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Bacteremic Cellulitis Caused by Non-Serogroup O1 *Vibrio cholerae* Acquired in a Freshwater Inland Lake

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The number of reported cases of infections with non-serogroup O1 *Vibrio cholerae* in the United States has increased recently. These cases have almost invariably been associated with travel, seawater exposure, or the ingestion of shellfish. We report a case of bacteremic cellulitis caused by non-O1 *V. cholerae* that was acquired in a freshwater inland lake in northern Illinois. The organism is more widely distributed than generally appreciated, and the potential for infection in patients without the usual risk factors exists.

In recent years, there has been an increase in the number of reports of infections with non-serogroup O1 *Vibrio cholerae* in the United States (6, 7, 9). Like *V. cholerae*, non-O1 *V. cholerae* can be found in coastal regions, and human infections occur in these areas in association with exposure to seawater or ingestion of seafood. We report a case of bacteremic cellulitis caused by non-O1 *V. cholerae* that was acquired in a freshwater inland lake in northern Illinois.

A 34-year-old male was admitted with fever, chills, nausea, vomiting, upper abdominal pain, and pain and swelling of both lower extremities. He had been fishing in Fox Lake (a freshwater lake in northern Illinois with an Na^+ concentration of 1.1 to 2.0 mmol/liter; U.S. Geologic Survey), wading in the lake without boots, 2 days prior to admission. While wading he had fallen and abraded his shins. In addition, he had numerous scratches on his legs from his dog. The next evening he awoke with fever, chills, and bilateral leg pain and swelling. Soon he developed nausea, vomiting, and upper abdominal pain. He admitted to heavy alcohol ingestion for the 2 days prior to admission but denied ingestion of water or fish from the lake. He had resided in Chicago, Ill., since moving there from Houston, Tex., in 1970 and had not traveled recently. Ten years earlier he had hepatitis B related to intravenous drug abuse and since then intermittent episodes of jaundice presumably owing to alcoholic liver disease.

On physical examination the patient appeared ill. His temperature was 101.7°F (38.7°C), his heart rate was 88 beats per min, his respiratory rate was 22 breaths per min, and his blood pressure was 130/80 mm Hg. Scleral icterus was noted. The abdomen was prominent with mild tenderness diffusely. The left leg was extremely tender, warm, erythematous, and swollen up to the inguinal ligament. The right leg was tender, warm, erythematous, and swollen to the knee. Scratches and abrasions were visible on both legs. The leukocyte count was 18,200/mm^3, with a differential of 82% polymorphonuclear leukocytes, 3% bands, 12% lymphocytes, and 1% monocytes. The serum aspartate aminotransferase was 99 IU, the serum alanine aminotransferase was 94 IU, the alkaline phosphatase was 188 IU, the amylase was 60 IU, and the bilirubin was 4.5 mg/dl. The total protein was 7.7 g/dl, and the albumin was 2.4 g/dl.

Intravenous antibiotic therapy with nafcillin was initiated for a presumed streptococcal or staphylococcal cellulitis. No attempt was made to aspirate the leading edge of the cellulitis. By the next morning the patient's abdominal complaints had resolved, but his temperature increased to 103.6°F (39.8°C) and the bilateral cellulitis appeared to be progressing. Clindamycin and gentamicin were empirically added, and his temperature returned to normal over the next 2 days. By the third hospital day, three sets of blood cultures from admission grew curved gram-negative rods identified as *V. cholerae*. Later the organism was identified as a non-serogroup O1 *V. cholerae* (confirmed by Matthew Lesko, Illinois Department of Public Health, Chicago; Table 1). The organism was negative for cholera toxin by enzyme-linked immunosorbent assay (I. K. Wachsmuth and J. J. Farmer III, Centers for Disease Control, Atlanta, Ga.). Antibiotic therapy was subsequently changed to oral tetracycline, 500 mg four times daily, and the patient received a total course of 4 weeks of antibiotics. The cellulitis gradually resolved, but he was left with permanent lymphedema of the left leg. He has since been treated for three episodes of cellulitis of the left lower extremity that occurred within 8 months of his initial presentation, presumably as a consequence of the severe lymphedema, which responded to empiric therapy with nafcillin. Currently he is given monthly intramuscular injections with benzathine penicillin to prevent streptococcal cellulitis, and he has not had any further episodes of cellulitis in the past 16 months.

Non-serogroup O1 *V. cholerae* does not agglutinate in type-O1 antisera, but biochemically the organism is indistinguishable from O group 1 *V. cholerae* strains, the causative agents of cholera. Like *V. cholerae*, the organism occurs in coastal areas, where it has been isolated from seawater and shellfish. The organism does not cause cholera but has been reported to cause sporadic cases and, rarely, outbreaks of diarrheal disease. The organism may account for a significant proportion of the sporadic cases of diarrheal disease in certain endemic areas (4). In the United States, however, gastroenteritis caused by non-O1 *V. cholerae* is rare, but the number of reported cases has been increasing. Most cases reported have been associated with travel, seawater exposure, or ingestion of shellfish. Of the 14 cases reported to the Centers for Disease Control in 1979, 5 were associated with foreign travel and all 9 cases acquired in the United States were related to the ingestion of shellfish (10). It is not clear whether the increase in reported cases is the result of an increased incidence of these infections. Hughes and coworkers have suggested that the increased number of re-

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TABLE 1. Characteristics of blood isolate identified as non-serogroup O1 *V. cholerae*

