Survival of a Patient with Intestinal Anthrax

DAVID R. NALIN, M.D.
Baltimore, Maryland

BEGUM SULTANA, M.B.B.S.
R. SAHUNJA, M.B.B.S.
A. K. ISLAM, M.B.B.
M. A. RAHIM, M.B.B.S.
M. ISLAM, M.B.B.S.
B. S. COSTA, M.B.B.S.
N. MAWLA, M.B.B.S.
Dacca, Bangladesh

WILLIAM B. GREENOUGH III, M.D.
Baltimore, Maryland

From The Johns Hopkins Center for Medical Research, The Cholera Research Hospital, The Holy Family Hospital, Dacca, Bangladesh; and The Johns Hopkins Hospital, Baltimore, Maryland. This work was supported by Research Agreement No. R07 AI10048-14 and No. 196802 of The National Institutes of Health, Bethesda, Maryland. Requests for reprints should be addressed to Dr. David R. Nalin, c/o The Johns Hopkins Center for Medical Research, 550 N. Broadway, Suite 115, Baltimore, Maryland 21205. Manuscript accepted January 30, 1976.

A patient with intestinal anthrax, the first documented surviving patient to be described in detail, presented with an acute condition within the abdomen. Intestinal anthrax should be considered in the differential diagnosis of abdominal conditions in areas in which anthrax is prevalent, especially when a history is available of ingesting putrid or improperly cooked meat. Clinical and therapeutic details are given as a guide in future cases.

Six cases of fatal intestinal anthrax and one case in which the patient survived have been reported [1,2]. We describe here in detail a second surviving patient who presented with an "acute abdomen, including prolonged abdominal pain of acute onset associated with tenderness, vomiting, distention and fever."

CASE REPORT

A 17 year old male Bangalee student at Dacca had three days of anorexia with constipation and temperature of 103° to 104°F, followed by very severe abdominal pain. The patient's history included childhood undernutrition, nummular eczema, malaria (cured) and inguinal lymphadenitis due to a gram-negative rod (presumably Ducrey's bacillus; cured with tetracycline). History was otherwise noncontributory except for ingestion of poorly cooked and malodorous beef and duck several days before the onset of disease.

The patient was prostrate and anxious; he had a temperature of 103°F, a pulse rate of 130/min and a blood pressure of 90/70 mm. Hg. He complained of constant generalized nonradiating abdominal pain with tenderness and rebound tenderness which was most severe in the epigastrium, and right upper and lower abdominal quadrants. Pain never localized in a single area. Dysuria was absent, as were contralateral rebound tenderness and aggravation of pain on straight leg raising or on medial thigh flexion. Slight flank tenderness was elicited, and bowel sounds and rectus muscular tone were moderately increased. There were no skin lesions, masses, organomegaly or ascites at this time. The findings on examination, including the heart, lungs, inguinal canal and rectum, were otherwise entirely within normal limits.

Oral ampicillin and water were given until the patient vomited guiac-positive coffee-grounds material and 3 liters of clear fluid, and passed 300 ml of foul, watery diarrhea. Wedge-shaped scleroconjunctival hemorrhages developed from the lateral corneal margin to the lateral angles of both eyes. Between the onset of symptoms and 16 hours after admission to the Cholera Research Hospital, the white blood cell count increased from 7,850 to 20,850/mm^3 with 68 per cent mature polymorphonuclear leukocytes, 22 per cent immature polymorphonuclear leukocytes and 10 per cent lymphocytes. The hematocrit value increased from 42 to 53 per cent, but plasma proteins decreased to

5 g/100 ml. Stool showed only mild hookworm infestation and urinalysis disclosed no abnormalities except for 1+ protein. Blood pressure decreased to 80/60 mm Hg; pulse rate was 130/min and respiratory rate 36/min. Oral intake of food, fluids and ampicillin was stopped and the patient was treated with intravenous fluids, dextrose, 6-hourly penicillin (initially 250,000 U, then 2.5 million U) and chloramphenicol (0.5 g). Blood pressure increased (100/60 mm Hg) and fever and pulse rate diminished over 24 hours (100° to 101°F; 90/min), but the respiratory rate remained 36/min.

