Non-O1, non-O139 *Vibrio cholerae* bacteraemia in a cirrhotic patient

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*Vibrio cholerae* serogroups O1 or O139 are the aetiological agents of cholera. The pathogenicity of non-O1, non-O139 *V. cholerae* is less well known. These worldwide bacteria are responsible for gastrointestinal infections or, more rarely, bacteraemia in patients with an underlying disease, leading to life-threatening complications. We report a case of non-O1, non-O139 *V. cholerae* bacteraemia due to a haemolytic strain in a cirrhotic patient. Early antibiotic therapy allowed a good outcome. The aim of this case report is to underline the virulence of non-choleragenic *Vibrio* strains, possibly linked to haemolysin production, and the potential danger of consuming undercooked seafood or exposing wounds to sea water in cirrhotic patients.

### Introduction

Vibrios are ubiquitous bacteria from aquatic environments. Strains of *Vibrio cholerae* that agglutinate with antisera O1 or O139 are the aetiological agents of cholera, a toxin-mediated acute diarrhoeal disease, with extremely rare bacteraemia in immunocompromised hosts. Non-O1 and non-O139 *V. cholerae* strains also cause diarrhoeal illness mediated by toxins distinct from the cholera toxin (CT) but bacteraemia is more frequent. However, the pathogenicity of those strains is less well known. This report concerns a cirrhotic patient with a non-O1, non-O-139 *V. cholerae* bacteraemia probably due to the consumption of undercooked seafood.

### Case report

A 63-year-old man managed for chronic liver disease, secondary to previous alcohol abuse, was referred for liver pre-transplant evaluation (Child–Pugh class C cirrhosis). At admission to the Gastroenterology Department at the University Hospital of Brest (Brest, France), the patient had signs of systemic infection (chills, fever at 39 °C), jaundice, ascites and encephalopathy without gastrointestinal symptoms. Laboratory tests revealed anaemia (8.8 g haemoglobin dl⁻¹), an increased white blood cells count (16.5 × 10⁹ cells l⁻¹), increased prothrombin time (29.5 s) and cholestasis. Hepatitis B and C serologies, and bacterial ascitic fluid cultures were negative. Stool samples were not collected in the absence of diarrhoea. Two sets of blood cultures (BacTalert; bioMérieux) yielded, after 24 h incubation, a curved Gram-negative and highly motile bacillus. Colonies grew on 5 % sheep blood agar with a marked zone of haemolysis and a greenish hue imparted to them. The isolate was rapidly oxidase-positive, susceptible to the vibriostatic agent O129 (Bio-Rad) and identified as non-O1 *V. cholerae* with the 32GN API system (bioMérieux) and the lack of agglutination with O1-specific antisera (Bio-Rad). Final identification of the non-O1, non-O139 and non-toxigenic *V. cholerae* strain was achieved by the French National Reference Center for Vibrios and Cholera (FNRC-VC), Institut Pasteur, Paris, France. The presence of an El Tor-like haemolysin was confirmed by PCR amplification of the *hlyA* gene (Rivera et al., 2001). The isolate was assessed by the Mueller–Hinton agar disc diffusion method to be susceptible to amoxicillin, cefotaxime, aminoglycosides, fluoroquinolones, doxycycline and co-trimoxazole.

Questioning of the patient for further information revealed both exposure to seawater and undercooked shellfish consumption 48 h prior to admission. Empiric parenteral treatment with ceftriaxone and metronidazole for 5 days, then with oral ofloxacin for a further 25 days, was successful.
Discussion

The genus *Vibrio* includes more than 70 species of bacteria living in a wide variety of water sources (seawater, warm coastal waters), in a free state or in close relationship with phytoplankton or zooplankton. Because water temperature and salinity govern their capacity for survival, their incidence in water increases during the summer months, especially in filter-feeding shellfish (Thompson et al., 2004).

