

## Case Report

# Two Rare Presentations of Fatal Anthrax: Meningeal and Intestinal

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### Abstract

Anthrax is an ancient disease of animals and men, caused by *Bacillus anthracis*. The diagnosis of cutaneous infection is relatively easy, but other clinical forms might escape recognition. We present two rare and fatal forms of anthrax: meningeal in a 33-year-old male shepherd and intestinal in a 4-year-old boy. The former was admitted to the hospital with complaints of headache, vomiting, fever, and decreased level of consciousness. The latter presented with abdominal pain and distension, vomiting, and fever. Both cases were proven by animal inoculation.

**Keywords:** anthrax, *Bacillus anthracis*, inhalational, intestinal, meningitis

### Introduction

Since the beginning of this century, anthrax has drawn universal attention due to its use as a biologic weapon. Anthrax is an acute infectious disease caused by *Bacillus anthracis*; a large gram-positive, non-motile, spore-forming, rod-like, and aerobic bacterium.<sup>1</sup> It can present different clinical forms in humans: cutaneous (95%), inhalational (5%), and rarely, gastrointestinal (GI)<sup>2-6</sup> as well as meningeal.<sup>2,7-10</sup> Inhalational anthrax (IA) has the highest mortality rate, followed by meningoenzephalitis and GI anthrax.<sup>1-4,11</sup> Diagnosis of the cutaneous form is rather easy because of its typical black ulceration.

However, diagnosis of rare forms is difficult.<sup>7</sup>

Anthrax meningitis (AM) is usually secondary to septicemia or associated with other forms of the disease.<sup>2,7,8,10-12</sup> Primary AM is extremely rare and only a few cases have been reported in English medical literature.<sup>9,13</sup> Intestinal anthrax is another quite rare presentation of anthrax that is caused by ingestion of bacteria.<sup>2-5,6</sup> These forms are usually fatal in the absence of antibiotic therapy and despite antibiotic treatment in advanced disease, particularly in children, the outcome is often fatal, as well.<sup>2-8,11,14</sup>

We report two rare presentations of fatal anthrax, with the purpose to mention the importance of considering it in as differential diagnosis in endemic areas because survival is possible with early diagnosis and prompt antibiotic therapy.<sup>2-4,9,12,14,15</sup>

### Case Report

#### Case 1

A 33-year-old man from Afghanistan, who worked as a shepherd in a suburb of Tehran, was admitted to our hospital emergency room with decreased level of consciousness and status epilepticus. Three days prior to admission, he experienced sustained headache, vomiting, and fever. He was referred to

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a General Practitioner who prescribed penicillin G and cephalexin. Two days later, his level of consciousness decreased and he developed respiratory distress and a tonic-colonic generalized seizure. His past medical history was unremarkable. On admission, temperature was 39°C, respiratory rate 55/min and pulse rate 130/min. He had localized response to painful stimuli, pupils were medium size and reactive to light, had neck rigidity and spastic extremities. Later, he developed decerebrate posturing despite receiving treatment for status epilepticus. Laboratory findings included: leukocytosis (WBC count: 35300/mm<sup>3</sup>), with normal hemoglobin, platelets, blood sugar, sodium, potassium, urea, and prothrombin time (PT). Chest X-ray was suggestive of pulmonary edema and bilateral pleural effusion. Brain CT scan showed evidence of subarachnoid hemorrhage (SAH). Lumbar puncture was bloody with the following results: 2000 WBC/mm<sup>3</sup> with 90% PMN and 10% lymphocytes; numerous RBCs, protein 800 mg/dL, sugar 160 mg/dL (blood sugar 275 mg/dL), and many gram positive bacilli. Intravenous ceftriaxone and clindamycin were administered with an impression of bacterial meningitis and superimposed aspiration pneumonia. Pleural tap was not performed. The next day, the patient hemodynamically deteriorated with anuria, hypotension, decreased platelet count, prolonged PT and metabolic acidosis; he expired 20 hours after admission to the ICU. CSF culture later grew 4 – 5 mm irregular flat colonies on blood agar at 35°C. On sheep blood agar the colonies had no hemolytic reaction. The organism showed no motility, positive lecithinase reaction on egg yolk agar, negative acid formation from salicin, positive nitrate reduction test, negative indole test, positive gelatin hydrolysis after seven days, and susceptibility to penicillin disk (10 U). Blood culture was negative and no skin or mucosal ulcers were detected on re-examination.

### Case 2

A 4-year-old boy was admitted to this center with a two day history of vague abdominal pain and distension, decreased bowel movement, vomiting, and fever. On admission, he was drowsy with a temperature of 38.5°C, pulse rate 125/min and respiratory rate 45/min, tense abdomen, shifting dullness, and decreased bowel sounds. At rectal exam, stool was grossly non-bloody. He was put on Ami-

kacin, Clindamycin, and ceftriaxone. Five hours later, his abdomen became tender with increased tenderness on deep palpation and no bowel sound. Plain abdominal radiography showed ascites and increased bowel thickness. Abdominal sonography revealed massive ascites. Chest X-ray was normal. CBC showed leukocytosis (WBC count: 44100/mm<sup>3</sup> with 77% neutrophils and 23% lymphocytes). Other routine tests were within normal limits. A diagnostic ascitic tap was turbid containing blood clots and 4200/mm<sup>3</sup> leukocytes with 85% neutrophils and gram positive bacilli which were thought to be contamination (*Bacillus cereus*, which is morphologically similar to *B. anthracis*). With a clinical impression of intestinal perforation and peritonitis, he underwent laparotomy and right hemicolectomy. Surgical findings included approximately two liters of turbid ascitic fluid, ileocecal intussusceptions, in addition to a fragile and edematous cecum with perforation. On histopathology examination, the bowel had transmural edema, hemorrhagic necrosis and many bacilli were seen. About forty mesenteric lymph nodes were detected, which showed hemorrhage and neutrophilic infiltration. Following surgery, the antibiotic regimen was changed to ampicillin, amikacin, and metronidazole. He developed hypotension with no response to dopamine and fluid therapy; his condition deteriorated and the patient expired 16 hours after admission. Blood and ascitic fluid later grew colonies with features as described in Case 1. A history of a possible contact with an animal carcass was given when investigating the source of infection; however, the definitive source of infection could not be identified. Other members of the family did not show any evidence of anthrax infection.

