Botulism Toxemia Following Laparoscopic Appendectomy

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We describe a case of botulism infection in a patient who had undergone laparoscopic appendectomy, an occurrence not previously described in the literature. This case exemplifies the need for coordination between clinical and public health personnel to ensure the immediate recognition and treatment of suspected botulism cases.

Botulism is a rare condition, with 121 total cases having been reported in the United States in 2009 [1]. Botulism develops from toxins produced by the spore-forming, obligate anaerobic bacillus Clostridium botulinum, leading to descending paralysis through blockade of acetylcholine release. Infant botulism comprises most reported cases (69% in 2009) [1] and develops from ingestion of spores that germinate, producing colonizing bacteria that release toxin and cause illness. Less commonly reported are food-borne botulism from preformed toxin in contaminated food, wound botulism caused by spore contamination of wounds, adult intestinal botulism that develops from ingested spores and subsequent colonization, and an iatrogenic form due to overdose with botulinum toxin. There are 7 genetically distinct botulinum neurotoxins, with type A being the most potent and longest lasting [2, 3]. The case fatality ratio for noninfant cases of botulism in 2009 was 11% [1].

Postoperative wound botulism is extremely unusual, with only 5 cases documented in 1 review covering 40 years [4]. We present a case of botulism toxemia in a patient who developed a botulinic pelvic abscess and paralysis following laparoscopic appendectomy.

METHODS

Clinical case data, including procedure reports, were obtained during patient’s hospitalization through medical chart review and interviews conducted with the patient, attending physicians, and the patient’s family. Laboratory assays were performed at the Michigan Department of Community Health (MDCH) Bureau of Laboratories, including the standard mouse bioassay [5, 6] using serum and ethanol spore-enrichment broth cultures of pelvic abscess fluid [7], the Centers for Disease Control and Prevention (CDC) proprietary polymerase chain reaction (PCR) on C. botulinum isolates (Brian Raphael, PhD, oral communication, 14 December 2009), diffusion-in-gel enzyme-linked immunosorbent assays (Dig-ELISA) on enrichment broth cultures from stool and abscess isolates [7, 8], and anaerobic cultures on stool and abscess specimens.

The public health investigation was initiated on receipt of the hospital case report, which fulfilled the epidemiological, clinical, and laboratory criteria as specified in the CDC’s “botulism, wound” and “botulism, other” case definitions used for public health surveillance and reporting [5, 9]. This study was approved by the hospital’s Institutional Review Board (IRB 6817), and the patient provided informed consent.

The patient was a 54-year-old, white woman who presented to the emergency department (ED) 6 days after laparoscopic appendectomy with progressive nausea, vomiting, abdominal pain, and dehydration without fever. At ED presentation, her medical history was notable for a 3-day hospitalization 6 weeks previously for a right lower quadrant abdominal abscess of unknown etiology that was treated with intravenous antibiotics, followed by several outpatient courses of broad-spectrum antibiotics, including metronidazole. Eight days before presenting to the ED, she underwent outpatient colonoscopy which revealed diverticulosis; an exploratory laparoscopy 2 days later showed right-sided intra-abdominal adhesions without evidence of infection. During the laparoscopy, an appendectomy was performed; the appendix was normal at pathologic examination. No complications were noted from either procedure.

The patient was admitted to general surgery and received intravenous metronidazole, ciprofloxacin, vancomycin, and pain medication for a presumptive ileus; no neurological deficits were noted. An abdominal computed tomographic (CT) scan, compared with a scan 6 weeks earlier, showed an increased fluid collection measuring 10 × 4.5 cm in the right lower quadrant, which was thought to be either hematoma or abscess.
On hospital day 1, the patient became acutely unresponsive, cyanotic, and pulseless. She was intubated, resuscitated, and found to be hypercarbic, which was consistent with respiratory failure attributed to oversedation with pain medication. On hospital day 2, she could not be weaned from the ventilator, exhibited bilateral ptosis, and could move only her hands and feet. Over the next 2 days, she experienced rapid neurological deterioration resulting in almost complete paralysis; her sensorium remained intact.

A brain-stem stroke was considered; brain CT and magnetic resonance (MR) imaging findings were negative. Neurological consultation was sought, and differential diagnoses included Guillain-Barré syndrome, myasthenia gravis, and botulism. Electromyography on hospital day 7 demonstrated a significant drop in motor nerve amplitude in all extremities, which was suggestive of atypical demyelinating disease; brain-stem auditory-evoked potentials showed no evidence of conduction suggestive of atypical demyelinating disease; brain-stem auditory-evoked potentials showed no evidence of conduction delay across the auditory pathways. Plasma exchange was empirically initiated for possible Guillain-Barré syndrome. Lumbar puncture showed clear fluid with normal cell count and glucose and protein levels. Results of cryptococcal antigen and Lyme antibody tests were negative. Cerebrospinal fluid cultures were negative, and MR images of the spine was unremarkable.