*Vibrio* infections include four types of syndromes (gastroenteritis varying from mild to severe, bacteraemia, soft-tissue infections, and otitis). Patient medical history often reveals recent ingestion of raw or undercooked seafood or exposure of traumatized skin to contaminated water. *V. cholerae* strains not agglutinating with O1 or O139 antisera are referred to as non-O1 and non-O139, but they are morphologically and biochemically indistinguishable. Only O1 and O139 serogroups of *V. cholerae* are responsible for the epidemic or pandemic cholera by secreting CT, a non-invasive enterotoxin. Because of the ability of the CT to suppress induction of inflammation during infection (Fullner et al., 2002), bacteraemia is rare. *V. cholerae* non-O1 and non-O139 may cause sporadic cases of diarrhoeal disease but may also lead to invasive extraintestinal illness and bacteraemia, especially in patients with underlying disorders. Although the virulence factors that allow non-O1 and non-O139 strains to invade the bloodstream are not well elucidated, it is speculated that the haemolysin produced by certain strains, such as the strain isolated in our cirrhotic patient, could contribute to invasive disease in immunocompromised hosts, due to its haemolytic property and to its ability to induce cell vacuolization (Restrepo et al., 2006). The presence and expression of *hlyA* genes has been reported in strains isolated from patients suffering acute diarrhoea without inducing extraintestinal effects (Ottaviani et al., 2009). The role of cytotoxin in conjunction with haemolysin, encapsulation and other potential virulence factors has been postulated in the enteroinvasiveness of some *Vibrio* isolates (Namdari et al., 2000).

*V. cholerae* non-O1, non-O139 bacteraemia is rare but potentially fatal. A few cases have been reported in the USA (Hlady & Klontz, 1996; Kontoyiannis et al., 1995; Namdari et al., 2000; Safrin et al., 1988; Patel et al., 2009), Taiwan (Ko et al., 1998; Lin et al., 1996) and Europe (Farmachidi et al., 2003; Halabi et al., 1997). In France, 16 cases of bacteraemia associated with 2 deaths were recorded among the 39 non-O1, non-O139 *V. cholerae* infections confirmed by the FNRC-VC from 1995 to 2003 (FNRC-VC data). The mortality rate depended on the studied cohort, and varied from 24 % (Lin et al., 1996) to 44 % (Hlady & Klontz, 1996) and 61.5 % (Safrin et al., 1988). The majority of reported cases occurred during the hot season in patients suffering from immunocompromising conditions such as liver cirrhosis (Hlady & Klontz, 1996; Ko et al., 1998; Halabi et al., 1997) or haematological malignancies (Safrin et al., 1988; Anderson et al., 2004; Dhar et al., 2004; Deris et al., 2009) associated with seafood consumption (Ko et al., 1998). Our patient, who lived near the Atlantic coast, had consumed shrimps and had dipped his legs in seawater 2 days prior to his admission to hospital. Because the skin of his legs was normal, a food-borne mode of contamination seemed most likely. Furthermore, a therapeutic reduction in stomach acidity can increase risk of colonization by acid-sensitive enteric pathogens like *V. cholerae*. Our patient had received proton pump inhibitor therapy for a duodenal ulcer.

Cirrhotic patients are at particular risk of non-O1, non-O139 bacteraemia. Among the 28 blood culture isolates of non-O1 *V. cholerae* identified by Lin et al. (1996) between 1989 and 1994, 75 % came from cirrhotic patients, with 6 classified as Child–Pugh class B and 15 as Child–Pugh class C. Contamination modes were seafood ingestion and direct contact with seawater. Bacteraemic episodes usually occurred between March and September. Our patient, identified as Child–Pugh class C, had become infected in August.

Non-O1, non-O139 *V. cholerae* is usually susceptible to most antimicrobial agents. Because of their rare occurrence, antibiotic guidelines for the treatment of these bacteraemias are not well established. While tetracyclines and co-trimoxazole are traditionally used for the treatment of cholera, non-O1 and non-O139 *V. cholerae* bacteraemia have been successfully treated with a parenteral treatment with third-generation cephalosporin, followed by oral fluoroquinolone (Ko et al., 1998; Anderson et al., 2004). Although the treatment duration for these bacteraemias has not been clearly defined, most of the patients received antibiotic therapy for at least 1 month (Anderson et al., 2004). The good outcome in our patient was probably due to the prompt start of antibiotics and early diagnosis of infection.

In conclusion, non-O1, non-O139 *V. cholerae* bacteraemia is a life-threatening infection that occurs mostly in immunocompromised and cirrhotic patients. Haemolysin could be one of the virulence factors that allows the strain to invade the bloodstream, and further studies to establish the mechanisms of virulence of these pathogens would be of interest. Such patients should be warned about the potential dangers of consuming raw or undercooked seafood, and advised to avoid the exposure of wounds to seawater.

References


