Alerts, Notices, and Case Reports

Necrotizing Fasciitis and Septic Shock Caused by *Vibrio cholerae* Acquired in San Diego, California

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NECROTIZING FASCIITIS is a disease that threatens life and limb by rapid invasion and destruction of the fascial planes by bacteria. Various pathogenic mechanisms enable the infectious process to spread uncontrollably, causing necrosis of the tissues, systemic and vascular collapse, and often death. This is a medical and surgical emergency requiring a team approach for effective treatment. Immediate, aggressive surgical intervention with wide debridement to healthy tissue is required, and subsequent "second-look" operations in one or two days is indicated. In some cases a third, fourth, and more operations are necessary.

Necrotizing fasciitis can be caused by a variety of bacteria, both gram-positive and gram-negative, aerobic and anaerobic, cocci and bacilli. Specific organisms include groups A, B, C, and F streptococci, peptostreptococci, clostridia, *Vibrio vulnificus*[1] and other noncholera *Vibrio* species, *Aeromonas hydrophila*,[2] and other synergistic combinations of aerobic and anaerobic bacteria.

Infection with *Vibrio vulnificus* and other noncholera *Vibrio* species is a well-described cause of necrotizing fasciitis[3] that has a higher incidence in patients with cirrhosis, hemochromatosis, and hematologic malignancy.[4] Most reports of this disease have been related to exposure of traumatized tissue or to the ingestion of oysters and other shellfish from the Gulf of Mexico.[5,6] In contrast, although *Vibrio cholerae* strains are frequently isolated in this region, we could not find any documentation of necrotizing fasciitis associated with this organism.

We report a case of fulminant necrotizing fasciitis and sepsis syndrome due to a *V cholerae* non-O1 acquired in the city of San Diego, California, where this organism is rarely encountered.

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Report of a Case

The patient, a 51-year-old man, presented to the emergency department after the sudden onset of exquisite right lower extremity pain, swelling, and advancing erythema that had awakened him from sleep approximately 12 hours earlier. The patient had insulin-dependent diabetes mellitus of adult onset, and because of a chronic plantar ulcer of the right foot and several past episodes of cellulitis and osteomyelitis, he had had a right transmetatarsal amputation and amputation of the fourth and fifth digits of his left hand. He had attended a "wild" social event at a men's bathhouse the night before his presentation that included the use of alcohol and amyl nitrite. He thought he was having another bout of cellulitis, although he reported much more severe lower extremity pain with this episode.

On physical examination in the emergency department, the patient was moderately obese, appeared acutely ill and anxious, and had a temperature of 39.2°C (102.6°F), heart rate of 130 beats per minute, respiratory rate of 30 breaths per minute, blood pressure of 140/90 mm of mercury, and normal oxygen saturation while breathing room air as measured by pulse oximetry. His lungs were clear, he was tachycardic, and his abdomen was normal without hepatomegaly. The right lower extremity showed his past transmetatarsal amputation, and the skin on his ankle and leg was warm, erythematous, swollen, and tense to the knee, but without crepitus or edema. There was extreme tenderness to the midthigh. There were no blisters or foul-smelling discharge, and pulses were not palpable below either inguinal region. On the right foot there was a purulent 2-cm plantar ulcer extending into the muscle. The left lower extremity was notable only for multiple scars on the lower leg from previous operations. His left hand had previous skin grafts, and the fourth and fifth fingers had been amputated.

The leukocyte count was 2.8×10^9 per liter (2,800 per mm^3) with a differential cell count of 0.71 (71%) polymorphonuclear leukocytes, 0.15 (15%) lymphocytes, 0.12 (12%) band forms, and 0.01 (1%) monocytes. The hemoglobin level was 147 grams per liter (14.7 grams per dl), the hematocrit was 0.435 (43.5%), and the platelet count was 154×10^9 per liter (154,000 per mm^3). The results of all other laboratory tests were initially normal. The patient was admitted for treatment of a presumed right lower extremity cellulitis, and a regimen of the combination of ticarcillin disodium and potassium clavulanate was started.

