SEPTIC SHOCK WITH DERMATITIS AND NECROTIZING MYOSITIS DUE TO *Vibrio vulnificus* INFECTION

(CASE REPORT)

Trinh Van Thong✉, Tran Van Thanh, Nguyen Ngoc Son, Nguyen Viet Thanh, Hoang Van Chau

Nghe An Friendship General Hospital

SUMMARY

Vibrio vulnificus (V. vulnificus) is a gram-negative bacterium that can cause serious, potentially fatal infections. V. vulnificus causes three distinct syndromes: Overwhelming primary septicemia caused by consuming contaminated seafood, wound infections acquired when an open wound is exposed to contaminated warm seawater, and gastrointestinal tract-limited infections. Case-fatality rates are higher than 50% for primary septicemia, and death typically occurs within 72 hours of hospitalization.

Risk factors for V. vulnificus infection include chronic liver disease, alcoholism, and hematological disorders. When V. vulnificus infection is suspected, appropriate antibiotic treatment and surgical interventions should be performed immediately. Third-generation cephalosporin with doxycycline, or quinolone with or without third-generation cephalosporin, may be potential treatment options for patients with V. vulnificus infection.

Keywords: *Septic shock, infection*

I. INTRODUCTION

Vibrio vulnificus (*V. vulnificus*) is a gram-negative, motile, halophilic bacterium commonly found in marine and brackish coastal waters. It can cause three distinct syndromes: gastroenteritis, primary septicemia, and wound infections, all of which have high mortality rates. The disease primarily affects individuals with chronic liver disease, immunocompromised states, or conditions associated with iron overload. Upon suspicion of *V. vulnificus* infection, based on patient history, epidemiology, clinical progression, and microbiological findings, prompt initiation of appropriate antibiotics and surgical intervention (when indicated) is crucial.

Vibrio vulnificus is a free-living organism found globally, primarily in saltwater and brackish environments, thriving in tropical and subtropical regions. Its optimal growth temperature is above 18^{0}C, with a preferred salinity range of 15 to 25 parts per thousand. This bacterium is ingested by filter-feeding animals such as oysters, clams, and mussels, with bacterial

[1] Chịu trách nhiệm: Trịnh Văn Thông, Bệnh viện Đa khoa Nghệ An

Email: thongmedical@gmail.com

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concentrations in their intestines reaching 1.0×10^3 to 1.0×10^6 cells per gram of oyster at warmer water temperatures. It is also present in the intestines of coastal and estuarine fish.

Vibrio vulnificus consists of 3 biotypes:

+ **Biotype 1:** The most common, primarily pathogenic to humans, with mortality rates exceeding 50% in wound infections and over 75% in cases of septicemia.

+ **Biotype 2:** Reported to cause disease in eels, with potential pathogenicity in humans.

+ **Biotype 3:** Believed to be a hybrid of biotype 1 and biotype 2, documented to cause infections in humans in freshwater environments in Israel.

Transmission Pathways: Infection occurs through the consumption of contaminated food (e.g., raw oysters) and exposure through skin wounds or mucous membranes (e.g., individuals frequently in contact with brackish or saltwater).

The disease typically manifests in individuals with chronic liver disease, alcoholism, immunosuppression, or conditions that lead to iron overload (e.g., thalassemia). The incidence is more common in middle-aged adults, likely due to the prevalence of chronic illnesses, cirrhosis, and alcoholism in this demographic. Males are affected more than females, possibly due to higher exposure to the bacterium from occupational activities and a greater prevalence of alcohol use and chronic diseases. Some studies in murine models suggest a protective role of estrogen against bacterial virulence.

The bacterium proliferates rapidly when transferrin saturation exceeds 70%. Many chronic liver diseases are associated with iron metabolism disorders, which partially explain the pathogenesis of the disease.

2. DISCUSSION OF CLINICAL COURSE AND TREATMENT METHODS

2.1. Case Progression

A 44-year-old male, a fisherman involved in aquaculture in Quynh Luu, Nghe An, was admitted at 14:50 on January 5, 2024. Three days prior to admission, he sustained a minor wound to his left thigh while inspecting a fish farm. Subsequently, he developed redness, swelling, and warmth in the left thigh, which progressively extended to the knee and lower leg. The following day, a necrotic area with black discoloration appeared at the wound site, accompanied by several brown-black vesicles measuring 4 x 5 cm surrounding the wound on the left thigh and lower leg. The patient experienced fever but reported no abdominal pain or diarrhea.