Test	Reaction
Hemolysis of sheep erythrocytes	+
Oxidase	+
Indole production	+
Voges-Proskauer (1% NaCl)[a]	+
Lysine decarboxylase	+
Arginine dihydrolase	−
Ornithine decarboxylase	+
Gas from glucose	−
Acid from glucose	+
Acid from sucrose[a]	+
Acid from salicin	−
Lipase[a]	+
Nitrate → nitrite	+
Growth in 0% NaCl	+
Growth in 10% NaCl	−
String test	+
Agglutination in O group 1 antiserum	−
Cholera toxin (ELISA)[b]	−

[a] Important in distinguishing *V. cholerae* from *V. mimicus*.
[b] ELISA, Enzyme-linked immunosorbent assay.

ported cases of non-O1 *V. cholerae* infections in the United States is the result of increased awareness of infections caused by vibrios other than *V. cholerae* and the increased use of selective media for isolating vibrios, such as thiosulfate-citrate-bile salts-sucrose (TCBS) medium, in clinical microbiology laboratories (7).

There is a wide spectrum of clinical illness with intestinal infection caused by non-serogroup O1 *V. cholerae* (2). Some patients with non-O1 *V. cholerae* in the stool are asymptomatic, and there are reports of prolonged carriage by asymptomatic patients. Zafari and co-workers reported that Iranian pilgrims returning from Saudi Arabia, an area endemic for non-O1 *V. cholerae*, frequently carried the organism in their stool but were asymptomatic (15). Over the next 12 months, contacts with patients carrying this organism were monitored, and secondary cases of diarrhea or asymptomatic intestinal infection were identified with serial stool cultures. The number of secondary cases increased gradually over the first 6 months, suggesting that the index patients carried the organism for prolonged periods. Isolation of non-O1 *V. cholerae* from bile of patients without diarrhea suggests that some individuals are chronic biliary tract carriers, as occurs with O group 1 strains (2, 7). Other patients develop more severe intestinal disease, and a substantial proportion of the patients reported have required hospitalization and intravenous fluid administration. Forty-six percent of the patients reported to the Centers for Disease Control in 1979 were hospitalized, but this probably reflects the increased severity of infection in persons seeking medical attention (10). In an outbreak of gastroenteritis in which most infected patients were identified, the rate of hospitalization was only 11% (1). Many patients have fever and bloody diarrhea, clinical features not associated with cholera (2, 6, 9, 10).

The pathophysiology of gastroenteritis caused by non-serogroup O1 *V. cholerae* is still not well understood (2, 6, 9). Some strains produce an enterotoxin that is antigenically similar to cholera toxin, but most strains isolated from persons in the United States lack this cholera-like toxin. These strains still produce diarrhea in infant rabbits and fluid accumulation in ligated rabbit ileal loops. Some strains produce other enterotoxins or cytotoxins or both. However, many strains do not produce toxin, and toxin elaboration is not required to produce diarrheal disease. Most non-O1 *V. cholerae* strains produce a hemolysin that is similar to that produced by the El Tor biotype of O group 1 *V. cholerae*. Investigators have shown that this hemolysin causes fluid accumulation in rabbit ileal loops and diarrhea in infant rabbits and suckling mice (8). At this time, however, the role of hemolysin in the pathogenesis of gastroenteritis is unclear and in vitro testing cannot accurately predict pathogenicity for non-O1 *V. cholerae* strains.

V. cholerae serogroup O1 strains do not invade the intestinal mucosa, and infection is limited to the intestinal and biliary tracts. However, extraintestinal infections caused by non-O1 *V. cholerae* do occur, most notably wound infections and bacteremias (2, 3, 7, 14). These infections are also associated with seawater exposure or shellfish ingestion. Bacteremias most often occur in immunosuppressed patients, such as patients with cirrhosis or hematologic malignancy, and our patient had evidence of chronic alcoholic liver disease (14). The organism has been recovered from the cerebrospinal fluid of a patient with a bacteremic wound infection (E. L. Fearrington, C. H. Rand, Jr., A. Mewborn, and J. Wilkerson, Letter, Ann. Intern. Med. **81**:401, 1974). It has also been isolated from patients with otitis media and aspiration pneumonia, but the significance of these isolates is unclear (2, 7). However, cases of pneumonia with bacteremia have been reported, indicating that pneumonia can occur with this organism (14). There are few previous reports of cellulitis caused by non-O1 *V. cholerae* (3). Tissue invasion occurs with non-O1 *V. cholerae* infections, and this clearly distinguishes the organism from O group 1 strains; but the mechanism of invasion is unknown.

Our patient is exceptional in that his infection was clearly associated with freshwater exposure. Infections with non-serogroup O1 *V. cholerae* have rarely been acquired in inland regions. Gelbart and Prabhudesai reported a case of cellulitis caused by non-O1 *V. cholerae* in a patient in Illinois without a history of travel, seawater exposure, or ingestion of seafood (5). Recently, Mulder and co-workers reported a patient with wound infection caused by non-O1 *V. cholerae* that occurred after exposure to lake water in Colorado and were able to culture the same organism from water samples from the lake (11). The organism is indigenous to certain inland bodies of water, especially brackish waters (Na^+, $\geq$25 mmol/liter), but can also be recovered from fresh water (Na^+, $\leq$5 mmol/liter). Rhodes and co-workers reported the isolation of non-O1 *V. cholerae* from herbivores with enteric disease in western Colorado and from surface waters from several sites within this same region (12, 13). None of these bodies of water could be considered brackish. Clearly, the organism is more prevalent in the environment than generally appreciated, and our case shows that the potential exists for infection with non-O1 *V. cholerae* in persons without the usual risk factors.

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