CASE REPORT

Vibrio vulnificus infection and liver cirrhosis: a potentially lethal combinationSalik Nazir,¹ Krysta Brown,¹ Ann Kyungwohn Shin,² Anthony A Donato¹¹Reading Hospital & Medical Center, Reading, Pennsylvania, USA²Department of Infectious Disease, Reading Hospital and Medical Center, Reading, Pennsylvania, USA**Correspondence to**
Dr Salik Nazir,
saliknazir133@gmail.com

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SUMMARY

We present a case of a 40-year-old man with decompensated alcoholic liver cirrhosis presenting with atraumatic cellulitis of one extremity and severe sepsis that rapidly progressed to compartment syndrome despite broad-spectrum antibiotics. Local cultures following debridement revealed *Vibrio vulnificus*, and subsequent history revealed consumption of raw oysters 48 h before presentation. Our case points out the unique susceptibility of those with cirrhosis and elevated iron saturation to *Vibrio* septicaemia, as well as the rapidity and severity of the disease progression.

BACKGROUND

Vibrio vulnificus is a Gram-negative bacterium that can cause serious wound infections, septicaemia and gastroenteritis.¹ Primary septicaemia with secondary skin and soft tissue infection usually follows ingestion of raw or poorly-cooked seafood and commonly occurs in people with underlying risk factors such as liver cirrhosis, haemochromatosis, diabetes mellitus, chronic renal failure and immunocompromised states.^{2–3} Primary septicaemia has a poor prognosis, with case fatality rates reaching up to 50% in these chronically ill patients.⁴ *V. vulnificus* infection should be suspected in patients with liver cirrhosis presenting with febrile illnesses and evidence of soft tissue infections, especially if temporally related with exposure to eating seafood or exposure of pre-existing wounds to seawater. A high index of suspicion is required for appropriate treatment, since doxycycline, which is the antibiotic of choice for *Vibrio*, is not usually part of empiric inpatient treatment for septicaemia nor for cellulitis.

CASE PRESENTATION

A 40-year-old man with decompensated alcoholic liver cirrhosis and known oesophageal varices presented to the emergency department, with acute onset of fever, left lower extremity pain and erythema over the previous 12 h. On initial vitals, he was found to have a blood pressure of 123/74 mm Hg (not orthostatic), heart rate of 104 bpm, respiratory rate of 22/min, temperature of 38.6°C and oxygen saturation of 96% while inspiring room air. On examination, he was conscious, alert and oriented to time, place and person. He looked in moderate distress due to left leg pain. His abdomen was distended and mildly tender in the right upper quadrant, with shifting dullness identified. His left lateral lower extremity had a 3–4 cm area of tender, non-blanching ecchymosis with

neither crepitus nor sensorimotor changes. Further history revealed that he was retired, with no significant exposures, no hobbies and no travel and he denied any ongoing drug or alcohol abuse.

INVESTIGATIONS

Laboratory investigation identified a white cell count (WCC) of 12 700/μL (normal: 4800–10 800/μL, differential: 79% polymorphonuclear leukocytes, 8% lymphocytes), creatinine of 1.22 mg/dL, (baseline: 0.7 mg/dL), arterial PH 7.303 (normal: 7.360–7.460), partial pressure of carbon dioxide in arterial blood 31.5 mm Hg (normal: 34–46 mm Hg), bicarbonate 16.2 meq/L (normal: 21–31 meq/L), sodium 127 meq/L (normal: 136–145 meq/L), glucose 316 mg/dL (normal: 70–99 mg/dL), serum lactate of 5.4 meq/L (normal: 0.5–2.2 meq/L), albumin 2.5 g/dL (normal: 3.5–5.7 g/dL), aspartate transaminase 85 IU/L (normal: 13–39 IU/L), alanine transaminase 44 IU/L (normal: 7–52 IU/L), alkaline phosphatase 198 IU/L (normal: 34–104 IU/L), total bilirubin 7.4 mg/dL (normal: 0.3–1.0 mg/dL), international normalised ratio 1.3 (normal: 0.9–1.0), platelet count 47×10³/μL (normal: 150–400×10³/μL), C reactive protein 7.69 mg/dL (normal: <1.00 mg/dL), erythrocyte sedimentation rate 18 mm/h (normal: 0–15 mm/h), ferritin 304 ng/mL (normal: 27–300 ng/mL) and iron saturation 85% (normal: 20–50%). Paracentesis revealed ascitic fluid cell count of 1217 WCCs, 72% polymorphonuclear cells on differential, red blood cell count of 1000, negative Gram stain and ascites fluid culture that returned negative on day 3 of admission. These initial laboratory findings were consistent with severe sepsis likely due to spontaneous bacterial peritonitis (SBP) or cellulitis and liver cirrhosis.

