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CASE REPORT

Case Reports

Fatal Necrotizing Fasciitis Caused by Aeromonas sobria in Two Diabetic Patients

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Abstract We report two rare cases of Aeromonas sobria necrotizing fasciitis with sepsis in patients with diabetes. In both cases, immediate fasciotomy was performed and appropriate empiric antimicrobial therapy and intensive care were administered. However, the two patients died on Day 2 and Day 11, respectively, after admission as a result of multiple organ failure. When patients present with a rapid onset of skin necrosis and progressive sepsis, an Aeromonas sobria infection or Vibrio infection should be considered in the differential diagnosis.

Introduction

Aeromonas species are Gram-negative bacilli that thrive in aquatic environments, especially in sewage, fresh or brackish water, soil, tap water, and nonfecal organic materials [7, 15–17]. Aeromonas species are known to cause diarrhea. They also cause necrotizing fasciitis and sepsis in patients with hepatic diseases, diabetes mellitus, and immunocompromised status [3, 10, 16, 17, 21, 24]. Most reported severe soft tissue infections have been caused by Aeromonas hydrophila [6, 7, 19, 20, 24, 26].

We report two cases of Aeromonas sobria necrotizing fasciitis and progressive sepsis. Fasciotomy was performed in the first patient and an above-knee amputation was performed in the second patient. However, both patients died of multiple organ failure.

Case Reports

Patient 1

A 66-year-old man presented to the emergency department with pain and bullous skin lesions on the right forearm. The patient was a farmer who had a history of diabetes mellitus that was not regularly controlled. He had abraded his right hand while working approximately 5 days before presentation. However, several discrete, black, necrotic bullae appeared on his forearm only approximately 2 days earlier. The patient appeared ill and was lethargic. His body temperature was 36.7°C and his blood pressure was 116/62 mm Hg.

The results of the laboratory tests were: hemoglobin, 12.1 g/dL; platelet count, 43,000/μL; albumin, 1.5 g/dL; and serum creatinine, 0.7 mg/dL. The leukocyte count was 3900 cells/mm^3 with 41% segmented neutrophils, 33% metamyelocytes, 1% myelocytes, 4% monocytes, 4% lymphocytes, and 17% band neutrophils. Necrotizing fasciitis of the right forearm with sepsis was diagnosed. We initiated broad-spectrum antibiotic therapy with cefuroxime (750 mg intravenously every 8 hours) and gentamicin (60 mg intravenously every 12 hours). Twelve hours after admission, the patient was taken to the operating room for decompression (Fig. 1). Extensive

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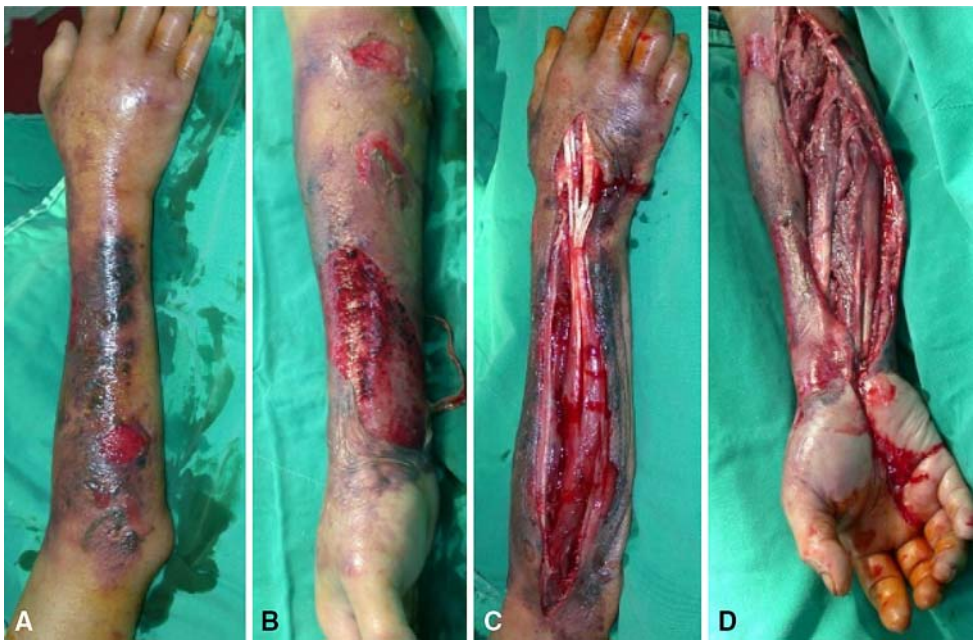

Fig. 1A–D Patient 1, a 66-year-old farmer was diagnosed with necrotizing fasciitis of the right forearm with sepsis. Preoperative photographs of the right arm show (**A**) hemorrhagic bullae and cyanotic skin lesions on the dorsal side, and (**B**) erupted vesicles on the medial side. After emergency fasciotomy, the forearm revealed (**C**) extensive skin necrosis on the dorsal side, and (**D**) the underlying flexor muscles revealed myonecrosis with cyanotic changes.

fasciotomy and débridement were performed along with removal of the necrotic skin. Extensive necrosis of the underlying skin and muscle also was noted. After surgery, he was taken to the intensive care unit for further management.