Upon arrival at Nghe An Friendship General Hospital, he was alert but severely fatigued, with complaints of headache and dizziness, alongside extensive lesions on the left thigh and lower leg, including hemorrhagic vesicles, swelling and tenderness in the lower leg, and ecchymosis with extensive necrotic lesions extending from the lateral thigh to the lower leg.

Vital signs were as follows: Blood pressure: 70/50 mmHg; Temperature: 40^0C; Respiratory rate: 28 breaths/min; Heart rate: 120 beats/min.

Initial laboratory test results upon admission: WBC: 22.86 G/L; NEU: 93.1%; Hb: 95 g/L; RBC: 2.82 T/L; HCT: 0.257 L/L; PLT: 29 G/L; Prothrombin time (PT): 15.2 s (by automated analyzer); PT ratio: 47.2%;

INR: 1.41; APTT: 32.7 s; APTT (control): 1.23; pO2: 88.1 mmHg; pCO2: 28.0 mmHg; Na: 127.3 mmol/L; K: 5.88 mmol/L; Cl: 94.4 mmol/L; HCO3: 20.9 mmol/L; Pro-calcitonin: 36.23 ng/mL; Serum albumin: 13.2 g/L; Total bilirubin: 33.3 µmol/L; Serum lactate: 6.14 mmol/L; ALT: 38.9 U/L; AST: 75.2 U/L; HBsAg (+), Anti-HBs (-), Anti-HCV (-), Elisa AFP (-); Electrocardiogram (ECG): Sinus tachycardia at a rate of 122 beats/min; ST segment is isoelectric. Doppler Ultrasound of Lower Limb Arteries and Veins: Atherosclerosis in the bilateral lower extremity arterial system.

The patient underwent blood cultures and drainage cultures from the vesicles and necrotic tissue for susceptibility testing prior to the initiation of antibiotic therapy. The patient had not received any antibiotics before this.

The patient has a history of alcohol use disorder, consuming approximately 250 mL of alcohol per day.

The assessment showed a qSOFA score of ≥ 2 and a SOFA score of > 2.

Diagnosis: Suspected skin-related septic shock due to *Vibrio vulnificus*, based on epidemiological characteristics, medical history, and disease progression. The patient was admitted to the ICU and immediately started on antibiotic therapy, including levofloxacin, metronidazole, and vancomycin, along with fluid resuscitation using 0.9% NaCl and human albumin to maintain a central venous pressure (CVP) of ≥ 12 mmHg. Additionally, levonordefrin (norepinephrine) and dobutamine were administered to ensure systolic blood pressure > 90 mmHg and mean arterial pressure > 65 mmHg.

At 21h30 on January 5, 2024, the patient was indicated for emergency continuous renal replacement therapy, which was completed at 02:00 on January 6, 2024. After the dialysis session, the patient was alert, with a heart rate of 100 beats/min, blood pressure of 110/70 mmHg, and a temperature of 37°C, breathing spontaneously with supplemental oxygen.

At 09h00 on January 6, 2024, a multidisciplinary consultation with the Burn Unit agreed on the need for emergency surgical debridement of necrotic tissue.

Figure 2.1. Preoperative images of the lesion

Figure 2.2. Post-debridement images of the necrotic tissue

After surgery, the patient received continuous irrigation of the wound with diluted Betadine and normal saline, with daily dressing changes.

Culture results from the necrotic tissue were positive for *Vibrio vulnificus* and demonstrated sensitivity to multiple antibiotics, including third-generation cephalosporins (Ceftazidime, Cefotaxime, Ceftriaxone), Carbapenems (Meropenem, Imipenem), Aminoglycosides (Gentamicin, Amikacin), and Fluoroquinolones (Levofloxacin, Ciprofloxacin). Vancomycin was discontinued, and treatment was switched to Ceftazidime at a dosage of 4 g/day based on the susceptibility results.

After six days of treatment, the patient was alert and breathing independently but appeared cachectic. The abdomen was soft, and there was no hepatosplenomegaly. Peripheral pulses were palpable, with no focal neurologic deficits. Vital signs were as follows: heart rate 95 beats/min, blood pressure 130/90 mmHg, temperature 37^0C, and urine output 2500 mL/24 hours.

