Purpura fulminans due to Vibrio vulnificus severe infection

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ABSTRACT

Purpura fulminans is a life-threatening disease, characterized by disseminated intravascular coagulation and endovascular thrombosis; can often occur secondary to heterogeneous etiologies, such as sepsis, and to a lesser extent, secondary to sepsis due to halophilic bacteria, such as V. vulnificus, found in marine environments. Patients with specific comorbidities are at the highest risk of worst scenarios, without prompt treatment, infection can rapidly evolve to fatal, with a mortality rate close to 100 %. We present a case of Purpura fulminans due to V. vulnificus septicemia.

Introduction

Purpura fulminans is a life-threatening disease, characterized by disseminated intravascular coagulation and endovascular thrombosis, can often occur secondary to heterogeneous etiologies, such as sepsis, and to a lesser extent, secondary to sepsis due to halophilic bacteria, such as V. vulnificus, found in marine environments. Patients with specific comorbidities are at the highest risk of worst scenarios, without prompt treatment, infection can rapidly evolve to fatal, with a mortality rate close to 100 %. We present a case of Purpura fulminans due to V. vulnificus septicemia.

Case report

52-year-old man, with type 2 diabetes and systemic arterial hypertension; bariatric surgery performed two years ago and history of raw seafoods consumption and skin trauma with an oyster while manipulating it ten days before to hospital admission.

Upon admission, he referred 7 days with throbbing pain and burning legs, exacerbated by walking and improvement with rest and non-steroidal anti-inflammatory analgesics ingestion; erythema and edema appeared later in both legs. During initial assessment, abnormal vital signs, such as, tachycardia, arterial hypotension, and undetectable oxygen saturation were found; physical examination highlighted a localized bilateral and symmetric dermatosis of the lower extremities constituted by edematous purpuric plaques with tense blisters of bloody content, excoriations, areas of necrosis and hyaline exudate (Fig. 1).

Laboratory findings suggested acute kidney injury, septic shock, and disseminated intravascular coagulation.

Doppler ultrasound of pelvic limbs reported edema of superficial tissues from knee to foot, with no evidence of thrombi; abdominopelvic computed tomography reported compatible findings with cellulitis of the left pelvic limb.

The patient rejected surgical treatment, and progressed to multi-organ failure, besides broad-spectrum antibiotics, and vasopressor therapy, and died 48 h after hospital admission.

After-death, V. vulnificus was isolated in blood and wound cultures; changes in relation to Purpura fulminans were described in skin biopsies (Fig. 1).

Discussion

Purpura fulminans (PF) is a life-threatening disease characterized by disseminated intravascular coagulation and endovascular thrombosis resulting in a cutaneous purpura pattern [1].

Clinically, early stages present as well-demarcated erythematous and...
painful macule that progress rapidly to irregular central areas of blue-black hemorrhagic necrosis, typically surrounded by a thin border of erythema that fades into adjacent uninvolved skin. Early lesions may be reversible with prompt therapeutic intervention, but established lesions often progress within 24–48 h to full-thickness skin necrosis or more extensive soft tissue necrosis that may require surgical debridement, fasciotomies, or amputation [1]. Histopathological findings include occlusion of small dermal vessels with microthrombi, capillary dilation and congestion with red cells in early PF. In later stages, an irreversible endothelial ischemic injury with extravasation of blood cells into the dermis and gangrenous necrosis, sometimes with secondary infection, appears. Activation of procoagulant pathways, dysfunction of anticoagulant pathways and endothelial damage characterized this entity [1]. PF requires prompt recognition and treatment, targeting the coagulation system and management of the underlying cause [1,2].

Although, PF may be triggered by several clinical scenarios, frequently occurs as consequence of infection, especially by gram-negative endotoxin-producing bacteria, but can also occur due to gram-positive, anaerobic, and viral infections. Less common cases of PF due to bacteria of genus vibrio have also been reported [1–3].

Vibrio vulnificus is a gram-negative, opportunistic bacillus responsible of wound infections, gastroenteritis, and septicemia. Inhabits saltwater flora and fauna, multiple cases have been reported annually [3,4] in regions with a subtropical climate [5]; however, in recent years significant increases in expansion of the geographic area have been observed in infections caused by this pathogen, probably due to global warming increasing ocean temperature [5,6].

This bacillus is the deadliest foodborne pathogen with a fatality rate greater than 30 %, however, severity of this condition will depend too on host’s comorbidities [7].

Two main routes of entry into the bloodstream have been identified in the development of this infection; ingestion of contaminated raw seafood, mainly oysters, and direct bacterial inoculation of skin wounds by direct contact between open wounds and contaminated seawater, or by skin trauma when fishing, handling, or preparation of seafoods [4,5,7].

