Case Report

Non-toxigenic Vibrio cholerae bacteraemia: case report and review of the literature

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Introduction

Vibrios are oxidase-positive Gram-negative bacteria commonly found in aquatic environments. Vibrio cholerae (toxigenic strains) remain a serious public health problem, responsible for devastating epidemics and pandemics worldwide. Non-toxigenic strains of V. cholerae, i.e. non-O1, non-O139, are also important causes of gastrointestinal infections but are usually associated with sporadic cases or small-scale outbreaks (Rozemeijer et al., 2009). Infections due to these non-toxigenic strains remain rare in Europe and are very infrequent in the UK, where they are usually associated with foreign travel. We report a case of non-O1, non-O139 V. cholerae bacteraemia and gastroenteritis in a patient with an underlying malignancy. To the authors’ knowledge this is the first reported, confirmed, non-travel-related V. cholerae bacteraemia in the UK.

Case report

A 74-year-old man with a past medical history of pancreatitis and bronchial carcinoma was admitted to the medical receiving wards with a 72 h history of severe watery diarrhoea with no blood and no vomiting. He had also complained in the days previously of dizziness and epigastric pain. On examination, he appeared lethargic. Examination of his cardiovascular and respiratory systems was unremarkable. His abdomen was soft with mild epigastric tenderness. C-reactive protein on admission was 66 mg l\(^{-1}\) (reference range <10 mg l\(^{-1}\)), white cell count was 13.6 \(\times\) 10\(^9\) l\(^{-1}\) (reference range 4–11 \(\times\) 10\(^9\) l\(^{-1}\)) and urea and electrolytes were normal. Liver function tests were within reference ranges aside from a gamma glutamyl-transpeptidase of 122 U l\(^{-1}\) (reference range <70 U l\(^{-1}\)). He was initially treated with intravenous (i.v.) co-amoxiclav 1.2 g three times daily, which was changed to i.v. ceftriaxone 2 g once daily on identification of the organism. He also required i.v. fluids with potassium supplementation. He recovered well and was discharged home on day five.

A public health investigation was undertaken. There was no history of foreign travel or sea or freshwater exposure. The patient did, however, consume a large amount of prawns, and to a lesser extent fish and other shellfish, on an almost daily basis. These were bought frozen from various retailers, defrosted at home and consumed without further heating, including within the incubation period (6–48 h). The patient also ate at a restaurant during this time. At the restaurant, the patient ate cooked frozen prawns that had been subject to further heating before eating (in a casserole). No one else ate the prawns he prepared at home, and there were no other cases or reports of illness (staff or customers) associated with the restaurant. National organizations (Health Protection Scotland and the Foods Standards Agency in Scotland) were informed.

Gram stain of the positive blood culture revealed classical curved Gram-negative rods. After 24 h incubation hae-molytic colonies grew on blood agar (Oxoid) and blue colonies were present on cysteine-lactose-electrolyte deficient agar (Oxoid), indicating the bacterium did not ferment lactose. Subculture onto thiosulfate-citrate-bile salts-sucrose agar (TCBS, Oxoid) revealed oxidase-positive yellow colonies. The organism was identified as V. cholerae by VITEK 2, VITEK MS and API 20E (bioMérieux). Although the patient had a history of severe watery diarrhoea, V. cholerae was not isolated from his stool specimen. Diagnostic microbiology laboratory protocols

Abbreviations: GBRU, Gastrointestinal Bacteria Reference Unit; i.v., intravenous; TCBS, thiosulfate–citrate–bile salts–sucrose agar.
recommend testing for *V. cholerae* only in patients who have recently travelled to regions where cholera is endemic.

The blood culture isolate was confirmed by the Gastrointestinal Bacteria Reference Unit (GBRU) at HPA Colindale as non-toxigenic *V. cholerae* non-O1, non-O139 using both traditional biochemistry and serology (Garrity, 2005) and a phenotypic microarray approach on the Omnilog platform (Biolog). Molecular tests included PCR for the ToxR regulatory gene and the ctxA cholera toxin gene. The ToxR gene in *V. cholerae* is well conserved among the species so is an ideal target for identification of *V. cholerae* to species level, whereas the ctxA gene is a marker for toxigenic strains (Ghosh *et al.*, 1997). The organism was susceptible to ceftriaxone, ciprofloxacin and azithromycin.

Environmental health officers obtained a sample of defrosted prawns, prepared around the time of admission, from his fridge. These were sent to Glasgow Scientific Services for microbiological culture (as above), which was negative. However, within the incubation period he likely consumed prawns from other bags that were not available for testing.

**Discussion**

Vibrio infections in humans arise as a result of exposure to contaminated water or ingestion of contaminated seafood. Filter feeding shellfish such as prawns and mussels are the most frequently contaminated seafoods (Petsaris *et al.*, 2010; Ottaviani *et al.*, 2009). Studies in Italy have demonstrated an increased incidence of seafood and water contamination with vibrios during summer months (Ottaviani *et al.*, 2009). Increased water temperatures and saline content favour proliferation of these organisms (Petsaris *et al.*, 2010).