On the second hospital day, the patient remained tachycardic and tachypneic, and fever, chills, and hypotension developed. A repeat leukocyte count was 6.6×10^9 per liter with a differential count of 0.33 polymorphonuclear leukocytes, 0.12 lymphocytes, and 0.55 band forms. The color of the right lower extremity had changed to a deep red with a faint blue hue to the midcalf, and several discrete, black, necrotic bullae had erupted along the anterior and medial aspect of his leg (Figure 1). There was no crepitus. A diagnosis of necrotizing fasciitis was

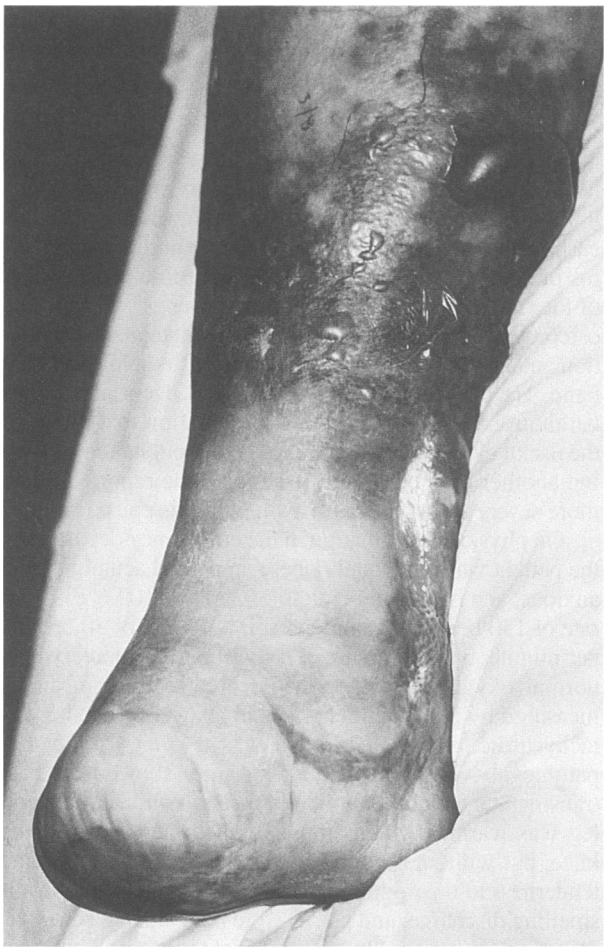

Figure 1.—The right lower extremity is shown. On the second hospital day, its color had changed to a deep red with a faint blue hue, and several discrete, black, necrotic bullae had erupted.

made. Cultures of two blood specimens drawn at the time of admission were reported to be growing oxidase-positive, gram-negative rods, and the antibiotic regimen was changed to the combination of imipenem and cilastatin sodium, plus gentamicin sulfate and clindamycin hydrochloride. An orthopedic surgeon (J.D.) was emergently consulted and immediately performed a below-the-knee amputation.

The postoperative course was eventful for disseminated intravascular coagulation and severe blood loss requiring 22 units of packed red cells, 20 units of fresh frozen plasma, and 18 units of platelets in the first 24 hours. The initial blood and surgical wound isolates were identified as *Vibrio cholerae* non-O1. This organism was also identified in a plantar wound culture, although not in pure culture. Other isolates included *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Enterococcus* species.

During the following week, the patient remained in critical condition and required multiple debridements. Cultures of wound specimens of healthy-appearing tissue from the first two debridements remained positive for *V cholerae* non-O1. On hospital day 9, the wound became more painful and developed a foul odor. At surgery, a knee disarticulation was necessary due to ascending subcutaneous necrosis. In the next few days, the patient's condition finally became stable, and he was able to provide the history of exposure of his plantar ulcer to sand at the bathhouse the night before admission. Investigation from the public health department discovered that this was untreated local sand that the proprietors had discarded before specimens could be obtained for culture. The patient was discharged on hospital day 22.

