CASE REPORT

Vibrio vulnificus septic shock due to a contaminated tattoo

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SUMMARY

We present a case of *Vibrio vulnificus* septic shock and cellulitis in a patient with chronic liver disease that occurred after obtaining a leg tattoo with subsequent seawater exposure in the Gulf of Mexico. Initial suspicion for *V. vulnificus* was high and he was started on empiric doxycycline and ceftriaxone at admission. Blood and wound cultures grew oxidase positive and comma-shaped Gram-negative rods ultimately confirmed to be *V. vulnificus*. Despite aggressive initial treatment, the patient developed septic shock and died. This case highlights the association of chronic liver disease and high mortality associated with infections of *V. vulnificus*. Health providers should remain vigilant for *V. vulnificus* infections in patients with chronic liver disease and raw oyster ingestion or seawater exposure.

BACKGROUND

Vibrio vulnificus is a halophilic comma-shaped Gram-negative bacteria common in coastal oceanic water.¹ The organism has been associated with gastroenteritis, cellulitis, necrotising fasciitis and septicæmia.¹ Infection with *V. vulnificus* carries a high mortality up to 50%–60% in all patients.^{1–3} Classic risk factors for infection include haemochromatosis and chronic liver disease.^{1–4} Prompt recognition of a *V. vulnificus* infection is important to reduce mortality and start appropriate empiric antibiotics which include doxycycline and a third-generation cephalosporin.¹ In the USA, most serious infections appear to occur with the ingestion of raw oysters along the Gulf Coast, as nearly all oysters are reported to harbour *V. vulnificus* during the summer months and 95% of cases were related to raw oyster ingestion.⁵ Infections can also occur with exposure of open wounds to contaminated salt or brackish water; however, this represents an uncommon mechanism of infection.¹ We present a case of septic shock from *V. vulnificus* due to a contaminated tattoo, which highlights the high mortality and association of chronic liver disease in *V. vulnificus* infections.

CASE PRESENTATION

A 31-year-old Hispanic man with a history of alcoholic cirrhosis presented with 1 day of rapidly worsening, severe bilateral lower extremity pain. Eight days prior to admission, he received a new tattoo on his right calf followed by a swim in the Gulf of Mexico 3 days prior to admission. One day prior to admission, he developed fevers and chills, followed

by the development of erythema over his tattoo site and other areas over his legs bilaterally. His review of symptoms was otherwise unremarkable. He took no medications or supplements and had no recent hospitalisations. Family history was unremarkable for any history of liver disease. His social history was notable for consuming six 12-ounce beers daily.

His admission vital signs were notable for: a temperature of 99.5°F, pulse 115 beats per minute, blood pressure 62/52 mm Hg and respiratory rate 22/min with an oxygen saturation of 99% on room air. His bilateral lower extremities demonstrated exquisite tenderness with well-circumscribed erythematous lesions over the greater trochanter of his right hip, his left medial and lateral calf, his left medial calf and his right lateral calf within the margins of a fresh tattoo (figure 1A, B). There was preserved sensation and distal pulses in his extremities. His abdominal exam was without ascites, distention, hepatosplenomegaly or tenderness to palpation. His remaining physical exam was unremarkable.

INVESTIGATIONS

His admission labs revealed an elevated alanine transaminase 64 U/L (normal 10–50 U/L), aspartate aminotransferase 80 U/L (normal 10–50 U/L), alkaline phosphatase 119 U/L (normal 40–129 U/L), total bilirubin 4.6 mg/dL (normal 0.2–1.3 mg/dL), international normalised ratio 1.5 (normal 0.9–1.3), albumin 2.8 g/dL (normal 3.5–5.2 g/dL) and 38×10^9 /L platelets (normal $160\text{--}383 \times 10^9$ /L) consistent with chronic liver disease. Admission labs were also notable for an acutely elevated creatinine 1.81 mg/dL (normal 0.67–1.17 mg/dL) and elevated lactate 4.2 mmol/L (0.5–2.2 mmol/L) concerning for septic shock. A ferritin level was 1943 (normal 30–400 ng/mL) with an iron saturation of 16% (normal 16%–50%) consistent with an acute phase reaction. An admission chest X-ray and ECG were unrevealing. Right and left tibia and fibula X-rays did not reveal subcutaneous gas or additional significant abnormalities. His lesions rapidly evolved developing central purple patches with dark black borders (figure 1C). Within 2–3 hours after admission, bullae began erupting over his lesions at an alarming rate (figure 1D).