On hospital day 9, an infectious disease consultant initiated penicillin therapy based on a clinical impression of botulism, and public health authorities were immediately contacted. MDCH arranged for delivery of botulinum antitoxin from the CDC, and the local health department began a field investigation to rule out potential food-borne etiologies. No other family or household members reported illness. The patient had no history of consuming home-canned or other inadequately processed food items.

On hospital day 10, the patient was transferred to hospital 2 with a diagnosis of probable botulism, and antitoxin was administered. At admission, she was alert with stable vital signs and paralyzed except for minimal finger and toe movement. Sensation was intact to deep and pinprick stimuli, reflexes were absent, and Babinski’s sign was equivocal. The patient’s pupils were equal and nonreactive, and her cranial nerves were paralyzed.

Repeated CT scans at hospital 2 revealed 2 pelvic fluid collections, 1 anterior collection measuring 7.9 × 6.2 × 12.0 cm, and 1 posterior collection measuring 6.0 × 4.2 cm. A pigtail catheter was placed in the anterior abscess, and 20 cc of fluid were drained and sent for culture and testing. Antimicrobial therapy was changed to piperacillin-tazobactam and vancomycin. On hospital day 31, the pelvic fluid collections had decreased in size, and clindamycin was added to the therapeutic regimen. Follow-up CT scans on day 39 revealed resolution of the anterior abscess and reduction of the posterior abscess to approximately 6 mm in diameter.

The patient was discharged after ~4 months of hospitalization on continuous positive airway pressure with ventilator assistance via tracheotomy. Nine months after hospitalization, she was at home with assistance and receiving outpatient rehabilitation weekly. She remained ventilator dependent during sleep, required catheter assistance to urinate, and was ambulating with a cane.

**RESULTS**

MDCH performed a mouse bioassay on serum specimens obtained on hospital day 9. Botulinum toxin serotype A was confirmed on day 7 of the patient’s stay in hospital 2. Ethanol spore enrichment broth cultures performed at MDCH were negative by Dig-ELISA for botulinum neurotoxin [5, 7]. The abscess broth culture was positive by Dig-ELISA for toxin types A and F; ultimately, the mouse bioassay confirmed toxin A only. The culture from the abscess drainage yielded *C. botulinum*. PCR identified an A(B) botulism strain. Stool cultures grew *Clostridium perfringens* and *Clostridium difficile* but not *C. botulinum*.

**DISCUSSION**

This patient exhibited a complex clinical picture most consistent with postsurgical wound botulism that presented as a toxin-filled pelvic abscess after laparoscopic appendectomy. The 2 possible alternate diagnoses, adult intestinal botulism or food-borne botulism, both seem highly unlikely, because serial stool cultures were negative for *C. botulinum*, which should be present in the former, and stool cultures were toxin negative, which is inconsistent with the latter. Instead, we hypothesize that the patient’s altered colonic anatomy and sustained course of antibiotics for treatment of diverticular disease created an environment conducive to *C. botulinum* growth at the time of laparoscopic instrumentation. This allowed for inoculation of tissues with already-present *C. botulinum* spores during her appendectomy, followed by development of a botulinum-filled pelvic wound abscess. Deep abdominal palpation at ED admission may have caused a bolus of toxin release from the abscess, which caused her sudden respiratory arrest and paralysis shortly after hospital admission.

Postsurgical wound botulism is rare. Only 5 of 47 confirmed wound botulism cases were postoperative wound botulism in a 40-year review by Weber et al [4]; these were attributed to postsurgical contamination from the patient’s gut, where *C. botulinum* spores may have resided without causing illness [4]. Although postsurgical wound botulism has been rarely documented after emergency laparotomies [4, 10], a laparoscopic procedure associated with wound botulism, as in this case, has not been previously described.
Whenever botulism is suspected, the clinician must rapidly decide whether antitoxin is needed; earlier administration is often associated with less extensive paralysis [11]. Antitoxin cannot reverse preexisting paralysis [5, 6, 11]. The mouse bioassay is the gold standard for diagnosis and requires ≥4 days for results [5]. Consequently, the decision to administer antitoxin must be made well before laboratory results are available. In this case, antitoxin was administered when paralysis was advanced and the patient was already on ventilator support. The prognosis for patients who develop botulinic paralysis is good if secondary complications are prevented. Continued neuromuscular recovery has been documented up to a year later [12]; our patient’s motor function continued to improve 9 months after paralysis onset.

A single case of botulism constitutes a public health emergency because of potential for additional cases of illness and death in the population [5, 6]. In Michigan, like most states [6], mouse bioassays and requests for CDC antitoxin are performed only by the state health department. Thus, immediate reporting to public health authorities by the diagnosing physician is the key to minimizing further exposures, identifying additional cases, and rapidly securing antitoxin for effective treatment.

Notes

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