Laboratory results included: pO2: 121.3 mmHg; pCO2: 34.3 mmHg; pH: 7.511; Na: 137.8 mmol/L; K: 3.88 mmol/L; Cl: 98.6 mmol/L; serum creatinine: 90 µmol/L; serum lactate: 5.11 mmol/L; RBC: 2.36 T/L; HGB: 77 g/L; HCT: 0.216 L/L; WBC: 17.67 G/L; %NEUT: 85.6%; PLT: 72 G/L; PT: 79.8%; INR: 1.10; APTT: 29.3 seconds; APTT ratio: 1.09.

Local necrotic tissue was beginning to develop granulation tissue, although there was still significant necrotic debris and exudate present.

On January 11, 2024, the patient was transferred back to the Burn Unit for further treatment.

In the Burn Unit, the patient continued on ceftazidime 4 g/day, human albumin 50 g twice daily, 5% amino plasma 500 mL/day, along with electrolyte replacement and daily dressing changes. By January 14, 2024, the patient was alert, with pale mucous membranes and a cachectic appearance. Laboratory results included: serum cortisol: 413.1 nmol/L; pro-calcitonin: 1.36 ng/mL; Na: 135 mmol/L; K: 4.05 mmol/L; Cl: 101.6 mmol/L; serum creatinine: 54 µmol/L; pre-albumin: 7.46 g/L; RBC: 2.56 T/L; HGB: 76 g/L; HCT: 0.279 L/L; WBC: 12.66 G/L; %NEUT: 75.6%; PLT: 98 G/L. Accordingly, the patient was indicated for a transfusion of 750 mL of red blood cells.

On January 16, 2024, the patient underwent thin split-thickness skin grafting to cover the skin defect on the left thigh and lower leg.

Figure 2.3. Preoperative images of the lesion before skin grafting

Figure 2.4. Post-skin graft images on the 6th day

After the skin graft procedure, the patient's overall condition improved, with increases in hemoglobin and hematocrit levels, as well as elevated albumin levels. Locally, the split-thickness skin graft adhered well, and the donor site healed satisfactorily.

On January 25, 2024, the patient was discharged with an outpatient management plan that included levofloxacin 0.5 g, two tablets daily, and a follow-up appointment scheduled for two weeks later.

2.2. Discuss of diagnosis and treatment

V. vulnificus infection is suspected based on clinical and epidemiological findings and is confirmed by bacteriological culture [1, 2]. Because bacteremia is common, routine blood cultures should be performed when *V.vulnificus* infection is suspected. Gram stain and culture of a specimen obtained from skin lesions such as abscesses or bullae are helpful to rapidly identify bacteria. Stool cultures are occasionally useful, requiring thiosulfate-citrate-bile salts-sucrose agar for isolation [1]. Culture tests using blood or skin lesion samples are the most important method for diagnosing *V. vulnificus* sepsis. However, since *V. vulnificus* is highly sensitive to antibiotic administration, it is necessary to check whether any antibiotic has been administered prior to performing the culture test.

Microbiological culture provides high specificity, but diagnosis takes a long time. Furthermore, *V. vulnificus* is susceptible to many antibiotics; therefore, infection in patients previously treated with antibiotics before culture is difficult to diagnose accurately [3]. Polymerase chain reaction (PCR) is also useful for early diagnosis of V. vulnificus infection, even in patients previously treated with antibiotics [3]. Using blood samples, the conventional PCR and nested PCR assays showed specificities of 100% and 73%, respectively. The real-time PCR assay had 100% sensitivity and specificity as a positive result using a cutoff value of < 38 cp [3]. The real-time PCR assay to detect *V. vulnificus* specific genes is not only the most sensitive and specific diagnostic method but also the most rapid technique [3].

In a recent study, *V. vulnificus* DNA copy numbers were higher in tissue samples than in blood samples from V. vulnificus-infected patients, showing that skin lesions are more useful than blood samples for PCR-based diagnosis of V. vulnificus-infected patients [4]. Real-time PCR using serum samples collected from 14 patients at admission showed a median *V. vulnificus* DNA load of 638.5 copies/mL of blood (interquartile range [IQR], 37 to 3,225), while real-time PCR using the initial tissue specimen at admission showed a median of 16,650 copies/mL of tissue fluid (IQR, 4,419 to 832,500; p = 0.022.

