

Vibrio Vulnificus Infection: A Rare Cause of Necrotizing Fasciitis

Hazem M Zakaria

Department Of surgery, College Of Medicine, King Faisal University, Dammam, Kingdom of Saudi Arabia

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Abstract

Necrotizing fasciitis may be caused by a variety of organism . The progression of the disease may be gradual or have a fulminant course. We report a case of septicemia, gangrene and fulminant necrotizing fasciitis caused by Vibrio Vulnificus with fatal outcome. The patient expired inspite of I.V antibiotics and amputation of the affected limb. Transmission to men is through contact with skin, mucosa or wounds exposed to sea water, and/or consumption of certain undercooked fish or raw shell , specially during the summer months. Significant risk factors for fulminant course of the disease include preexisting liver disease and immunocompromised states. This infection should be clinically suspected and recognized from its typical history of exposure to sea water and fulminant clinical progress as a delay in diagnosis and treatment may result in considerable mortality.

Introduction

Necrotizing fasciitis is a necrotizing soft tissue infection (NSTI) spreading along fascial planes, with or without overlying cellulitis; also called Meleney's ulcer. Necrotizing fasciitis is severe manifestation of lymphangitis that progresses in a frightening manner within a short period. Tissue necrosis develops rapidly behind advancing wall of inflammation that limits penetration by antibiotics [1].

Necrotizing fasciitis due to Vibrio Vulnificus, the awareness of which has evolved during the last 30 years, can produce an overwhelming toxic shock-like syndrome that results in rapid deterioration and death [2,3]. It is especially fatal in subjects who have chronic liver disease such as cirrhosis caused by chronic hepatitis B or C infection. Other high-risk conditions that predispose to severity of infection with Vibrio Vulnificus include iron overload states (hemochromatosis), concurrent malignancy, human immunodeficiency virus infection (AIDS) and other immunocompromised states, chronic renal failure, thalassemia and diabetes [4-5]. A recent study showed that people with these pre-existing medical conditions were 80 times more likely to develop Vibrio Vulnificus septicemia with grave consequences than were healthy people [6].

Rapid diagnosis and treatment is life saving. As yet, no superantigen has been implicated as a cause of this form of necrotizing fasciitis. The current literature suggests that

host factors play a large role in the fulminant nature of the disease in these susceptible patients [3,6].

Vibrio Vulnificus is a rare cause of disease. Between 1988 and 1991, there were only 21 reported cases of Vibrio Vulnificus infection in the United States. Most cases occur in coastal states. The incidence of serious Vibrio Vulnificus infection has been reported between 0.4 and 1.9 cases/100,000 [7].

Vibrio Vulnificus infection is an acute illness, and those who recover should not expect any long-term consequences. The organism rapidly crosses the gut mucosa and invades the bloodstream without causing any significant gastrointestinal symptoms [8].

Among healthy people, ingestion of Vibrio Vulnificus can cause vomiting, diarrhea, and abdominal pain. In immunocompromised persons, particularly those with liver disease, Vibrio Vulnificus can invade the blood stream, producing a severe and life-threatening illness characterized by fever and chills, hypotension (septic shock), and blistering skin lesions [1,5]. Initial skin lesions begin as erythematous subcutaneous nodules that spread to the dermis and muscle. Overlying hemorrhagic vesicles or bullae arise which frequently develop into necrotic ulcers [4,8].

Vibrio Vulnificus infection is diagnosed by routine stool and wound culture. The laboratory should be notified

when this infection is suspected by the physician, since a special growth medium can be used to increase the diagnostic yield. The treating clinician should have a high suspicion for this organism when patients present with gastrointestinal illness, fever, or shock following the ingestion of raw seafood, especially oysters, or with a wound infection after exposure to seawater [4,9].

Vibrio Vulnificus is well endowed with an array of virulence mechanisms including multiple invasive enzymes and endotoxins containing the core lipoprotein characteristic of most gram-negative bacteria. Lipoprotein alone or in concert with other substances such as proteases act as the triggering mechanism for a complex series of events that eventually lead to hypotension, insufficient tissue perfusion, uncontrollable bleeding and multiple organ system failure caused by hypoxia, metabolic acidosis and other severe alterations in metabolism [3,9].