TREATMENT

The patient was started on ceftriaxone for SBP and vancomycin to cover empirically for cellulitis. Despite antibiotics, the patient's condition continued to rapidly decline over the next 12 h, with progression of leg pain, persistent fever, increasing WCC (14 600/μL, differential: 80% PMNs, 4% lymphocytes), worsening acidosis (PH 7.293 and bicarbonate 16.4 meq/L), rising creatinine (1.6 mg/dL) and elevated C reactive protein (11.80 mg/dL). Repeated examinations revealed increased tension on left lower leg compartments, including pain with passive range of motion prompting concern for compartment syndrome, and urgent surgical consultation was sought. Four-compartment fasciotomy with surgical debridement was performed the following day,

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which identified dusky, necrotic tissue involving skin, subcutaneous tissue and underlying fascia consistent with necrotising fasciitis. Blood and tissue cultures both returned positive for *V. vulnificus* at 36 and 40 h, respectively, however, the ascitic fluid cultures were negative. Culture sensitivities revealed that *V. vulnificus* was sensitive to ceftazidime, tetracycline, ciprofloxacin and piperacillin. Doxycycline 100 mg intravenous two times a day was added to intravenous ceftriaxone, and vancomycin was discontinued. Subsequent history revealed that the patient and his daughter had consumed raw oysters 48 h before admission, and that his daughter was asymptomatic. Following 2 weeks of intravenous antibiotics, the patient was transitioned to doxycycline orally 100 mg two times a day and renally-adjusted ciprofloxacin 250 mg two times a day.

OUTCOME AND FOLLOW-UP

The patient recovered slowly over the next 6 weeks, requiring multiple operative surgical debridements. Doxycycline and ciprofloxacin were continued until his lower extremity wound was covered with granulation tissue for a total antibiotic duration of 6 weeks.

DISCUSSION

V. vulnificus is a deadly pathogen transmitted by ingestion of raw or undercooked seafood and by exposure to warm seawater where *V. vulnificus* thrives.⁵ *V. vulnificus* has several pathologic mechanisms that enable it to evade host defences. It is able to up-regulate the production of several enzymes, which allow it to survive in the harsh acidic environment of the stomach and enter the bloodstream through the intestine.^{6–8} Dysregulation of cytokine activity that leads to sepsis syndrome is another key feature.⁹ Animal studies have found a specific drop in tumour necrosis factor α in response to challenge with *Vibrio* species in hepatic dysfunction, which may be a clue to a potential mechanism.¹⁰ Disrupted iron physiology common in chronic liver disease may enhance the growth of the bacteria and affect neutrophil activity by interfering with oxygen radicals during infection.¹¹ It is known that elevated serum ferritin and percentage of transferrin iron saturation do correlate positively with survival of *V. vulnificus* in whole blood, while phagocytosis by neutrophils is decreased and correlates negatively with *V. vulnificus* survival.¹² Furthermore, patients with cirrhosis often have dysregulated immune function, decreased complement activity, and aberrant phagocytic and chemotactic mechanisms that make them more susceptible to *V. vulnificus* infection.¹³ Finally, murine models show depletion of lymphocytes in active *Vibrio* infection, which suggests a direct cytotoxicity to this cell; some authors believe this may contribute to the severity of disease.¹⁴ In our case, we noted a significant drop in lymphocytes, which did not normalise until hospital day 5.

Nine hundred cases of infection with *V. vulnificus* were reported to the US Centers for Disease Control and Prevention, from 1998 to 2006. The Centers for Disease Control (CDC) developed a mandatory reporting system for *V. vulnificus* in 2007, as a result of an increase of reported cases.¹⁵ *V. vulnificus* remains a rare but quite deadly infection. The most recent data for the USA indicate that, in 2013, of the 1176 cases of reported *Vibrio* infections, 137 (12%) were *V. vulnificus*, of which 32/115 (28%) were fatal.¹⁶ Data gathered prior to mandatory reporting reveal that primary septicaemia, wound infections and gastroenteritis were the most common manifestations of *V. vulnificus* infection.^{1–5} Necrotising fasciitis, as seen in our patient, has been reported quite commonly following wound infections.¹⁷ However, necrotising fasciitis and SBP occurring

spontaneously from septicaemia without previous injury or trauma is infrequently reported. Meningitis, septic arthritis and other illnesses in more rare sites of infection have also been reported.^{18–19} A history of ingestion of raw seafood within 7 days of illness onset was found in a remarkable 96% of patients in one study.⁵ US CDC data also indicate that chronic liver disease increases the risk of developing the infection by a factor of 80 and increased death by a factor of 200 compared to those patients without history of chronic liver disease.²⁰ Prompt treatment has repeatedly been demonstrated to be essential to survival. In one case series, primary septicaemia led to death in 55% of cases, while wound infection was responsible for death in 24% of cases. In this same case series, fatality was significantly increased with delay in antibiotic treatment. Thirty-three per cent of patients died if antibiotics were initiated within 24 h while 53% and 63% died if antibiotics were initiated between 24–48 h and 48–72 h, respectively.³

Infection by *V. vulnificus* is a rare but potentially deadly infection in patients with liver disease who ingest raw seafood. A thorough dietary and travel history should always be taken to identify risk factors for infection. While *Vibrio* is an uncommon cause of patient presentations with cellulitis, physicians should include *V. vulnificus* as part of the differential diagnosis in the patient with severe sepsis or severe wound infection in order to provide prompt treatment, and reduce morbidity and mortality.

Learning points

- ▶ Patients with liver disease are susceptible to lethal infection by *Vibrio vulnificus* if they consume raw or undercooked seafood.
- ▶ Infection with *V. vulnificus* commonly manifests as local wound infection, gastroenteritis or primary septicaemia.
- ▶ Prompt recognition of risks for *Vibrio* infection and thorough exposure and dietary history are essential in patients with chronic liver diseases presenting with signs of severe infection.

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