DIFFERENTIAL DIAGNOSIS

Given the rapidly progressing skin lesions in a patient with cirrhosis and recent exposure to seawater with a recent tattoo, overwhelming

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Figure 1 (A) Picture of recent tattoo on the right leg, which was the suspected portal of entry with erythema around tattoo margins. (B) Admission image of our patient's painful right medial calf. (C) Patient's right hip with rapidly progressing purple patch with necrotic centre noted approximately 2 hours after admission. Findings were not present on admission exam. (D) Patient's left medial calf with new bullae, expanding erythema and pain approximately 2 hours after admission. Findings were not present on admission exam.

infection due to *V. vulnificus* was suspected and doxycycline with a third-generation cephalosporin was immediately added to his antibiotic regimen. Spontaneous and secondary bacterial peritonitis were considered less likely due to a benign abdominal exam with the lack of ascites. Due to the concern for necrotising fasciitis, he was taken emergently to the operating room the night of admission to inspect the fascial planes, which were intact. Two sets of admission blood cultures and deep tissue surgical wound cultures were positive for oxidase positive comma-shaped Gram-negative rods within 24 hours of sample collection. These organisms were confirmed to be *V. vulnificus* (figure 2), confirming the diagnosis of septic shock due to *V. vulnificus*.

TREATMENT

Within 24 hours, his clinical status declined with progressive septic shock requiring multiple vasopressors and multi-organ system failure including acute renal failure requiring

Figure 2 Image of comma-shaped Gram-negative rods identified as *Vibrio vulnificus* obtained from the patient's positive blood culture.

Figure 3 (A) Picture of the suspect tattoo, the lateral portion of his right leg after fascial exploration 2 weeks after admission. (B) Picture of his right lower extremity 2 weeks after fascial exploration with progressing bullae and expanding erythema distal to the tattoo site.

continuous renal replacement and hypoxic respiratory failure requiring mechanical ventilation. Repeat blood cultures obtained 48 hours after admission were negative and vasopressors were gradually titrated off. His initial wounds continued to progress, developing more bullae and discoloration (figure 3A, B). Over the following 14 days, his clinical status improved with aggressive bedside debridement of necrotic lesions, wound care, life support and antibiotics. His lesions eventually progressed to dry gangrene with several eschar plaques on his right hip and bilateral lower extremities, but distal lower extremity circulation, strength and sensation remained intact. Deep surgical necrotic wound debridement and bedside lower extremity amputations were considered; however, due to chronic liver disease, his surgical risk was considered prohibitively high.

OUTCOME AND FOLLOW-UP

He was extubated on the 18th day of admission and began aggressive rehabilitation. Unfortunately, his clinical status subsequently deteriorated, ultimately leading to his death due to a myriad of complications related to cirrhosis, renal failure and necrotic skin lesions approximately 2 months after admission.

DISCUSSION

V. vulnificus is classically associated with sepsis and soft tissue infections in patients with chronic liver disease after exposure to seawater or ingestion of raw oysters. Risk of infection is also increased in patients with immunodeficiency, haemochromatosis, end-stage renal disease and diabetes mellitus.¹⁻⁴ Healthy patients appear to account for <5% of all reported cases of *V. vulnificus* sepsis in the USA.⁶ Haemochromatosis has long been recognised as a risk factor for developing severe *V. vulnificus* infections; however, the relationship between iron metabolism and the bacteria is unclear.¹ Chronic liver disease is associated with impaired iron metabolism and may account for some of the increased risk for patients with chronic liver disease.⁶

In one case series, *V. vulnificus* infections in 62 patients presented predominantly with primary sepsis (61%), skin soft tissue infections (27%) and isolated gastrointestinal infections (11%).³ Sepsis typically presents with fever, lethargy, chills and can result from primary skin infections.¹ Cutaneous skin lesions such as bullae, cellulitis and ecchymosis typically occur on the lower extremities or the trunk and may represent primary or metastatic sites of infection. These lesions can progress to necrotic ulcers, necrotising fasciitis, necrotising vasculitis or myonecrosis.¹ Soft tissue infections are often accompanied by

swelling and severe pain out of proportion to the exam.¹ Symptoms can rapidly progress to septic shock during the first 12 hours of presentation which represents a very poor prognosis.¹ The mortality rate for sepsis due to *V. vulnificus* is high with reported rates of 50%–60% in all patients.^{1–3} Gastrointestinal symptoms may present with abdominal pain, cramping, vomiting, diarrhoea and fever. Disease can occur in immunocompetent patients and symptoms are usually self-limited, although rare deaths have been previously reported.¹