Case Report

A 54-year-old fisher man was admitted to our hospital with left lower-extremity pain and shortness of breath starting approximately 24 h prior to admission. He also complained of subjective fever and resolved watery diarrhea. His medical history was significant for obesity, chronic obstructive pulmonary disease and chronic liver disease. He smoke one pack of cigarettes per day for more than 30 years. The patient was hospitalized with a diagnosis of cellulitis of the left leg, ulceration with necrotizing fasciitis; blood cultures were obtained and IV cefazolin at 1 g administered three times per day. Physical examination revealed a morbid obese man in mild distress from lower extremity pain. His temperature was 38.7 °C, his respiratory rate was 20 breaths/min, his pulse was 110 beats/min, and his blood pressure was 110/60 mm Hg. The patient was alert and oriented. His cardiorespiratory system examination was non contributory. His liver edge was palpable 3 cm below the right costal margin. On his ankle, two deep ulcers measuring 3 × 2 × 3 cm, with elevated margins and surrounding erythema were present. The entire left leg was swollen and the area around the wound was tender to palpation. Findings from a chest x-ray and an electrocardiogram were unremarkable.

The patient's initial laboratory analysis (compared to normal values) revealed white blood cell count, 14.3×10^3 cells/UL (3.9×10^3 to 10.3×10^3 cells/UL) with a left shift; hemoglobin, 8.4 g/dl; hematocrit, 25.2%; platelets, 133,000/UL (135,000 to 370,000/UL); bicarbonate, 14 mmol/liter (23 to 30 mmol/liter), pH 7.34; and erythrocyte sedimentation rate 157 mm/h. Blood urea nitrogen, 28 mg/dl (5 to 22 mg/dl); creatinine 1.9 mg/dl (0.7 to 1.2 mg/dl). Serum glucose was 65 mg/dl (70 to 110 mg/dl); international normalized ratio, 1.8; and total bilirubin, 2.8 mg/dl (0.2 to 1.2 mg/dl). and his albumin was 2.8 mg/dl

(3.5 to 4.8 mg/dl). The patient had a single episode of watery diarrhea (a stool sample for C/S was obtained which revealed no growth).

During the following 24 hours, the patient remained febrile, complaining of increasing pain and numbness over the left calf. After adequate hydration, serum creatinine and serum urea nitrogen returned to the normal range. He became progressively obtunded. He was shifted to the intensive care unit for further evaluation and management of presumed septic shock. His blood pressure was 90/50 mm Hg on dobutamine infusion. Respiratory rate was 26, and his SpO₂ was 93% on 3 liters per minute by nasal cannula. Over the next 12 hours, the patient's requirement for inotropic support increased to maintain his blood, and the patient had to be intubated...Meanwhile, the patient's lower-extremity lesions enlarged and progressed further, with the formation of hemorrhagic bullae, thrombosis of superficial veins, and skin necrosis. The distal lower-extremity pulses became feeble, and his condition continued to deteriorate. In view of his rapid deterioration and worsening clinical features of the limb, it was decided to perform an above knee amputation. He continued to deteriorate despite increased inotropic support and expired 48 hours following operation. Blood cultures were reported as growing *Vibrio* spp., identified as *Vibrio Vulnificus*.

Histological sections of the surgically amputated lower leg showed subepidermal bullae formation with the presence of an intense mononuclear inflammatory infiltrate, present in the dermis, subcutaneous adipose tissue, and the muscles.

Discussion

Vibrio Vulnificus is an opportunistic halophilic (those which require salt), lactose fermenting, highly motile gram-negative bacillus in the same genus as that cause cholera. It is found in marine or brackish waters in the coastal areas. It grows best in warmer waters (temperature >20°C) with salt level ranging from 0.7%-1.6% [6-8].

Most cases of *Vibrio Vulnificus* infections occur during the warm summer months between May and October. In some epidemiologic studies, greater than 50% of shellfish and 11% of crabs were found to harbor the organism during warmer months when the incidence of the infection also shows a significant rise [9,10].

The coastal areas of the Arabian Gulf countries also share the geographical distribution of warm water especially during the summer months.

Of the 422 cases of *Vibrio Vulnificus* infection reported to the CDC over a 9-year period, 43% were primary septicemia, 45% were wound infections, 5% were gastroen-

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teritis, and in 7%, the source could not be determined. Overall case fatality rate was 25% and history of sea food ingestion was present in 90% of all deaths [11].

Risk factors for developing this infection include the ingestion of seafood, especially crabs, lobsters, and raw oysters, poor refrigerating and handling of seafood and history of injury during sea water exposure [4,5,12]. Primary septicemia is seen without an apparent source of infection and is attributed to ingestion of contaminated sea food particularly in patients with pre-existing liver diseases.

