Vibrio vulnificus Infection: An Important Cause of Septicemia in Patients With Cirrhosis

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ABSTRACT: *Vibrio vulnificus*, a virulent gram-negative organism, is a normal inhabitant of coastal waters, including the Gulf of Mexico. *Vibrio vulnificus* infection has been recognized as a cause of fatal septicemia in chronically ill patients, particularly those with chronic liver disease. We report the case of a patient with chronic liver disease who had *V vulnificus* septicemia 2 days after eating raw oysters harvested in the Gulf Coast. *Vibrio vulnificus* septicemia should be suspected in all patients with underlying medical illnesses, particularly cirrhosis, who present with a febrile illness days after eating seafood or being exposed to saltwater. Physicians should advise their patients with cirrhosis and other chronic debilitating illnesses not to eat raw or undercooked seafood.

VIBRIO VULNIFICUS is a virulent gram-negative bacterium that is a normal inhabitant of coastal waters.[1,2] Studies from Gulf states estimate the incidence of serious *V vulnificus* infection between 0.4 and 1.9 cases/100,000.[3] *Vibrio vulnificus* has been recognized primarily as a cause of local wound infection after direct contact with contaminated marine water,[4] however, in some patients, infections may lead to only a mild gastrointestinal (GI) illness. Recently, *V vulnificus* infection has been identified as a cause of fatal septicemia in patients who are immunologically compromised or chronically ill, especially those patients who have cirrhosis.[5] Recognizing the possibility of this serious infection in susceptible individuals is most important, since it affects directly the choice of initial antibiotics used for empiric treatment. Doxycycline, the antibiotic of choice for the treatment of *Vibrio* infections, is usually not used empirically in patients admitted with a febrile illness. We report the case of a patient who had *V vulnificus* septicemia and review the epidemiology, risk factors for infection, clinical presentation, and treatment of this serious disease.

CASE REPORT

A 43-year-old white man came to our emergency department with diffuse abdominal pain, nausea, vomiting, fever, chills, and severe lower extremity pain of 24 hours' duration. Medical history revealed cirrhosis and portal hypertension due to alcohol abuse and infection with hepatitis B and C viruses. One month earlier, he had been hospitalized for treatment of an upper GI hemorrhage due to esophageal varices and had been treated with sclerotherapy. He denied current alcohol or intravenous drug use and reported no signs or symptoms of active GI bleeding.

Physical examination revealed a well-developed man in mild distress from lower extremity pain. His blood pressure was 134/68 mm Hg, pulse rate 118/min, temperature 101°F, and respiratory rate 22/min. Pertinent physical examination findings included a tachycardia with no murmurs. Lungs were clear to auscultation. Abdominal examination revealed hepatosplenomegaly, a diffusely tender abdomen, and physical signs of ascites. Rectal examination was normal, and the stool tested negative for occult blood. Lower extremities exhibited moderate-to-severe edema and were markedly tender to palpation. Laboratory values included a normal white blood cell count of 8,300/mm^3, and the platelet count was decreased at 82,000/mm^3. Other values were serum bicarbonate 19 mEq/L (normal, 22 mEq/L to 32 mEq/L); serum aspartate aminotransferase 83 U/L (normal, 15 U/L to 37 U/L); alanine aminotransferase 60 U/L (normal, 35 U/L to 60 U/L); alkaline phosphatase 122 U/L (normal, 50 U/L to 136 U/L); serum bilirubin 2.9 mg/dL; direct fraction 2.1 mg/dL; and albumin 2.1 mg/dL (normal 3.4 mg/dL to 5.0 mg/dL). Prothrombin time was prolonged at 17.2 sec; INR was 1.97. Ascitic fluid analysis revealed a total nucleated cell count of 315/mm^3, with an absolute polymorphonuclear count of 302/mm^3. Ascitic fluid total protein was <2.0 g/dL and the serum ascites albumin gradient was 1.7, consistent with portal hypertension.

A diagnosis of spontaneous bacterial peritonitis was made; after obtaining blood, urine, and ascitic fluid cultures, we started the patient on intravenous ceftriaxone. Abdominal ultrasonography was significant only for the presence of ascites. The patient had systemic hypotension and respiratory insufficiency, necessitating vasopressive medications and mechanical ventilation. Blood and ascitic fluid cultures were positive for gram-negative organisms. Antibiotics were changed to piperacillin and ceftazidime. Twelve hours after admission, the patient had large bullous lesions on the lower extremities, which were extremely tender. At that time, blood and ascitic fluid cultures were

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Reprinted from the Southern Medical Journal, Journal of the Southern Medical Association, Volume 90, Number 10, October 1997, Pages 1040-1042,

TABLE. Conditions That Predispose to *Vibrio vulnificus* Septicemia

Chronic liver disease
Diabetes mellitus
Alcohol abuse
Hemochromatosis
Chronic renal disease
Immunosuppressive drugs
Immunodeficiency syndromes
Hemolytic anemia
Hypochlorhydria
Cancer

reported as growing *V vulnificus*. Antibiotics were changed to doxycycline and ciprofloxacin. The patient continued to deteriorate and died 36 hours after admission. On further questioning, the patient's family admitted to eating raw oysters 2 days before the patient's presentation. No other family members became ill.