V. vulnificus appears to cause virulence through several different mechanisms which include activation of cytokines, accumulation of iron via siderophores and the production of toxins. *V. vulnificus* appears to be a potent activator of systemic inflammatory response via cytokine activation of interleukin (IL)-1b, IL-6, IL-8 and tumour necrosis factor alpha (TNF- α).¹ In patients with chronic alcoholic liver disease and *V. vulnificus* infection, deficiencies of proinflammatory cytokines may result in a less brisk immune response leading to increased bacterial proliferation and worse clinical outcomes.⁷ Furthermore, patients with chronic liver disease have decreased neutrophil activity which is theorised to further reduce the bacterial clearance.¹ Disease states with abnormal iron metabolism particularly haemochromatosis, chronic liver disease and end-stage renal disease on dialysis are well-recognised risk factors for *V. vulnificus* infections.¹ The exact pathophysiology remains unclear; however, *V. vulnificus* is known to produce at least two siderophores that have been shown to enhance growth in a mouse model.⁸ At least three different toxins, RtxA1, VvpE and VvhA, appear to play a significant role in organism virulence.¹ RtxA1 appears to be a potent activator of reactant oxygen species that leads to necrotic cell death in experimental models.¹ VvhA is a protein that facilitates haemolytic activity, cell death via cellular membrane pore formation and assists with liberation of iron from red blood cells.¹⁰ VvpE is an extracellular metalloprotease that causes tissue necrosis, increased vascular permeability and bullous lesions similar to those seen in systemic *Vibrio* infections in experimental models.¹⁰ Experimental animal models without all three toxins (RtxA1, VvpE and VvhA) have been found to be devoid of toxicity, further implicating these toxins in systemic disease.¹¹

V. vulnificus infections should be suspected in patients with liver cirrhosis presenting with sepsis or soft tissue infections with the appropriate temporal association to raw oyster ingestion or seawater exposure.⁴ A high index of suspicion is imperative as empiric treatment with doxycycline is not routinely initiated for sepsis.⁴ *V. vulnificus* is typically susceptible to third-generation cephalosporins, beta-lactam beta-lactamase inhibitors, tetracyclines, fluoroquinolones and carbapenems.¹ The Centre for Disease Control currently recommends dual treatment with doxycycline and a third-generation cephalosporin for 7–14 days in addition to surgical debridement for soft tissue infections.¹ In a review of patients presenting with symptoms of severe soft tissue skin infections and necrotising fasciitis, outcomes including mortality and severity of symptoms were significantly improved with early debridement and fasciotomy within 24 hours of presentation.¹² Surgical debridement is important for severe soft tissue infections and necrotising fasciitis to remove necrotic tissue and improve source control of sepsis.¹ Antimicrobial therapy without debridement is usually insufficient to achieve

local wound therapeutic levels.¹ Extensive skin debridement will sometimes require skin grafting for wound healing.

In sum, *V. vulnificus* infections are associated with a high mortality in patients with chronic liver disease. A high level of clinical suspicion is required to promptly start appropriate empiric antibiotics with doxycycline and a third-generation cephalosporin. Surgical wound debridement for soft tissue infections or necrotising fasciitis should ideally occur within 24 hours of presentation to maximise the chances of survival. All patients with chronic liver disease and haemochromatosis should be instructed to avoid raw oyster ingestion and avoid swimming in seawater with open skin wounds.

Learning points

- *Vibrio vulnificus* infections should be suspected in patients with chronic liver disease presenting with septic shock after raw oyster ingestion or seawater exposure.
- Empiric antibiotics for presumed infection should include a third-generation cephalosporin and doxycycline.
- Prompt surgical debridement of necrotising soft tissue infections within 24 hours appears to improve survival.

Contributors NH authored several drafts of the clinical vignette and obtained patient consent. SS edited the drafts and provided feedback in addition to obtaining clinical images. CSG was the senior author who critically reviewed the drafts and verified our citations serving as the guarantor of content. All authors approve the current draft for submission and resume responsibility for the accuracy and integrity of the manuscript.

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