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RESEARCH ARTICLE

Septicaemia due to *Vibrio vulnificus*: A tropical infection not to be taken lightly

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ABSTRACT

Vibrio vulnificus is a halophilic gram-negative bacillus that can cause fulminant septicaemia in immunocompromised patients. A 67-year-old man who was immunosuppressed as a result of cytotoxic chemotherapy presented with a brief history of fever, lethargy, myalgia, and reduced oral intake. He had recently travelled to the beach to consume seafood. His blood pressure was 81/47 mm Hg, necessitating fluid resuscitation followed by inotropic support and admission to the intensive care unit. His blood culture was positive for curved gram-negative bacilli. The isolate was oxidase-positive and produced an acid butt with an alkaline slant in triple sugar iron agar. Matrix-assisted laser desorption ionization-time of flight mass spectrometry conclusively identified the isolate as *V. vulnificus*. Intravenous ceftazidime plus ciprofloxacin were administered, and by the fifth day of admission, he was successfully transferred out to the general ward. In total, the patient completed a 14-day course of antibiotic therapy.

Keywords: Ceftazidime; ciprofloxacin; seafood; septicaemia; septic shock; *Vibrio vulnificus*.

INTRODUCTION

Vibrio vulnificus was first isolated by the United States Centres for Disease Control and Prevention (CDC) in 1964, initially as a mistakenly identified virulent strain of *V. parahaemolyticus* (Strom & Paranjpye, 2000). It was only recognised as a distinct *Vibrio* species half a decade ago, after it was noted to possess characteristics unique from other *Vibrio* species. However, like *V. cholerae* (arguably the best-known member of the Vibrionaceae family), *V. vunificus* is also a halophile and can be isolated from marine and brackish environments, especially where the water temperature exceeds 20°C (Liu *et al*., 2006). The bacterium would therefore be of particular significance in tropical countries with miles and miles of coastline such as Malaysia. While the other members of its family (i.e., *V. cholera* and *V. parahaemolyticus*) cause mostly acute gastroenteritis, *V. vulnificus* can cause, in addition to gastroenteritis, more serious infections such as skin and soft tissue infections or even primary septicaemia (Yun & Kim, 2018). We report a case of *V. vulnificus* septicaemia in an immunocompromised man following the ingestion of seafood.

CASE REPORT

We present the case of a 67-year-old man who arrived at the emergency department of Hospital Canselor Tuanku Muhriz with a brief history of fever, lethargy, myalgia, and reduced oral intake. He was diagnosed with nasopharyngeal carcinoma three years ago and had undergone surgery and adjuvant chemotherapy. Additionally, he was also diagnosed with pancreatic carcinoma (pT3N0M0) recently and had a Whipple's procedure six months prior. He was started on cisplatin and gemcitabine chemotherapy two months prior to admission – his fourth cycle was administered just five days before admission.

Upon presentation, the patient had a blood pressure of 81/47 mm Hg, a heart rate of 109 beats/minute, and a temperature of 39.0°C. He had recently travelled to the beach to eat seafood just three days prior to admission. Resuscitation with 2 L of crystalloid fluids transiently improved his haemodynamics. However, he experienced a sudden episode of loss of consciousness accompanied by bradycardia and hypotension unresponsive to intravenous atropine. Consequently, he was intubated for airway protection. Alas, following intubation, his blood pressure dropped further, necessitating an increase in inotropic support. He also developed transient ventricular tachycardia, which spontaneously resolved, alongside acute kidney injury and transaminitis following this event. Imaging studies showed no remarkable findings on chest X-ray. His biochemical parameters showed elevated C-reactive protein and serum creatinine levels, increasing from 6.6 to 24.24 mg/dL and 91.6 to 112.5 µmol/L, respectively.

Intravenous piperacillin-tazobactam was initiated, but as his haemodynamics deteriorated, it was escalated to intravenous meropenem. Our provisional diagnosis was now septic shock in an immunocompromised host. After discussions with the oncology and medical teams, it was decided to transfer the patient to the intensive care unit for close monitoring. On the fourth day of admission, his blood culture was positive for curved gram-negative bacilli

(Figure 1). The bacterium grew as haemolytic mucoid grey colonies on blood agar. It was also oxidase-positive, motile in semisolid agar and produced an acid butt with an alkaline slant in triple sugar iron agar (Figure 2). The isolate's identity was confirmed by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) (Bruker-Daltonics, Germany), which matched its mass spectral pattern with that of *Vibrio vulnificus* DSM 10143T DSM with a score value of 2.20. Antibiotic susceptibility testing was performed using the disk diffusion method on Mueller-Hinton agar and interpreted according to breakpoints provided by the Clinical and Laboratory Standards Institute (CLSI) in its M45 document (CLSI, 2015). The isolate was susceptible to ceftazidime, cefotaxime, tetracycline and ciprofloxacin (i.e., all four antimicrobial agents recommended for primary testing by the CLSI).