Data on 62 cases of *V. vulnificus* infection reported by Florida health authorities showed that the mortality rate was 33% when antibiotics were administered within 24 hours after admission, but increased to 63% and 100% when antibiotic administration was delayed to 48 to 72 and > 72 hours post-admission, respectively [5]. These results demonstrate the importance of timely early antibiotic administration.

V. vulnificus is sensitive to most antibiotics in vitro, except for colistin; antibiotics that are effective against *V. vulnificus* in vitro are third-generation cephalosporins ceftriaxone, cefotaxime, or ceftazidime), Piperacillin-Tazobactam, Carbapenems (Imipenem or Meropenem), Tetracyclines (Doxycycline or Tetracycline), aminoglycoside (gentamicin or amikacin), fluoroquinolones (ciprofloxacin, levofloxacin, or moxifloxacin), and Sulfamethoxazole-Trimethoprim [6].

In most in vitro or in vivo mouse model experiments on antibiotic susceptibility, tetracyclines are reported to have significantly higher efficacy than penicillin or cephalosporins. This has been attributed to the fact that the tetracycline class of antibiotics achieves better penetration into tissues with poor perfusion when V. *vulnificus* infection occurs, and has inhibitory effects against the synthesis of proteins, such as various toxins and enzymes produced by *V. vulnificus* [7].

The CDC recommends doxycycline 100 mg intravenously or orally twice a day plus ceftazidime (or any other third-generation cephalosporin) 1 to 2 g intravenously every 8 hours for the treatment of *V. vulnificus* infection [8]

Case fatality rates for V. vulnificus infections have been shown to increase with delays between the onset of illness and the administration of antibiotics. Therefore, if a patient is suspected to be infected with V. vulnificus, appropriate antibiotic treatment should be immediately administered [5, 9].

Furthermore, in many patients with serious skin and soft tissue infections such as necrotizing fasciitis, surgical interventions such as debridement or fasciotomy are necessary in addition to antibiotics treatment to remove necrotic tissue and bacteria [6, 9]. A retrospective study on necrotizing soft-tissue infections including *V. vulnificus* related necrotizing fasciitis in 65 patients demonstrated the importance of early surgical intervention based on the time from admission to surgery (25 ± 39 hours in the survival group and 90 ± 95 hours in the mortality group) [10].

3. LESSONS LEARNED

Vibrio vulnificus is a gram-negative, halophilic, motile bacterium primarily found in warm coastal waters. It has the potential to cause illnesses ranging from mild to severe, including gastroenteritis and septic shock. Severe infections often occur in patients with chronic liver disease, immunocompromised states, and conditions leading to iron overload in the body. Despite the number of individuals at risk of exposure to V. vulnificus, the incidence of related illnesses remains relatively low. Cases tend to occur during warmer months when bacterial counts increase. The primary routes of infection are through the consumption of raw or undercooked seafood or through direct contact via open wounds when wading, fishing, or handling infected seafood.

Vibrio vulnificus possesses several virulence factors, including resistance to gastric acid, endotoxins, exotoxins, a capsule, flagella, pili, and siderophores. It is characterized by three syndromes: gastroenteritis, primary sepsis, and wound infection. Diagnosis is based on clinical symptoms, epidemiology, and microbiological testing, with real-time PCR showing high sensitivity and specificity. Early antibiotic therapy is strongly recommended and should be combined with surgical intervention in severe cases. Several antibiotics show in vitro sensitivity to V. vulnificus, with ceftazidime in combination with doxycycline being recommended by the CDC. Comprehensive care, along with patient education, guidance, and counseling, is essential and crucial for improving patient outcomes and preventing complications such as necrotizing fasciitis and secondary infections with other dangerous bacteria.

Patients with a presumptive diagnosis of V. vulnificus infection should be immediately started on antibiotics therapy and surgical interventions if needed. The recommended antibiotics treatment regimen is ceftriaxone plus doxycycline or ceftriaxone plus ciprofloxacin. pH level upon admission, APACHE II score, and V. vulnificus DNA load can help predict the prognosis for patients with V. vulnificus infection.

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