Discussion

It is not well known to the medical community that cholera and noncholera *Vibrio* strains are present in the western United States coastal regions. Further, these organisms are not generally recognized as pathogens that can be acquired in California. Our case is one of two San Diego County cases of waterborne non-O1 *Vibrio cholerae* disease identified by the Department of Public Health. *Vibrio cholerae* strains are found in several areas of the world, including the United States.[3,6,7] All *V cholerae* are similar with regard to structure, biochemistry, and ability to produce enterotoxins. They are oxidase-positive, gram-negative rods and are classified as O1 or non-O1 depending on whether they agglutinate in cholera polyvalent O1 antiserum; O1 organisms are agglutinated by antiserum, and non-O1 isolates are not.[8] More than 72 serotypes of *V cholerae* are classified as non-O1.[8]

The O1 strains typically cause the cholera epidemics in developing countries but do not cause disease outside the gastrointestinal tract. In contrast, non-O1 strains have been isolated from specimens of blood,[9-11] ear tract,[12] cellulitis,[13,14] cholecystitis,[15] and meningitis.[16] Fulminant *V cholerae* non-O1 necrotizing fasciitis has not been reported, however.

Infection from non-O1 *V cholerae* results from open wound exposure to infested sand or saltwater, estuary exposure, or from ingesting contaminated seafood. The pathogenic mechanism may reside partly in its ability to produce a number of extracellular toxins, including an enterotoxin similar to the cholera toxin,[17] cytolysins,[18] and a hemagglutinin or protease that is structurally, functionally, and immunologically similar to the elastase of *Pseudomonas aeruginosa*.[19] Further, established risk factors for non-O1 infection include immunocompromise, cirrhosis, or hematologic malignancy,[4,20,21] but the reasons for increased risk are not clear. Immunocompromised patients with human immunodeficiency virus (HIV) infection or a malignant neoplasm are more susceptible to bacterial infections from deficient cellular immunity. Patients with liver disease may have a defective chemotactic defense against infection.[22]

In conclusion, we report the first documented case of fulminant necrotizing fasciitis due to *Vibrio cholerae* non-O1. Our report describes an immunocompetent host (who tested negative for HIV during his hospital stay) with dia-

betes mellitus who has a history of many bacterial infections. The exposure of a chronic plantar ulcer to sand at a bathhouse infested with non-O1 *V cholerae* is the probable mechanism of entry that led to necrotizing fasciitis and septic shock. The history of pain out of proportion to physical findings suggested a deeper infection of the fascia that spread rapidly and resulted in septic shock. The inability to control necrotizing fasciitis despite surgical intervention often leads to amputation of extremities or death with involvement of abdominal or chest wall fascia. An aggressive medical-surgical team approach is necessary for the survival of the patient.