Autopsy was not performed in either patient. Specimens from both cases were sent for animal inoculation. In the first case, two guinea pigs were used, and for the second case, rats were inoculated by the bacteria and one was used as a negative control. Approximately 24 and 48 hours later, the inoculated animals died. Blood taken from the hearts of the dead animals were positive for *Bacillus anthracis*.

### Discussion

Anthrax is a zoonotic disease; humans can become infected when they come into contact with infected

animals or their products. Areas of high prevalence include the Middle East, Africa, South America, and New Zealand.<sup>1,9,12</sup> Anthrax is an endemic disease in Iran.<sup>2,3,15,17</sup>

*Bacillus anthracis* has three major virulence factors: an antiphagocytic capsule (protective antigen) and a toxin complex containing two exotoxins (lethal and edema). The protective antigen binds to target cell surface receptors, allowing the lethal and edema factors to bind and enter the cell. These contribute to the septic syndrome which can lead to multiorgan failure and death.<sup>1,11,12</sup>

Anthrax meningitis is very rare with just over 100 reported cases in the world literature.<sup>1,2,7-11,13</sup> It is usually a rare complication of other forms of the disease, mostly cutaneous (80%), followed by pulmonary (5%), and GI (5%).<sup>1,7,8,10,11</sup> However, *de novo* cases are reported and are called primary anthrax meningitis.<sup>9,13</sup> The major neurological complication of anthrax is a fulminant and rapidly fatal hemorrhagic meningoencephalitis with SAH.<sup>2,7,8,10,11,13</sup> In cases with acute neurologic deterioration, gram-positive rods in CSF, and multifocal intracerebral hemorrhage on CT scan; anthrax should be considered in the differential diagnosis since hemorrhagic changes in acute meningitis are relatively unusual.<sup>11</sup> The mortality rate is very high (>95%) and death usually occurs within a week.<sup>1,2,7,8,10,11,13</sup>

IA presents with a rapidly progressive course characterized by fever, fatigue or malaise, nausea or vomiting, cough, shortness of breath, and/or abdominal symptoms. X-ray findings are characteristically mediastinal widening and pleural effusion, which is hemorrhagic.<sup>2,12</sup> IA may be particularly potent in causing neurologic complications, followed by death within a week.<sup>11</sup> The overall mortality rate is 97% without antibiotic treatment and greater than 40% with antibiotic therapy.<sup>2,4,12</sup>

Our patient presented with signs and symptoms of meningitis; respiratory distress developed during the course of the disease. Chest X-ray showed pleural effusion, which was suggestive of an IA in the present case. Since a pleural tap was not performed, the diagnosis of IA was not confirmed in our case. However, the possibilities are that he had simultaneous IA and AM. On the other hand, since neurologic manifestation in meningitis following IA could be prominent and may be the initial symptom leading to the diagnosis of anthrax<sup>11</sup>, the other pos-

sibility was that our patient had IA with secondary neurologic involvement.

GI anthrax is also extremely rare and has been reported in less than 1% of all cases.<sup>1,2,6</sup> GI anthrax occurs more commonly than IA in the developing world and is extremely rare in developed countries due to effective protection of the food supply.<sup>2,4-6,16</sup> It mainly occurs in two different clinical forms, oropharyngeal and intestinal<sup>1-5,16</sup>; a few cases of gastric anthrax have also been reported.<sup>6</sup>

Kanafani et al.<sup>5</sup> reported three clinical phases in GI anthrax. At phase I, the patient had fainting spells, low grade fever, headache, facial flushing, and red conjunctiva. Phase II started 24 hours later, with abdominal pain and distension, nausea, vomiting, and mild diarrhea. Phase III was marked by rapid increase in abdominal distension, paroxysms of abdominal pain and occasionally GI bleeding. Shock, ascites, flushed face, and red conjunctiva were frequently present. Death was more common in phase III patients and those who were only treated with antibiotics (no surgery). Surgery saved some of the patients. The mortality rate is less than 40% with antibiotic treatment.<sup>2-5</sup> The signs and symptoms in our patient included abdominal pain and distension, fever, decreased bowel movement, and ascites. Diarrhea was not present and the stool was grossly non-bloody, most likely due to obstruction.

Diagnosis is rarely made before death.<sup>2,4-6,15</sup> Radiographic examination of the abdomen usually is non-diagnostic and shows nonspecific findings in favor of obstruction or ascites,<sup>2,4</sup> as was in our case.

The involved intestine, usually in the region of the ileum and cecum, and/or ascending colon, shows ulceration and edema accompanied by hemorrhagic lymphadenitis caused by dissemination of bacilli to the regional lymph nodes.<sup>2-5,16</sup> Death due to sepsis usually occurs before bowel perforation or obstruction secondary to intestinal wall edema.<sup>4,5</sup> Our patient had similar pathologic findings in addition to ileocecal intussusceptions and perforation.

Because of the rarity of GI and meningeal anthrax, the diagnosis is not quickly suspected. Early diagnosis and antibiotic therapy could be lifesaving.<sup>2-4,9,12,14,15</sup> These cases are presented to emphasize the inclusion of anthrax in the differential diagnosis in areas where the disease remains endemic, such as our country.

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