaminated remains unknown. The cheese sauce probably became contaminated with spores after the can was opened. The low acidity (pH, 5.8) and high water activity \( (A_w, 0.96) \) of this cheese sauce are factors known to favor spore germination and toxin production (9), and the oily consistency of the cheese and plastic lid may have provided the necessary low-oxygen environment. Previous studies have shown the potential for the production of botulinum toxin in processed cheeses contaminated with *C. botulinum* spores (10–13). A failure in the process used by the manufacturer to produce the cheese sauce seems unlikely. Two other cans from the same lot were not contaminated, no other outbreaks of botulism associated with this product have been reported, and the persons who ate the same cheese sauce before 1 October did not become ill.

Potatoes may have been the original source of spores. *Clostridium botulinum* is a common soil organism in the United States (14, 15), and spores are often present on the surfaces of raw potatoes (16). Potatoes have been implicated in several large outbreaks of botulism (17–19). In addition, type A *C. botulinum* was cultured from the surfaces of leftover uncooked potatoes and from the cutting board on which the potatoes were prepared. No subtyping method is currently available to determine whether the organisms on the potatoes were genetically identical to those cultured from the cheese sauce.

This outbreak might have been prevented if the cheese sauce had been adequately refrigerated. Although the owner of the delicatessen insisted that the cheese had been kept refrigerated, the inoculation experiments showed that the outbreak strain did not produce botulinum toxin at a temperature of 5°C. These experiments also showed that this cheese sauce does support the germination and growth of *C. botulinum* spores and that it can become toxic without appearing spoiled when it is kept at room temperature for 8 days. This is about the amount of time that elapsed between the reopening of the delicatessen and the exposure date in the first case. The inoculation experiments also showed that *C. botulinum* spores remain viable and dormant in refrigerated cheese for at least 120 days. Similar inoculation studies done with other types of processed cheese have shown that spores survive and that toxin can be recovered after 6 years (20). The cheese sauce may have been opened and contaminated with spores months before the delicatessen reopened.

The thermal process used to make the cheese sauce is designed to yield a sterile, shelf-stable product, but it provides no assurance that the cheese will remain uncontaminated after the can has been opened. Prevention of botulism depends entirely on the consumer's understanding of the need to keep such products adequately refrigerated and to keep them away from sources of spores. Unfortunately, “Refrigerate After Opening” instructions listed in fine print on food labels do not provide sufficient warning of the potential danger of allowing products, such as this cheese sauce, to remain at room temperature. The number of commercial products that have a composition similar to that of this cheese sauce is unknown. If preservatives
that provide an additional intrinsic barrier to the production of botulinum toxin were added to this and similar products, future outbreaks might be prevented.

This outbreak shows that detecting and reporting even mild cases of botulism can stop outbreaks and prevent severe illness and deaths. Botulism should be considered early in the differential diagnosis of patients presenting with signs or symptoms of ocular or bulbar dysfunction. Patients with cranial nerve symptoms should be specifically asked about gastrointestinal symptoms and should be examined carefully for subtle neurologic findings. A detailed food history and inquiries about the health of family members and recent meal companions may lead to the correct diagnosis and the source of the illness.

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