Late-onset *Vibrio vulnificus* septicemia without cirrhosis

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ABSTRACT

Recent surveillance from the Centers for Disease Control and Prevention indicates rising annual incidence rates of *Vibrio vulnificus* infection. Unfortunately, this infection is often excluded from the differential diagnosis in lesser known at-risk populations. Transmission occurs via wound exposure or ingestion, with *V. vulnificus* foodborne illness having the highest mortality rate of all *Vibrio* species. Fatality rates of *V. vulnificus* rival those of Ebola and bubonic plague, so timely treatment is imperative. Current literature favors surgical debridement with a third-generation cephalosporin plus intravenous doxycycline or fluoroquinolone. Cephalosporin monotherapy is discouraged due to rising resistance. This case features *V. vulnificus* septicemia with prolonged incubation time in a noncirrhotic patient.

KEYWORDS Necrotizing fasciitis; septicemia; *Vibrio* infections; *Vibrio vulnificus*

In *Epidemics Book I*, Hippocrates described the final days of Criton, a food critic living by the Aegean Sea, who developed a sudden onset of “violent pain in the foot while walking,” diarrhea, and dark bullae and perished from sepsis days later. This work likely depicts the first recorded *Vibrio vulnificus* fatality. Today, these motile gram-negative bacilli are a leading cause of seafood-associated deaths in the United States. Clinical decompensation may occur within days, though ingestion-related infections are often more dramatic and classically feature hemorrhagic bullae with gastrointestinal illness preceding rapid-onset sepsis. Unfortunately, when initial presentation lacks common themes of cirrhosis, oyster ingestion, or open wounds, treatment is delayed. This report describes a case of late-onset *V. vulnificus* septicemia in a noncirrhotic patient presenting with abdominal complaints and new dermatological findings.

CLINICAL PRESENTATION

A 60-year-old man with uncontrolled hypertension and diabetes mellitus presented with a 3-day history of intractable vomiting, right leg pain, and painful rash. Two weeks prior, he had visited Galveston for wade fishing and a seafood

cookout. No skin injuries or illness occurred in the days prior to or during the trip. At admission, he was hemodynamically stable but febrile (102.4°F). Exam showed bilateral pitting edema to mid-shins with tender erythematous patches and hemorrhagic bullae involving the right leg (*Figure 1a*). Laboratory results revealed lactic acidosis with leukocytosis; an HIV test and hepatitis panel were negative. The patient denied any history of alcohol abuse, and review of primary care records indicated intact liver function per serology without transaminitis. Recent abdominal imaging corroborated these findings without echotexture abnormalities or concerning findings at the hepatic surface or hepatocellular level.

Initial management included intravenous fluids with broad-spectrum antibiotics (vancomycin, cefepime, clindamycin). On hospital day 4, cultures showed lactose-negative, oxidase-positive gram-negative bacilli; given potential infection with *Aeromonas* or *Vibrio*, doxycycline was added. Leukocytosis and fevers persisted despite resolving symptoms, and sudden clinical decompensation occurred on hospital day 5. The patient developed hypotension refractory to fluids and ecchymoses with enlarging bullae (*Figure 1b*). Prompt reevaluation was concerning for rapidly progressing

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Figure 1. Right lower extremity (a) at emergency department triage, with nonblanching, erythematous patches and hemorrhagic bullae and (b) on hospital day 4, with clinical decompensation with ecchymoses and enlarging bullae.

necrotizing fasciitis. A below-knee amputation was performed and the patient gradually improved without postoperative complications. *Vibrio vulnificus* was identified from blood cultures, and antibiotics were changed to ceftriaxone and doxycycline.

DISCUSSION

V. vulnificus infection has been commonly associated with cirrhosis. Its virulence increases with underlying hepatic insufficiency due to (1) decreased glutathione and cytokine production and (2) decreased hepcidin production. The first effect produces an immunocompromised state with poor pathogen clearance from the bloodstream.¹ Hepcidin, a peptide hormone secreted by hepatocytes, regulates iron levels essential for growth and pathogenicity of siderophilic bacteria, including *Vibrio* spp. It also exhibits direct bactericidal effects in vitro.^{2,3} Other at-risk conditions include HIV, end-stage renal disease, diabetes, malignancy, asplenia, and postmenopause.^{4–9} Interestingly, estrogen is protective against *V. vulnificus* infection through unclear mechanisms.

Foodborne *V. vulnificus* illness often initially manifests as gastroenteritis; exam characteristically reveals hemorrhagic bullae.¹⁰ Dissemination across gastrointestinal mucosa occurs days later, producing a primary septicemia.^{11–13} Our patient's course fit the description but with an unusually prolonged incubation time (1.5 weeks versus 1–3 days). In contrast, wound-exposure infections often fare better. Complications include necrotizing fasciitis or secondary septicemia following primary cellulitis.^{14,15} In susceptible populations, like people with diabetes, acquisition may occur without obvious skin ulcerations.¹⁶ Differences aside, both transmission routes usually feature symptoms peaking within days of exposure.^{10,12,14,17}

Contrary to past practices, cephalosporin monotherapy is strongly discouraged with increasing beta-lactam resistance and its inability to halt toxin production. Current evidence shows decreased mortality using two-agent therapy with third-generation cephalosporin plus doxycycline or fluoroquinolone.^{18,19} In refractory cases, tigecycline has been reportedly used as an alternative salvage agent.^{5,20,21}

With global warming and pollution disrupting the marine microbiome, *V. vulnificus* incidence rates will continue to rise. For the clinician, obtaining a thorough epidemiological history will avoid unnecessary antibiotic delays. If *V. vulnificus* involvement is suspected, prompt initiation of a two-agent regimen (third-generation cephalosporin plus doxycycline or fluoroquinolone) improves survival.

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