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Vibrio vulnificus septicemia in a hospitalized patient with hepatitis B virus-associated cirrhosis: A case report

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ABSTRACT

Vibrio vulnificus is usually transmitted by consumption of raw or undercooked seafood or exposure to seawater and can causes gastroenteritis, wound infection, and even sepsis. However, atypical or unclear sources of *V. vulnificus* infection have been reported. Here, we report a case of *V. vulnificus* infection presenting as septicemia in a 53-year-old man with hepatitis B virus-associated cirrhosis. The source of infection remained unclear as the patient reported no consumption of seafood or contact with seawater. Treatment with antibiotics was initiated prior to confirmation of *V. vulnificus* infection. This report provides an important reference for the diagnosis and treatment of *V. vulnificus* infection.

1. Introduction

Vibrio vulnificus is a Gram-negative, motile, halophilic, pathogenic bacterium commonly found in warm coastal waters worldwide that causes acute gastroenteritis by consumption of raw or undercooked shellfish, necrotizing wound infections by exposure of open wounds to seawater, and invasive sepsis in those with compromised immune systems or chronic liver disease [1]. *V. vulnificus* is subdivided into three biotypes based on biochemical characteristics. Biotype 1 strains, which are responsible for the majority of human infections, including fatal septicemia, are further classified into clinical (C) and environmental (E) genotypes based on the virulence-correlated gene *vcg* (*vcgC* and *vcgE*, respectively) [2]. *V. vulnificus* is the most deadly foodborne pathogens with a fatality rate of >50% in high-risk individuals, especially those with liver disease [3]. Hence, rapid diagnosis and treatment are critical to improve survival [3]. However, atypical clinical symptoms or unclear sources of exposure can delay diagnosis and treatment [4–6]. Here, we report a case of *V. vulnificus* septicemia in a cirrhotic patient with no history of contact with seawater or consumption of seafood.

2. Case presentation

A 53-year-old man with chronic hepatitis B virus (HBV) infection (>30 years) presented on May 9, 2018 with chief complaints of weakness, bloating, anorexia, and decreased urine output for 10 days. He denied any history of infectious disease, such as typhoid or tuberculosis, chronic disease, such as hypertension or diabetes, or recent surgery or trauma. Laboratory findings on admission were as follows: alanine aminotransferase, 160 (reference, 0–40) U/L; aspartate transaminase, 167 (reference, 0–40) U/L; serum albumin

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(ALB), 28 (reference, 40–60) g/L; total bilirubin, 77.4 (reference, 5.1–19) μmol/L; direct bilirubin, 22.4 (reference, 0–6) μmol/L; white blood cell (WBC) count, 3.51 (reference, 3.5–8.5) $\times 10^9$/L; absolute neutrophil count (ANC), 58.1% (reference, 55%–70%); lymphocyte percentage, 22.25% (reference, 20%–40%), hemoglobin, 112 (reference, 120–165) g/L; platelet count, 74 (reference, 125–350) $\times 10^9$/L; thrombocytocrit, 0.033% (reference, 0.11–0.28%); and ascites cell count, 200/μL. Abdominal ultrasound revealed liver cirrhosis and ascites with a maximum anteroposterior diameter of 132 mm. The diagnosis on admission was decompensated cirrhosis resulting from chronic HBV infection with possible abdominal infection. Routine culture of 50 mL of ascites fluid was free of bacteria. His blood pressure on admission was 153/89 mmHg. The initial treatment regimen included propranolol, furosemide, spironolactone, compound glycyrrhizin, polydilute phosphatidylcholine, piperacillin sodium, and tazobactam sodium. His ALB level was only 25.8 g/L on May 12, thus ALB infusion was initiated. His liver function improved as compared to May 17. HBV DNA was 1.88 $\times 10^6$ U/L, thus anti-viral treatment with entecavir was initiated. The patient developed a transient fever (37.8 °C) on May 26, which was not treated. On May 29, abdominal ultrasound revealed a decrease in ascites volume (maximum anteroposterior diameter, 20 mm). ALB infusion was performed again on May 30, but discontinued and piperacillin was administered. From June 1 to July 3, treatment included only several infusions of ALB and abdominal ultrasounds for observation of ascites.

On July 15, he developed a fever (39 °C), which began the day before, with obvious tenderness of the left lumbar vertebra. Subsequent laboratory findings were as follows: blood pressure, 120/75 mmHg; WBC count, 6.93 $\times 10^9$/L; ANC, 82.6%; hemoglobin, 110 g/L; platelet count, 58 $\times 10^9$/L; procalcitonin (PCT), 1.62 (reference, <0.1) ng/mL; serum C-reactive protein (CRP), 61.1 (reference, <10) mg/L; prothrombin time, 17 (reference, 11–13) s; and D-dimer, 1.61 (reference, <0.2) mg/L. A secondary diagnosis was bacteremia, but no specific treatment was given. The patient also complained of worsening low back pain overnight.

On the morning of July 16, his temperature was 40.2 °C, which was accompanied by chills, unbearable low back pain, and forced position. Approximately 40 mL of blood was drawn for routine culture. Subsequently, he was given ceftazidime, vitamin B6, vitamin C, and "*zhengchaihuyin*" granules. Follow-up laboratory test results were as follows: WBC count, 6.92 $\times 10^9$/L; ANC, 84.71%; hemoglobin, 105 g/L; platelet count, 44 $\times 10^9$/L; PCT, 2.12 ng/mL; and CRP, 77.3 mg/L. Ultrasound showed no abnormalities of the kidneys of ureters. Injection of dexamethasone at 5 mg reduced his temperature to 38.5 °C. However, the overall condition of the patient did not significantly improve. Therefore, on the afternoon of July 16, piperacillin-tazobactam in addition to β-lactam/β-lactamase inhibitors were administered as antibacterial agents. On the night of July 16, his temperature gradually decreased to normal and the low back pain had improved.

