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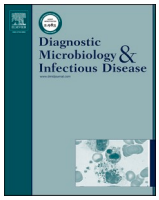

Vibrio cholerae bacteraemia: A case report on an unusual presentation

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ABSTRACT

Infections by non-O1/non-O139 serogroups of *Vibrio cholerae* (NOVC) are increasing worldwide. Infected patients usually display self-limiting diarrhoea or external ear and wound infections. We present a rare case of bacteraemia secondary to NOVC infection. A 39-year-old male presented with acute onset of dyspnoea, chest pain, vomiting, diarrhoea and chronic bipedal oedema. He was hypoxic, acidotic, tachypnoeic, displayed tachycardia and an altered level of consciousness. The patient was assessed to be in congestive cardiac failure with acute gastroenteritis and hypoglycaemia, and was started on empiric co–amoxiclav. The blood culture flagged positive with *Vibrio cholerae* which was toxin negative and typed as NOVC. Unfortunately, the patient deteriorated in the emergency department and demised despite resuscitation efforts. This case demonstrates the possible severity of NOVC bacteraemia and its associated mortality, highlights the need for identification of potential risk factors and emphasizes the importance of sending appropriately collected samples for laboratory testing.

1. Background

Cholera, an acute diarrhoeal illness, has been known since days of yore with Sanskrit texts describing typical cholera symptoms as early as 400 B.C. [1,2] *Vibrio cholerae*, the bacterium causing cholera, belongs to the *Vibrionaceae* family. It is a facultative anaerobic, halophilic, curved gram-negative bacterium that is naturally found in aquatic environments. [3] It can spread directly from person-to-person or indirectly from contaminated water or food.[4]

There are over 200 serotypes of *V. cholerae* differentiated by the major surface O-antigen. [5] Serogroups O1 and O139 are typical choleragenic strains. They produce the cholera toxin which results in secretory diarrhoea characteristic of the disease and accountable for epidemic cholera.[3] Bacteraemia caused by choleragenic strains is rare, likely due to the suppression of the inflammatory response by the cholera toxin. Non-choleragenic vibrios include non-O1/non-O139 serogroups of *V. cholerae* (NOVC) and other *Vibrio* species such as *V. vulnificus* and *V. parahaemolyticus*.[5]

NOVC is postulated to be increasing worldwide due to environmental and climate change.[5,6] Most do not produce the cholera toxin itself and thus do not have epidemic potential, making them less of a public health concern than O1 and 0139 *V. cholerae*.[4,6] They may exist as colonizers of the gastrointestinal tract and the majority of NOVC cases present with self-limiting diarrhoea, external ear and wound infections. Although infrequent, they could cause noteworthy human infections of varying severity. [4,5] We present an unusual case of bacteraemia caused by NOVC.

2. Case presentation

A 39-year-old male patient was referred from a local clinic to the Emergency Department of a regional hospital with a two-day history of difficulty in breathing, chest pain on exertion, diarrhoea and vomiting. The patient was a truck driver and had travelled from a coastal town in South Africa. He had no known co-morbid medical or surgical conditions but did report a two-month history of swollen legs.

None of his family members had similar symptoms.

On initial assessment, he was tachypnoeic with a respiratory rate of 28 breaths per minute, had an oxygen saturation of 83% on O_2 via face mask, pulse rate of 105 beats per minute, temperature of 36 degrees

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Celsius and blood pressure of 126/92 mm Hg. He had bilateral pedal oedema, generalised respiratory crackles and a GCS of 14/15. His heart sounds and abdomen were normal with no hepatosplenomegaly.

Blood gas analysis revealed a decreased pH of 7.078, pO_2 of 29.8 mmHg, sodium of 130mmol/L glucose of 0.2mmol/L and an elevated lactate of 12mmol/L.

A preliminary assessment of congestive cardiac failure, acute gastroenteritis and hypoglycaemia was made and 50ml of 50% dextrose water was administered. A complete blood count, liver and renal function tests and blood cultures were collected. The patient was booked for an echocardiogram and was empirically administered 1.2g co-amoxiclav intravenously. Stool for microscopy, culture and susceptibility testing was not requested.