The patient's condition quickly deteriorated, and chest radiography revealed consolidation in both lung fields. Mechanical ventilation support was required as a result of respiratory failure. During the next 24 hours, multiorgan failure developed and the patient died on Day 2 after admission.

Two days after the patient's death, a wound culture confirmed the presence of Aeromonas sobria, and blood culture showed no bacteria growth.

Patient 2

A 79-year-old man was referred to the emergency room on referral from a local hospital. He reported patchy erythematous and bullous skin lesions of the left leg accompanied by cyanosis and tenderness of the left foot. He was a farmer with a history of diabetes mellitus. A day before admission, he had gone to work; multiple bullous skin lesions with swelling and tenderness appeared on the left lower leg at night. He did not recall having sustained any injury.

Physical examination revealed patchy erythema and bullous skin lesions extending to the left thigh. His blood pressure was 100/62 mm Hg and his body temperature was 36.8°C. Laboratory values were: hemoglobin, 6.9 g/dL; platelet count, 60,000/μL; creatinine kinase, 1582 U/L; albumin level, 1.3 g/dL; and serum creatine level, 1.4 mg/dL. The leukocyte count was 600 cells/mm^3 with 66% segmented neutrophils, 4% myelocytes, 11% lymphocytes, and 2% band neutrophils. We diagnosed necrotizing fasciitis of the left leg with sepsis and began empiric antibiotic therapy with vancomycin (1 g intravenously every 12 hours) and ceftazidime (2 g intravenously every 8 hours). Three hours after admission to the emergency room, an above-knee amputation was performed as a result of the severe septic status. The patient then was transferred to the intensive care unit for further treatment.

On the second hospital day, the patient's vital signs became more stable after surgery; however, the chest radiography revealed consolidation of both lung fields with pleural effusion. Subsequently, wound and blood cultures confirmed an Aeromonas sobria infection, and the antibiotic coverage was changed to ceftriaxone and metronidazole based on antibiotic sensitivities. The repeat leukocyte count was 900 cells/mm^3 with a differential count of 66% polymorphonuclear leukocytes, 11% lymphocytes, and 11% band forms; a low platelet count of 24,000/μL was observed. Chest echography was performed on the fifth hospital day as a result of poor recovery of pulmonary function, and it revealed bilateral pleural effusions with collapse of the left lung. Although the left thigh stump wound showed improvement, Acinetobacter baumannii was isolated from a sputum culture, and the chest radiograph revealed progressive infiltration (Fig. 2). The patient died 11 days after admission to the hospital as a result of respiratory failure and pancytopenia.

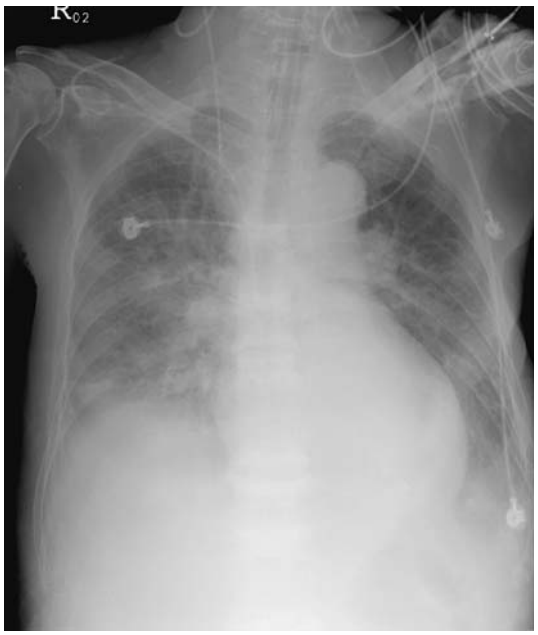

Fig. 2 Patient 2, 79-year-old farmer was diagnosed with necrotizing fasciitis of the left leg with sepsis. A chest radiograph reveals bilateral pleural effusion with collapse of the left lung and progressive infiltration on the ninth day after admission.