On July 18, blood culture results revealed bacterial infection. Blood cultures were analyzed with the BacT/ALERT® 3D system (bioMérieux, Marcy-l'Étoile, France). Subsequently, species identification was performed with a VITEK® 2 system (bioMérieux). Antibiotic susceptibility testing showed that the isolate was susceptible to ampicillin, ampicillin/sulbactam, piperacillin-tazobactam, cefuroxime, cefuroxime axetil, ceftazidime, ceftriaxone, and levofloxacin. In addition, cultures on blood agar and thiosulfate–citrate–bile salts–sucrose agar showed grayish white colonies and green colonies, respectively, consistent with *Vibrio* (supplementary Figure 1). The isolate was confirmed as *V. vulnificus* by 16S rRNA sequencing (GenBank accession number: OR192851). In addition, the genome of the isolate was positive for the *vvhA* (cytolysin/hemolysin), *vcgC*, *nanA* (N-acetylneuraminate lyase), *mtlABC* (mannitol/fructose-specific phosphotransferase system IIA protein), *ary* (arylsulfatase), and *cps1* (capsular polysaccharide) (Fig. 1 and supplementary Figure 2), confirming that the *V. vulnificus* isolate was the C-genotype [7]. However, the patient denied having contact with seawater or consuming seafood.

Treatment was initiated with piperacillin-tazobactam and levofloxacin. Laboratory findings on July 24 were as follows: WBC count, 3.58 $\times 10^9$/L; ANC, 64.2%; PCT, 0.271 ng/mL; and CRP, 23.2 mg/L. Laboratory findings on July 28 were as follows: WBC count, 2.77 $\times 10^9$/L; ANC, 61.3%; PCT, 0.096 ng/mL; and CRP, 13.7 mg/L. Notably, no bacteria were detected in the blood. Laboratory findings on August 13 were as follows: WBC count, 2.12 $\times 10^9$/L; ANC, 45.7%; hemoglobin, 104 g/L; platelet count, 60 $\times 10^9$/L; PCT, 0.02 ng/mL; and CRP, 23.2 mg/L. Thereafter, his body temperature and inflammatory indicators returned to normal, and liver function had improved, thus the patient was discharged.

3. Discussion

V. vulnificus primarily inhabits coastal environments and can be easily isolated from shellfish during warmer months [8]. Most clinical cases of *V. vulnificus* infection are associated with either the consumption of raw or undercooked seafood or exposure of open wounds to seawater [1]. We encountered a case of *V. vulnificus* septicemia in a 53-year-old man with a history of HBV-associated cirrhosis. Blood samples of patients with hepatic cirrhosis usually have significantly high iron concentrations, which promote rapid

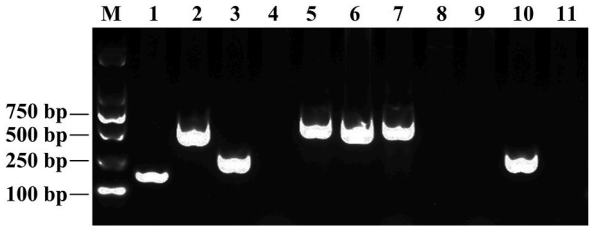

Fig. 1. Specific gene identification by PCR. Lane M: DL2000 DNA ladder. Lanes 1–11: 16s-rDNA, *vvhA*, *vcgC*, *vcgE*, *nanA*, *mtlABC*, *ary*, *bt2*, *serE*, *cps1*, and *cps2*, respectively. The primers used for PCR analysis are listed elsewhere [7].

proliferation of *V. vulnificus* [9,10]. Thus, *V. vulnificus* septicemia is strongly associated with hepatic cirrhosis.

Although the patient was admitted on May 9, *V. vulnificus* infection was not confirmed until July 20. The cause of *V. vulnificus* infection was undetermined as the patient denied consumption of raw seafood or contact with seawater. Unknown sources of *V. vulnificus* infections are not uncommon clinically, as insect vectors, such as a bee sting, have been reported [4]. Moreover, *V. vulnificus* strains belonging to the C- and E-genotypes have been isolated from freshwater environments [11]. A previous study reported *V. vulnificus* infection after exposure to freshwater in China [12]. The isolate in this study was a C-genotype strain (Fig. 1). Thus, a freshwater source could not be ruled out. The rapid development and high mortality rate of *V. vulnificus* sepsis should serve as reminders of the importance of timely diagnosis and treatment of *V. vulnificus* infection. The best choice of antibiotics may be a combination of third-generation cephalosporins and quinolones. Overall, this report provides an important resource for the clinical diagnosis and treatment of *V. vulnificus* infection.

Ethics approval and consent to participate

The publication of this case study was approved by the Committee on Human Rights Related to Research Involving Human Subjects of the Affiliated Nantong Hospital 3 of Nantong University (Nantong, Jiangsu, China).

Consent for publication

The patient consented to publication of potentially identifying information.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e18905.

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