The next morning, bowel sounds disappeared and massive ascites and scrotal edema developed, but abdominal pain decreased and results of a repeat rectal examination were normal. A chest film showed a raised diaphragm, and an abdominal film showed a diffuse ground-glass appearance with widening of spaces between bowel loops but no free air; scant intralumenal colonic and jejunal gas was present. Serum sodium was 131 meq/liter, sodium bicarbonate 20.9 meq/liter, creatinine 1.3 and amylase 120 units/ml. The hematocrit value was now 51 per cent and the white blood cell count 21,950/mm^3 with 42 per cent mature polymorphonuclear leukocytes, 46 per cent immature polymorphonuclear leukocytes and 12 per cent lymphocytes. A laparotomy was performed at Holy Family Hospital.

At laparotomy the peritoneal cavity was full of semipurulent turbid brown fluid (culture sterile). Gram stain showed polymorphonuclear leukocytes but no organisms were seen. The mesenteric lymph nodes were enlarged (1 to 3 cm) and firm, and the mesentery was scarlet with confluent petchiae. Otherwise viscera appeared normal. A lymph node biopsy specimen showed nonspecific inflammatory changes including edema, vessel dilatation and proliferation of reticulum cells and lymphocytes. No organisms were seen.

Both of two preantibiotic blood cultures yielded a gram-positive bacillus. Initially considered a contaminant, it was later identified as Bacillus anthracis by bacteriologic tests including bacteriophage reaction and guinea pig inoculation. The organism was sensitive to penicillin, ampicillin, tetracycline, erythromycin, chloramphenicol, kanamycin, oxacillin and streptomycin. The minimum inhibitory concentrations for chloramphenicol and erythromycin were 12.5 μg/ml and 0.8 μg/ml, respectively.

The postoperative course was complicated by a drug reaction, pneumonitis and a gastrointestinal hemorrhage. Two days after the operation 1 to 3 mm erythematous macules, papules and hemorrhagic vesicles appeared on the arms and trunk. Antibiotic therapy was changed to streptomycin (2.0 g/day intramuscularly) and pyrrolidinomethyl tetracycline (1.1 g/day intravenously). The dose of streptomycin was reduced to 1 g/day after three days due to vertigo. A fever with temperatures of 101° to 102°F. with a 6 P.M. peak persisted for nine more days. Nonpitting edema over most of the lower posterior thoracic and lumbosacral areas was present from the first to the fourth postoperative day.

Five days after the operation, rales at the base of the right lung and dullness with scant white sputum developed without dyspnea. Roentgenograms showed diffuse infiltrates of the upper and middle lobes of the right lung which resolved over four days.

From four to 11 days after the operation, melena necessitated a 10 unit transfusion of fresh and banked blood. Prothrombin time and platelet count were normal (13/13 sec and 276,000/mm^3, respectively). Antacids and vitamin k_1 were given. The hematocrit value stabilized after treatment with oral thrombin (Topostasin® three times a day), intramuscular lipid thromboplastin (25 mg twice a day) and epsilon-aminocaproic acid (100 mg twice a day) [3]. An x-ray series of the gastrointestinal tract showed duodenal bulb ulceration.

A grade 2/6 systolic ejection murmur was attributed to anemia and fever; it disappeared during convalescence. The patient was discharged on the seventh afebrile day on a regimen of oral tetracycline (2.0 g/day).

Eight days later, recurrent fever and severe headache with percussion tenderness in the right frontotemporal area led to the patient's readmission. Coughing or neck flexion increased headache. Papilledema, neck stiffness and focal neurologic signs were absent, but the pulse rate was slow (60 beats/min) in relation to fever (oral temperature, 103°F). The next day the patient had a grand mal convulsion. The white blood cell count was 6,300/mm^3 with 62 polymorphonuclear leukocytes, 9 immature polymorphonuclear leukocytes, 19 lymphocytes and 10 eosinophils. Examination and cultures of cerebrospinal fluid, blood and urine were otherwise within normal limits. A presumptive diagnosis of focal anthrax cerebritis and/or meningitis was made.