Recent investigations have shown *Vibrio Vulnificus* undergoes a period of "bacterial hibernation" in which the organism is not viable below 10°C. However, upon warming to room temperature the organism becomes viable. ⁽¹³⁾ Organism proliferates at room temperature but is readily killed by boiling or freezing [12].

Infection with this bacterium, especially septicemia primarily occurs through ingestion of contaminated raw seafood. Raw oysters are the usual source, although other seafood can carry and transmit the organisms. Symptoms characterized by gastroenteritis is presumably an aftermath of seafood ingestion. In such cases the organism can be cultured from stool specimen but there is no wound infection. Wound infection is caused by direct inoculation of the bacteria and results in tissue necrosis and bacteremia.

Other types viz, pneumonia and endometritis have also been reported [13,14]. Since the organism is naturally found in warm marine waters, people with open wounds who come in contact with sea water especially fishermen can be exposed to *Vibrio Vulnificus* infection through direct contact, There is no evidence of person to person transmission of *Vibrio Vulnificus* [3,4,9].

Vibrio Vulnificus secretes a variety of toxins that have been instrumental in bacterial virulence and pathogenesis of severe manifestations. Iron has been shown to play a significant role in the pathogenesis of virulent infection as has been immunocompromised states. It has been postulated that the bacterium recruits iron to accelerate its growth and can quickly reach concentrations where the tumor necrosis factor- α released by its overwhelms the immune system [4].

The reported case-fatality rate from raw oyster and shellfish associated *Vibrio 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 [14].

This is relevant to Singapore where 6% of the population are hepatitis B carriers [15]. Several theories exist to ex-

plain the increased virulence of *Vibrio 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 *Vibrio Vulnificus*. [2,5,15].

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 *Vibrio Vulnificus* septicemia if they come in contact with the organism. They described 27 cases during a 5-year period from May 1985 to July 1990 and demonstrated three major discernible syndromes: primary septicemia, wound infection, and gastrointestinal diseases. The disease had a high mortality rate (41%). [16,17]

Clinical manifestations of pain, hyperpyrexia, and chills are severe. Wound infections and primary septicemia caused by this organism classically produce hemorrhagic bullae. Widespread vasculitis, thrombosis and vascular necrosis are the major features of skin lesions which severely hinder penetration by the antibiotics. Such lesions are associated with necrotizing fasciitis, cellulitis or pyomyositis [18].

Hence early and thorough surgical debridement should be a part of the planned treatment. This also helps in delivering the antibiotics to the areas where it is most needed. The presence of significant lower extremity pain at presentation and the subsequent development of lower extremity skin lesions, as seen in our patient, suggests *Vibrio Vulnificus* septicemia. Patients who get the infection through an open wound may have a compartment syndrome on the affected extremity, requiring surgical debridement and or amputation [4,5]. Decision to debride the wound should be made within the first 24 hours of admission to improve chances of survival.

One-third of patients are often accompanied by thrombocytopenia and evidence of disseminated intravascular coagulation. About 75% of patients have bullous skin lesions that range from mild lesions to rapidly progressive cellulitis and myositis [1,5].

Virulence of *Vibrio 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 *Vibrio 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 *Vibrio Vulnificus* than total iron stores [19,20].

Appropriate antibiotics should be administered without delay for soft tissue infections and septicemia and include doxycycline in combination with a third generation cephalosporin such as ceftazidime, an aminoglycoside or possibly chloramphenicol [4,8]. Surgical debridement of soft tissue infections is indicated early if the disease progression is rapid, surgical amputation of gangrenous limbs is often required [4,15]. The course of illness is often rapid and about 50% of cases are fatal.

The histopathology of *Vibrio Vulnificus* is usually revealed as an intense cellulitis involving the skin and subcutaneous tissues in a septal distribution [16]. Numerous bacteria are found in the superficial dermis, and bullae that form at the dermal-epidermal interface are devoid of inflammatory cells. The infiltrate is usually neutrophilic, which makes our case unusual in that the infiltrate was composed of mostly mononuclear cells [1,16].

Conclusion

Vibrio Vulnificus can be the cause of necrotizing fasciitis in the arabian gulf region especially in immunocompromised patients with chronic liver disease. These patients, who ingest undercooked or raw seafood or come in contact with the sea water, must be advised to seek medical care as soon as possible if they have skin lesions with fever and pain.

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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Correspondence:

Hazem Zakaria
Department of Surgery
King Faisal University
Kingdom of Saudi Arabia
P.O Box 40081, Al-Khobar 31952
Saudi Arabia

Phone: +966505963022; Fax: +96638649635
e-mail: hazakaria@yahoo.com