Discussion

Aeromonas species, members of the Vibrionaceae family, are Gram-negative bacteria that exhibit positive oxidase activity and glucose fermentation [7]. The aeromonads are distributed worldwide and proliferate mainly in fresh water, sewage, and soils. They often cause disease in fish, amphibians, and reptiles [15]. Human illnesses typically caused by Aeromonas species are uncommon and may present as various diseases, including acute gastroenteritis, wound infection, endocarditis, peritonitis, meningitis, and primary septicemia [13, 20, 21, 24, 29]. Aeromonas hydrophila, Aeromonas sobria, and Aeromonas caviae frequently are reported in association with human diseases, especially in patients with chronic illnesses such as liver cirrhosis, alcoholic liver disease, malignancies, gouty arthritis, chronic renal failure, diabetes mellitus, or chronic steroid use [7, 13–17, 20]. Aeromonas species were susceptible to cefuroxime, cefepine, aztreonam, piperacillin/tazobactam, amikin, and gentamicin [3, 29].

Aeromonas species can produce many virulence factors, including hemolysin, cytotoxin, aerolysin, enterotoxin, endotoxin, protease, adhesins, leukocidin, and lipases [1, 11, 14, 20, 23, 29, 30]. Aeromonas hydrophila is the most commonly reported pathogen that causes Aeromonas necrotizing fasciitis and septicemia; these conditions often occur after soft tissue trauma with exposure to contaminated water or nonfecal organic materials and produce skin lesions similar to those observed in infections caused by Vibrio species [7, 19, 21, 24, 26, 28]. Brenden and Huizinga [2] reported endotoxins of Aeromonas hydrophila intramuscularly inoculated in mice caused the pathogenesis of sepsis; moreover, endoxemia appeared to damage the liver, kidneys, and pulmonary function, resulting in septic shock and multiple organ failure [2, 9].

Aeromonas wound infections typically occur within 72 hours after injury and are characterized by pain, swelling, hemorrhagic bullae, subcutaneous bleeding, purpura, necrosis, and gangrene, which can be severe, with myonecrosis and gas production resembling those caused by Clostridia [7, 16]. Aeromonas hydrophila is frequently isolated in polymicrobial infections and, along with Gram-negative bacilli and Clostridium species, can cause synergistic necrotizing fasciitis [6, 7, 27]. The fatality rate of Aeromonas soft tissue infections and bacteremia is high and reportedly ranges from as much as 28% to 73% [7, 15–17, 24, 28]. Thus, early diagnosis and prompt aggressive débridement are essential and critical for survival.

Infections resulting from Aeromonas sobria most commonly present as gastroenteritis and diarrhea [1, 14, 15, 23]. Aeromonas sobria was reported to account for 25% to 27% of extraintestinal aeromonas infections [15, 28]. Aeromonas sobria has been isolated most frequently from patients with bacteremia and was reported to produce more enterotoxigenic, pathogenic, and cytotoxic activity than Aeromonas hydrophila [5, 14, 16, 23]. However, Aeromonas sobria necrotizing soft tissue infections rarely have been reported [12, 14, 18, 23, 25]. Aeromonas sobria can produce myonecrosis with gas gangrene resembling that caused by Clostridia. It may cause extensive cellulitis, rhabdomyolysis, and epidermolysis in patients with liver cirrhosis and hematologic malignancies [12, 18, 22].

Aeromonas sobria hemolysin and cytolytic enterotoxin possess enterotoxic activity and are the major virulence factors that cause diarrhea [11, 23, 30]. Yokoyama et al. [30] reported Aeromonas sobria protease may enhance vascular permeability and bullous formation by stimulating the bradykinin release pathway in rat skin through the plasma kallikrein activation and histamine release. Imamura et al. [11] reported Aeromonas sobria can secret serine proteinase and may induce vascular leakage through prekallikrein activation and kinin release to cause lethal hypotension and septic shock. However, the virulence factors and pathogenesis responsible for human extraintestinal infections remain unclear [29].

Necrotizing fasciitis and fatal sepsis caused by Aeromonas sobria have been reported in patients with cirrhosis as a result of impaired phagocytic activity of the reticuloendothelial system; however, they rarely have been reported in patients with diabetes [9, 12, 14, 18]. Our two patients had no history of hepatic dysfunction. They

experienced fatal sepsis despite rapid initiation of broad-spectrum antibiotic therapy and emergent surgical fasciotomy. Diabetes mellitus results in peripheral vasoocclusion and "sugar-coated capillaries" limit the blood supply to the superficial and deep structures. Subsequent invasion of the bloodstream by virulence factors released from gangrenous tissues can easily cause fulminant sepsis in patients with diabetes with necrotizing faciitis [4, 8].

We report two rare cases of Aeromonas sobria necrotizing fasciitis with fatal sepsis in patients with diabetes. Early diagnosis, immediate fasciotomy, appropriate empiric antimicrobial therapy with third-generation cephalosporins and aminoglycosides, and intensive care should be given to patients with underlying chronic illnesses, particularly liver cirrhosis and diabetes mellitus. When patients present with a rapid onset of necrotizing skin necrosis and progressive sepsis, an Aeromonas sobria infection or Vibrio infection should be considered in the differential diagnosis.

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