In the UK between 2004 and 2011, 403 isolates of *V. cholerae* non-O1, non-O139 were submitted to the GBRU by local diagnostic microbiology laboratories in England and Wales, averaging 49 isolates per year. Of these 403, 375 were from faeces, two were cultured from a wound, one was cultured from an ear swab and three were isolated from blood cultures. No source was stated for 22 isolates. Of the three bacteraemia cases, two reported recent travel to India and for the third case no travel history information was available. All three patients were male and aged between 50 and 62 years old. Recent travel abroad was reported in 375 (93 %) of the 403 cases; no travel histories were available for the remaining 28 isolates. Between 2002 and 2012 the number of samples referred to the GBRU for confirmation of *V. cholerae* has remained consistent with no recent increase.

In the USA, non-O1, non-O139 serogroups of *V. cholerae* are the fourth most common cause of vibriosis (Newton *et al.*, 2012). Surveillance from the US indicates that vibriosis is on the increase and warming of costal waters has been postulated as a reason for this (Newton *et al.*, 2012). In Europe, non-toxigenic strains of *V. cholerae* have been found in aquatic environments, such as the Mediterranean Sea. A study in Italy demonstrated that 3.4 % of acute diarrhoeal cases were secondary to infection with non-O1, non-O139 strains of *V. cholerae* (Ottaviani *et al.*, 2009). Non-toxigenic strains have also been found in lakes in Poland and resulted in two bacteraemias in different parts of the country during the summer months of 2006 (Stypulkowska-Misiurewicz *et al.*, 2006). Also in 2006, three infections were reported in Finland, and subsequently Baltic Sea water, which all the patients had contact with, was found to be contaminated with vibrios (Lukinmaa *et al.*, 2006) Overall, in Europe infections due to non-O1, non-O139 *V. cholerae* remain rare.

Non-toxigenic strains of *V. cholerae* have been reported to cause gastrointestinal infection and extraintestinal manifestations such as bacteraemia, wound infections, external ear and neurological infections (Kadkhoda *et al.*, 2012). A well-established risk factor for non-O1, non-O139 *V. cholerae* bacteraemia is the presence of underlying liver disease. Ko *et al.* (1998) found a predominance of non-O1, non-O139 infections in patients with underlying liver cirrhosis in Taiwan over an 8 year period. Why this patient group are at increased risk of bacteraemia is unclear but may relate to elevated serum iron levels or impaired hepatic filtration (Halabi *et al.*, 1997). Case fatality rates in this particular study for patients with bacteraemia and underlying liver cirrhosis were high at 47 %. Patients with underlying malignancy or immunosuppression are also at increased risk of infection with non-toxigenic *V. cholerae* and there have been sporadic cases of bacteraemia among this group of patients reported from Europe (Petsaris *et al.*, 2010; Stypulkowska-Misiurewicz *et al.*, 2006; Halabi *et al.*, 1997).

The majority of reported bacteraemic patients have had a history of seafood consumption, sea or fresh water exposure, or travel. Our patient gave a history of consumption of large amounts of seafood. The source and processing of seafood in the UK can originate from either local or tropical waters. Sampling of remaining prawns did not detect the organism; however, these may not have been from the same packet as those consumed during the incubation period.

While the exact nature of the exposure in our patient remains unknown, it is possible that the prawns consumed during the incubation period may have been contaminated with a small amount of bacteria that remained post-cooking (prior to freezing) at source, or in the water mixed with them. It is postulated that this might have been sufficient to cause infection in an immunocompromised individual, particularly if the prawns had been consumed sometime after defrosting.

Little has been established in relation to virulence factors in non-O1, non-O139 *V. cholerae*. Haemolysin has been proposed to be of importance in blood-stream invasion (Petsaris *et al.*, 2010). In addition, cytotoxin production
may also play a role (Ottaviani et al., 2009). Some cases of bacteraemia have occurred in patients receiving proton pump inhibitors and it is possible that reduced gastric acid may be a predisposing factor (Petsaris et al., 2010). Our patient was not on any medication.

There is no consensus on treatment choice or duration for non-O1, non-O139 V. cholerae infections. Treatment of self-limiting gastrointestinal infection is usually not required. In patients who require treatment tetracyclines are effective. Agents that have been used successfully for non-O1, non-O139 bacteraemia include extended spectrum cephalosporins and fluoroquinolones (Ko et al., 1998). Our patient responded well to therapy with i.v. ceftriaxone.

As laboratories move increasingly towards automation the ability to confirm the identity of more unusual results may be lost. In this particular case we had to request TCBS plates from a neighbouring laboratory. Furthermore, we were unable to process the stool samples from the patient as we no longer stock alkaline peptone water.

With increased globalization and climate change having an impact on water temperatures, it is likely that nontoxigenic strains of V cholerae will be detected more frequently as the cause of gastroenteritis in patients with or without a travel history. Routine diagnostic laboratories should therefore ensure they have the capability to detect such isolates.

References