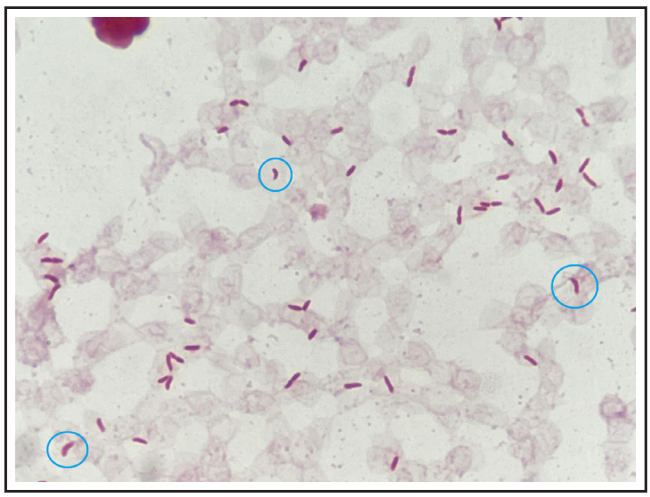

Figure 1. A Gram stain (1000x magnification) of the positive blood culture revealed curved gram-negative bacilli (circled).

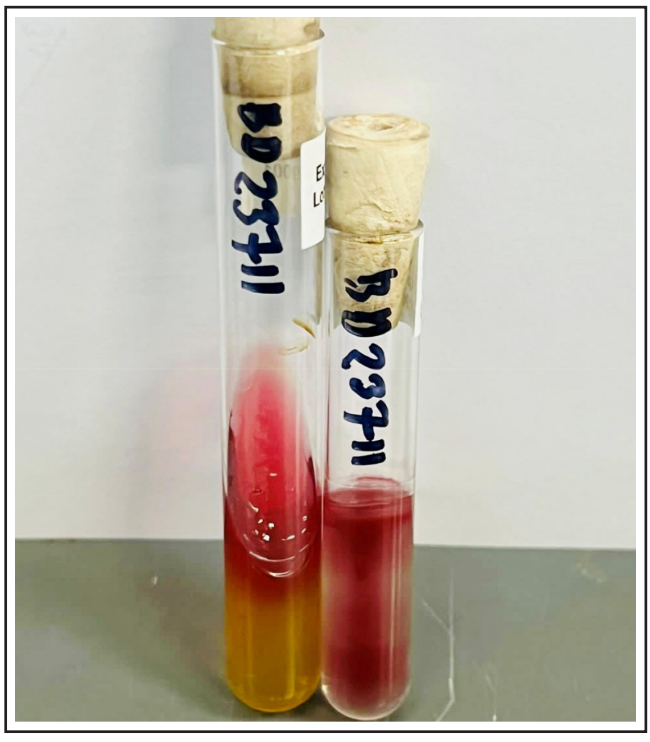

Figure 2. The bacterium produced an acid butt with an alkaline slant in triple sugar iron agar (left tube) and was motile in semisolid agar (right tube).

Following the release of the blood culture report, the patient's antibiotic regimen was changed to intravenous ceftazidime and ciprofloxacin. His clinical condition began to improve, and he was successfully weaned off mechanical ventilation and inotropic support. On the fifth day of admission, he was finally extubated and transferred out from the intensive care unit to the general ward. In total, the patient completed a 14-day course of antibiotic treatment.

DISCUSSION

In the diagnostic laboratory, the finding of an acid butt in triple sugar iron agar customarily suggests the presence of a fermentative gram-negative bacilli (GNB) from the Enterobacteriaceae family (e.g. *Escherichia coli*). These bacteria ferment either glucose alone or glucose plus lactose and/or sucrose. On the other hand, oxidase-positivity typically suggests the presence of a non-fermentative GNB (such as *Pseudomonas aeruginosa*). Thus, a fermentative GNB which is also oxidase-positive is a relatively uncommon occurrence and narrows-down the identification to the *Vibrio*, *Aeromonas* and *Plesiomonas* genera (Bravo *et al*., 1993). The microscopic visualisation of curved (or comma-shaped) GNB would be the "smoking gun" implicating *Vibrio* spp. as both *Aeromonas* spp. and *Plesiomonas* spp. are relatively straight GNB (Greiner *et al*., 2021). Although we relied on MALDI-TOF MS for conclusive identification, commercial biochemical identification kits such as API 20 NE or API 20 E (bioMérieux) and automated identification systems such as VITEK 2 (bioMérieux) may be utilised as well (Liu *et al*., 2006; Zetti *et al*., 2009; Narendrakumar *et al*., 2021).