Three biotypes of *V. vulnificus* strains are known. Biotype 1 strains are responsible of most infections in humans, while biotype 2 strains (non-pathogenic for humans) are responsible for infections in marine eels. The strains of biotype 3, which cause fewer skin infections in humans, have been limited to people who handle fish [6,7].

*V. vulnificus* has virulence factors that cause direct cellular damage, including cytolsin, toxin A1, and extracellular proteases. In addition, *V. vulnificus* contains immunogenic lipoprotein A, which acts as an adhesin and immunogen to activate intracellular pathways, triggering an inflammatory cascade [6,8,9].

*V. vulnificus* can cause mild infectious diseases in healthy hosts, which can resolve spontaneously without antibiotic treatment; however, in immunocompromised individuals, severity of the disease becomes much worse, with bacteremia being common, with a mortality rate greater than 50 % [10]; fatal cases without prompt treatment who evolves to septic shock, mortality rate is close to 92 % [11,12].

In case of oral ingestion, gastroenteritis may occur in the best-case scenario, meanwhile, wound infection can manifest heterogeneously, from mild symptoms with well-defined erythematous lesions, blisters, and cellulitis to deep infections such as myositis, necrotizing fasciitis, and purpura fulminans [11]. Less common pneumonia, osteomyelitis, ocular infections, meningitis, peritonitis, and endocarditis may occur [12,13].

Septicemia may occur through both: ingestion of the microorganism and its passage into the bloodstream through the ileum or cecum, or as infected wounds and the ascent of the bacillus to the circulation [13], however, of patients with chronic diseases, those with chronic liver disease, have an 80-fold higher risk of developing septicemia due to *V. vulnificus* compared to the rest of people with chronic affections, which place them at the top of the list [12].

Cornerstone in the diagnostic approach, are both clinical presentation and epidemiological background. Growth of *V. vulnificus* in culture samples confirms the diagnosis. Other valuable diagnostic tests are conventional and real-time polymerase chain reactions (PCR), of which

![Fig. 1. Clinical and histopathological findings. a) Purpuric plaques characterized by hemorrhagic bullae, ulceration, necrosis, and diffuse edema on the left pelvic limb. b) and c) Biopsy sections of the patient’s left thigh and left foot dorsum observed by electron microscopy. b) Dermoepidermal infarction with detachment of the superficial layer of the epidermis. c) Purpuric dermatitis associated with nascent thrombi in the deep vascular plexus.](image-url)
real-time PCR is characterized by its high sensitivity and specificity, as well as rapid execution and results, making it useful in patients with atypical manifestations or with recent antibiotic treatment [13,14].

Centers for Disease Control and Prevention (CDC) recommends the combine use of third generation cephalosporins and doxycycline for 7–14 days on the treatment of *V. vulnificus* infections [14]. Patients with deep skin and soft tissue infections will often require urgent surgical debridement or amputation, in addition to promptly establishment of antibiotic therapy [13,14].

**Conclusion**

Sepsis and septic shock produced by *V. vulnificus* have a high fatality rate despite surgical and targeted antimicrobial treatment. In patients with immunosuppressive conditions, especially those with chronic liver disease, mild infections can easily evolve to catastrophic scenarios, since these people, constantly present high levels of transferrin saturation indexes, which favors the growth and reproduction of the microorganism and, with it, its blood dissemination.

*V. vulnificus* infection should be suspected in immunocompromised patients with painful skin lesions and a history of raw shellfish ingestion, handling, or exposure of skin wounds to seawater.

It is extremely important to inform vulnerable population about the importance of the use of protective gloves when handling shellfish for consumption or sale, as well as to avoid intake of raw shellfish, as well as exposition of open wounds to seawater.

**Ethical approval**

This protocol was carried out in strict adherence to current regulations, considering the Declaration of Helsinki, Good Clinical Practices, International Ethical Guidelines for Biomedical Research and Experimentation on Human Beings and the Regulations of the General Health Law on Research for health.

This protocol corresponds to an investigation without risk, since the information collected was carried out using retrospective documentary research techniques and methods (clinical file review) and no intentional intervention or modification was made in the physiological, psychological, and social variables of the individual who participated in the study.

**Consent**

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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All authors contributed equally to this paper.

**CRediT authorship contribution statement**

**Xochipilli Delgado**: Writing - Original draft preparation, Investigation, and Visualization, **Paul Osua**: Investigation, Conceptualization, and Resources, **Edgar Carrillo**: Investigation, Writing - review, and editing, **Gabriel Alejandro Núñez**: Investigation and Resources, **Suria Loza**: Investigation and Supervision, **Luis Guillermo Castellanos**: Investigation and Resources.

**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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