REFERENCES

1. Blake PA, Weaver RE, Hollis DG: Diseases of humans (other than cholera) caused by vibrios. Annu Rev Microbiol 1980; 34:341-367
2. Hennessy MJ, Ballon-Landa GR, Jones JW, Farrell T: *Aeromonas hydrophila* gas gangrene: A case report of management with surgery and hyperbaric oxygenation. Orthopedics 1988; 11:289-293
3. Blake PA, Allegra DT, Snyder JD, et al: Cholera—A possible endemic focus in the United States. N Engl J Med 1980; 302:305-309
4. Siegel MI, Rogers AI: Fatal non-O1 *Vibrio cholerae* septicemia in chronic lymphocytic leukemia. Gastroenterology 1982; 83:1130-1131
5. Wilson R, Lieb S, Roberts A, et al: Non group O1 *Vibrio cholerae* gastroenteritis associated with raw oysters. Am J Epidemiol 1983; 114:293-298
6. Morris JG Jr, Black RE: Cholera and other vibrioses in the United States. N Engl J Med 1985; 312:343-350
7. Hughes JM, Hollis DG, Gangarosa EJ, Weaver RE: Non-cholera vibrio infections in the United States—Clinical, epidemiologic, and laboratory features. Ann Intern Med 1978; 88:602-606
8. Smith HL Jr: Serotyping of non-cholera vibrios. J Clin Microbiol 1979; 10:85-90
9. Guard RW, Brigden M, Desmarchelier P: Fulminating systemic infection caused by *Vibrio cholerae* species which does not agglutinate with O-1 *V cholerae* antiserum. Med J Aust 1980; 1:659-661
10. Rabadan PM, Vilalta E: Non-O:1 *Vibrio cholerae* bacteremia (Letter). Rev Infect Dis 1989; 11:667
11. Platia E, Vosti KL: Noncholera vibrio septicemia. West J Med 1980; 132:354-357
12. Hansen W, Crokaert F, Yourassowsky E: Two strains of *Vibrio* species with unusual biochemical features isolated from ear tracts. J Clin Microbiol 1979; 9:152-153
13. Pitrak DL, Gindorf JD: Bacteremic cellulitis caused by non-serogroup O1 *Vibrio cholerae* acquired in a freshwater inland lake. J Clin Microbiol 1989; 27:2874-2876
14. Gelbart SM, Prabhudesai MM: *Vibrio cholerae* non-O1 cellulitis. Arch Pathol Lab Med 1986; 110:1182-1183
15. Peterson EM, Jemison-Smith P, de la Maza LM, Miller D: Cholecystitis: Its occurrence with cholelithiasis associated with a non-O1 *Vibrio cholerae*. Arch Pathol Lab Med 1982; 106:300-301
16. Fearrington EL, Rand CH, Mewborn A, Wilkerson J: Non-O1 vibrio septicemia and meningoencephalitis (Letter). Ann Intern Med 1974; 81:401
17. Robins-Browne RM, Still CS, Isaacson M, Koornhof HJ, Appelbaum PC, Scragg JN: Pathogenic mechanisms of anon-agglutinable *Vibrio cholerae* strain: Demonstration of invasive and enterotoxigenic properties. Infect Immun 1977; 18:542-545
18. McCardell BA, Madden JM, Shah DB: Isolation and characterization of a cytolysin produced by *Vibrio cholerae* serogroup non-O1. Can J Microbiol 1985; 31:711-720
19. Hase CC, Finkelstein RA: Comparison of the *Vibrio cholerae* hemagglutinin/protease and the *Pseudomonas aeruginosa* elastase. Infect Immun 1990; 58:4011-4015
20. Dhar R, Ghafoor MA, Nasralah AY: Unusual non-serogroup O1 *Vibrio cholerae* bacteremia associated with liver disease. J Clin Microbiol 1989; 27:2853-2855
21. Yang PM, Huang GT, Lin JT, et al: Ultrasonography in the diagnosis of benign diffuse parenchymal liver disease: A prospective study. Taiwan I Hsueh Hui Tsa Chih [J Formosa Med Assoc] 1988; 87:966-977
22. DeMeo AN, Andersen BR: Defective chemotaxis associated with a serum inhibitor in cirrhotic patients. N Engl J Med 1972; 286:735-740

Hyperammonemia With Severe Methanol Intoxication

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METHANOL POISONING leads to a well-described syndrome of metabolic acidosis with elevated anion gap and osmolar gap, vision impairment often leading to blindness, and in severe cases, progressive central nervous system dysfunction, renal and hepatic failure, and death.[1,2] The neurologic damage brought about by methanol poisoning, particularly that of the vision system, has been ascribed to the effects of formic acid, the principal toxic metabolite of methanol. Hyperammonemia, to our knowledge, has not been reported as a presenting feature of methanol toxicity. We report a case of severe methanol poisoning associated with hyperammonemia in the presence of near-normal liver function test results.

Report of a Case

The patient, a previously healthy 16-year-old boy, presented to the emergency department with symptoms of impaired vision and stupor. Two nights before admission, according to his family, the patient had been out drinking with friends. Subsequent investigation revealed that he had ingested methanol intended for use as a cleaning solvent but unaccountably stored in a vodka bottle. On the day before admission, the patient felt ill and vomited several times, but ascribed his symptoms to a hangover. On the day of admission, he was too ill to attend school and continued to have nausea and vomiting. While watching television that evening, he complained that he "couldn't see" and became progressively somnolent. On arrival at the emergency department, he was able to stand with assistance, but within moments of arrival became obtunded and had an apparent seizure. An endotracheal tube was inserted and supportive care begun.

The patient's initial vital signs included a blood pressure of 169/125 mm of mercury and a heart rate of 100 beats per minute. Arterial blood gas measurements with the patient receiving bag ventilation with 100% oxygen revealed a pH of 6.84, a P_{CO_2} of 19 mm of mercury, a P_{O_2} of 456 mm of mercury, and a calculated base excess of −31.3 mEq per liter. Diazepam and phenytoin were given to prevent further seizures. Administering

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