DISCUSSION

Vibrio vulnificus is a halophilic, lactose fermenting, highly motile gram-negative bacillus found in coastal waters, including the waters of the Gulf of Mexico. It grows best in warmer waters (temperature >20°C) with low salinity.[6-8] Most cases of *V vulnificus* infections occur during the warm summer months between May and October.[4] Infection may result in mild gastroenteritis, a severe local wound infection, or septicemia.[4,6,9] Primary septicemia is seen most commonly in patients with certain underlying illnesses. Conditions that predispose to *V vulnificus* septicemia are shown in the table. The disease has a higher mortality in patients with underlying illnesses, in particular, cirrhosis. The reported case-fatality rate from raw oyster–associated *V vulnificus* septicemia in Florida among patients with preexisting liver disease was 67%, compared with 38% among those who were not known to have liver disease.[2] Based on the prevalence of predisposing diseases in the general population, it is estimated that 3.8% of the population is at risk of having *V vulnificus* septicemia if they come in contact with the organism.[5]

Septicemia usually follows ingestion of raw or poorly cooked contaminated seafood. During the summer months, more than 50% of oyster lots from Florida estuaries[10] and 11% of crabs sampled from Galveston Bay, Texas,[11] are found to be culture-positive for *V vulnificus*. The presence of *V vulnificus* in saltwater is not related to fecal contamination.[12] Oysters harvested from approved sites free of fecal contamination may be contaminated with *V vulnificus*. Among *V vulnificus* deaths reported in Florida, 88% were associated with raw oyster consumption.[2] The organism proliferates at room temperature but is readily killed by boiling or freezing.[4] Consequently, consumption of fresh, raw seafood poses the greatest risk for infection. Because of the increasing number of reported cases of *Vibrio* septicemia due to raw oyster ingestion, several states, including Florida, Louisiana, California, and Mississippi, require that a statement detailing the risks of raw shellfish consumption be attached to oyster lots or be visible in areas where raw oysters are served for consumption.

Septicemia usually develops 24 hours to 48 hours after a person eats contaminated food[6] but may occur up to 7 days after the ingestion.[13] Presenting symptoms include abdominal pain, watery diarrhea, fever, chills, and intense lower extremity pain. Skin lesions are usually localized to the lower extremities and develop within 24 hours to 48 hours, ranging from echymotic bullous lesions to necrotic ulcers with bacteria but without inflammatory cells.[14] The presence of significant lower extremity pain at presentation and the subsequent development of lower extremity skin lesions, as seen in our patient, suggests *V vulnificus* septicemia. Patients who get the infection through an open wound may have a compartment syndrome on the affected extremity, requiring surgical debridement.

Clinical course is one of rapid deterioration, with disseminated intravascular coagulation and hypotension. In patients with underlying illnesses, mortality rates exceed 50%; without appropriate treatment, the mortality rate is 100%. The treatment is supportive in nature with early use of intravenous antibiotics. Current recommendations for treatment include doxycycline in combination with ciprofloxacin or an aminoglycoside.[6,14]

In patients with cirrhosis, the mortality rate of *V vulnificus* septicemia is increased 200-fold.[16] Several theories exist to explain the increased virulence of *V vulnificus* in patients with liver disease. Cirrhotic patients often have immune system dysfunction: decreased complement levels, reduced phagocytic activity, chemotaxis, and opsonization, thus promoting the virulence of *V vulnificus*.[17,18] In the presence of portal hypertension, bacteria that enter the body through the portal system may bypass the hepatic reticuloendothelial system.

The virulence of *V vulnificus* in humans is associated with the availability of iron. Patients with increased iron stores, such as seen in hemochromatosis, alcoholic liver disease, or

hemolytic anemia, are susceptible to septicemia with *V vulnificus*. The organism is unable to use transferrin-bound iron for growth; however, in patients with iron overload and transferrin saturation of 75% or higher, free iron is available for use by the organism. Therefore, transferrin saturation is a more important growth variable for *V vulnificus* than total iron stores.[19,20] These findings may explain the unusual susceptibility of patients with chronic liver disease and elevated serum iron to having *V vulnificus* septicemia.

In summary, *V vulnificus* is a ubiquitous virulent gram-negative bacterium that should be suspected as the cause of sepsis in patients who present with fever, chills, lower extremity pain, and a history of underlying medical disease, in particular, cirrhosis. If there is a history of recent ingestion of raw or improperly cooked seafood, empiric antibiotic therapy should cover for *V vulnificus* infection. It should be a standard practice for physicians to advise patients with underlying medical illnesses, particularly cirrhosis or immunosuppression, against the ingestion of uncooked or undercooked seafood or exposure of wounds to seawater.

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