Chloramphenicol was given intravenously (6.0 g/day for five days, then 4.0 g/day for 18 days). After five days the patient was symptom-free. From days 23 to 43, oral erythromycin (4.0 g/day) was substituted for chloramphenicol due to marrow suppression.

After six weeks of antibiotic therapy, the patient was sent to Johns Hopkins Hospital where skull films, electroencephalogram and brain scan were found to be within normal limits, and neurologic examination showed minimal right-sided upper motor neuron signs. A repeat series of the gastrointestinal tract showed healing. The patient remains well without medication.

Serum specimens collected one week before illness and 27 days later were tested by the indirect microhemagglutination test for anthrax by courtesy of Dr. James C. Feeley of the Center for Disease Control, Atlanta, Georgia. The reciprocal titer rise from 0 to 4, although not very great, was considered diagnostic since the test is highly specific [4].

COMMENTS

Six fatal cases of gastrointestinal anthrax and one in which the patient survived have been reported. The clinical findings in a fatal case in Iran [1] were very similar to ours. The appearance of the mesentery and nodes at laparotomy, as well as the nonspecific histologic features of the node biopsy specimen are consistent with previous observations [2].

Intestinal anthrax is fulminating, mimics other disorders and can be rapidly fatal. Diagnosis is difficult and can easily be missed. The usual practice of thorough cooking of meat in areas where anthrax is prevalent must prevent many cases, since spore- or bacilli-contaminated meat from sick animals is marketed by un-

scrupulous vendors and probably was the vehicle of infection in our patient. Outbreaks of intestinal anthrax after eating condemned meat have occurred in Thailand and Pakistan [5].

Gastrointestinal bleeding was noted in two previous cases, but in one it was attributed to an old ulcer [1]. Our patient's "coffee-grounds" vomitus and later melena were attributed to hemorrhagic necrosis at the primary site of infection of the upper gastrointestinal tract, i.e., a "malignant carbuncle" of the duodenum [2]. From there dissemination apparently proceeded via lymphatics to the blood. The bleeding after three weeks suggests a parallel with typhoid or intestinal tularemia. Therapy with epsilon aminocaproic acid, thrombin and thromboplastin was used on the assumption that fibrinolysis at the bleeding site could account for the recurrent bleeding [3]. Although the rationale is hypothetical, the temporal sequence of treatment and effect was dramatic after a long course of intestinal hemorrhage.

Wedge-shaped scleral hemorrhages are considered pathognomonic of sandfly fever ("Pick's sign") but their significance in our patient is obscure. The cause may have been bacterial embolism. The patient had no generalized bleeding tendency despite several focal hemorrhagic lesions during his illness.

Prompt antibiotic therapy may have been life-saving. The organism was sensitive to the antibiotics used, but the initial clinical response was slow, perhaps due to dissemination of organisms and prior liberation of anthrax toxins. After 48 hours, the temperature levels fell but bowel sounds disappeared and ascites, scrotal and truncal edema supervened, possibly due to bacilli blocking perivascular lymphatics [1,2]. The node biopsied was peripheral to the most inflamed area, which lay over large blood vessels; this or prior antibiotic therapy may explain the absence of bacteria in sections stained by Gram's and Brown and Brenn's methods. The administration of antibiotics probably reduced the serologic response, but other patients have had similar titers [4]. The results indicate that the serologic response to gastrointestinal anthrax is not very great.

Previous workers have suggested that electrolyte imbalance and renal failure are the main causes of death in patients with anthrax treated with antibiotics [2]. The present report confirms this contention, since the patient's survival depended not only on the antibiotic therapy, but also on prompt restoration of losses of plasma proteins and blood, maintenance of fluid and electrolyte balance, and relief of respiratory embarrassment due to effusions complicating affected nodes.

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