V. vulnificus septicaemia cases from Malaysia have been rarely reported in the medical literature but include a fatal case by Zetti *et al*. (2009) and a non-fatal case by Zainuddin *et al.* (2023) – however, only the latter had a history of consuming raw seafood. Being halophilic, *V. vulnificus* has been found in a wide variety of seafood, such as oysters, mussels, cockles, crabs, squid and shrimp (M Kurdi Al-Dulaimi *et al*., 2019). A study conducted by Paydar & Thong (2013) revealed that in general, 13% of seafood in Malaysia harboured *V. vulnificus*. However, among the various seafood, oysters appear to have an exceptionally high likelihood of harbouring *V. vulnificus*, with freshly harvested oysters from India and the Gulf of Mexico recording jaw-dropping contamination rates of up to 75% and 100%, respectively (Heng *et al*., 2017). The bacterium can be transmitted to humans either by handling or consuming contaminated seafood. We hypothesise that our patient contracted the infection during his trip to the beach, where seafood was consumed. Other known risk factors for *V. vulnificus* infection are age above 40 years, male gender (six times more likely to be infected than females), diabetes mellitus and chronic liver disease (such as cirrhosis) (Li *et al*., 2019; Strom & Paranjpye, 2000). While our patient was not known to have either diabetes mellitus or chronic liver disease, he was a male in his 60s. Additionally, receiving cytotoxic chemotherapy would have heightened his risk of infection, as nearly all patients with *V. vulnificus* sepsis are immunocompromised (Liu *et al*., 2006).

The septicaemia caused by *V. vulnificus* is typically primary, without any definite nidus of infection. The organism's presumed portal of entry into the bloodstream is either the ileum or caecum (Heng *et al*., 2017). Typically, severe *V. vulnificus* septicaemia in an immunocompromised patient presents with an abrupt onset of fever and chills within 7 days of ingesting tainted seafood (Strom & Paranjpye, 2000; Liu *et al*., 2006). Within 24 hours, cutaneous lesions such as cellulitis, bullae or ecchymoses may start to appear on the patient's extremities as a form of metastatic infection (Heng *et al*., 2017; Yun & Kim, 2018). These lesions may evolve to become necrotic (e.g. necrotising fasciitis), necessitating surgical debridement or even amputation (Strom & Paranjpye, 2000). Septic shock, with a systolic blood pressure of less than 90 mm Hg, has been reported in up to 60% of patients (Strom & Paranjpye, 2000). The development of hypotension following admission heralds a poor

prognosis, as the risk of death in these patients is doubled compared to normotensive patients (Heng *et al*., 2017). While our patient was fortunate to not develop cutaneous lesions, he had septic shock and required inotropic support.

The importance of early antibiotic administration in a case of *V. vulnificus* septicaemia cannot be overemphasised. Even with timely administration (i.e. within 24 hours of admission), the mortality rate is 33% – this rate increases to 63% and 100% when antibiotic administration is put off by 48 and 72 hours, respectively (Klontz *et al*., 1988). Although *V. vulnificus* is susceptible to many antibiotics, it is resistant to colistin, an antibiotic typically employed to manage infections caused by multidrug-resistant GNB (Yun & Kim, 2018). The combination of a third generation cephalosporin (TGC) and ciprofloxacin has been shown to result in synergistic in vitro bactericidal activity against *V. vulnificus* (Kim *et al*., 2019). However, the CDC recommends a TGC plus doxycycline as the first-line treatment of *V. vulnificus* infections (Yun & Kim, 2018). The rationale of selecting doxycycline (a tetracycline analogue) is the relatively higher tissue penetration of tetracyclines in the setting of poorly perfused necrotic cutaneous lesions (Liu *et al*., 2006). Nonetheless, when these two regimens were compared in a mouse model of foodborne *V. vulnificus* septicaemia, the survival rate of the ceftriaxone (a TGC) plus ciprofloxacin group was 100%, while that of the ceftriaxone plus doxycycline group was 91% (Trinh *et al*., 2017). Thus, since our patient did not have cutaneous lesions, we administered a TGC (in the form of ceftazidime) plus ciprofloxacin.

CONCLUSION

Time is of the essence when dealing with *V. vulnificus* septicaemia. A history of ingesting seafood (particularly if raw or undercooked) in an ill immunocompromised patient should prompt close monitoring of vital signs in anticipation of septic shock. The finding of curved GNB in a clinical sample is a red flag that should be communicated immediately to the attending physician to facilitate the administration of life-saving antibiotics. While *V. vulnificus* is not habitually regarded as a multidrug-resistant organism, the combination of a TGC with either a fluoroquinolone or a tetracycline drug should be administered for synergistic action.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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