2.1. Investigations

The complete blood count revealed a normal white cell count (8.22×10^{9}/L), anaemia (haemoglobin 10.9 g/dL), reduced haematocrit (0.328 L/L) and thrombocytopenia (platelets 37×10^{9}/L). The liver function tests were deranged with a hypoalbuminemia (12 g/L), and elevated total and conjugated bilirubin (69 umol/L and 44 umol/L respectively). The liver enzymes were elevated (alanine transaminase 88 U/L; aspartate transaminase 256 U/L; gamma-glutamyl transferase 138 U/L). Sodium (130 mmol/L), chloride (97mmol/L) and bicarbonate (11mmol/L) were low. The anion gap (27 mmol/L), serum urea (8.9 mmol/L) and creatinine (331 umol/L) were elevated. C-Reactive protein was elevated at 105 mg/L.

Of the two blood culture bottles that were sent to the laboratory, the anaerobic bottle flagged positive within two hours of incubation in the BacTAlert (BioMérieux®). Gram stain revealed curved Gram-negative bacilli. Following overnight incubation, growth was seen on the 5% blood, chocolate, and MacConkey agars. The isolate was oxidase and rapid indole positive, and was identified on Vitek®2 as *Vibrio cholerae* (96% probability).

The National Institute of Communicable diseases (NICD) and Infection Prevention & Control (IPC) Units were notified. Serotyping performed by the NICD revealed non-O1/non-O139 *Vibrio cholera*e. PCR was positive for *Vibrio cholerae* but negative for cholera toxin.

Contact tracing was performed by the epidemiologists and IPC teams whilst awaiting serotyping results. It revealed that six people were in contact with the patient since the onset of diarrhoea.

None of the contacts reported diarrhoea and screening swabs performed on all contacts were negative for *Vibrio cholerae*.

2.2. Outcome

The patient's clinical condition deteriorated whilst still at ED. Despite timely initiation of CPR, he became unresponsive and subsequently demised.

3. Discussion

Non-O1/non-O139 *V. cholerae* has been implicated as a causative agent of intestinal and extra-intestinal illnesses. While the former is more common and often self-limiting, we present a case of extra-intestinal NOVC infection in a patient who travelled from a coastal area in South Africa. Our patient presented with acute gastroenteritis with previously undiagnosed and untreated congestive cardiac failure.

As of July 2024, 14 countries in the WHO African region have been affected by the 2024 cholera outbreak, including South Africa. While most cases in South Africa are imported from other African countries, occasional indigenous cases have been reported.[7,8] Most of the data available for vibriosis are regarding toxigenic *V. cholerae*. NOVC is rarely reported since the infections are usually self-limiting and of minimal public health significance. As per a 2015 review, only 2 cases were reported from Africa. [5]

Despite several patients not having any obvious exposure, seawater and inadequately cooked seafood have been described as the most likely sources of NOVC, particularly in cases of bacteraemia [5,9,10]. In addition, reduced gastric acid due to the use of proton pump inhibitors, can predispose to NOVC infections.[11] In our patient, history of the aforementioned exposures is not available.

NOVC bacteraemia has been most commonly described among males aged 55 years and older. The best described risk factor for NOVC bacteraemia is liver cirrhosis. Others include alcoholism, liver transplantation, diabetes, haematological malignancies, nephropathy, malnutrition and immunocompromising conditions including HIV, corticosteroid therapy, chemotherapy, splenectomy, intravenous drug abuse and systemic lupus. [5,12] Although not listed as a risk factor for NOVC bacteraemia, undiagnosed and untreated cardiac failure can be considered an immunocompromising condition, and is associated with increased susceptibility to infections. Infection, in general, is a common reason for hospitalisation among patients with cardiac failure. [13]

The virulence factor that has been most described to facilitate NOVC bacteraemia is haemolysin. Other virulence factors include a heat-stable enterotoxin and hemagglutinin protease. However, due to the under-reporting and insufficient research, there could be other virulence factors that are yet to be described. [5]

Regarding antimicrobial susceptibility testing in the laboratory, both the Clinical Laboratory and Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility testing (EUCAST) provide guidelines for *V. cholerae*.[14,15] However, there are no guidelines available regarding the optimal antibiotic choice or duration of therapy for NOVC bacteraemia. Extrapolating data from infections caused by toxigenic *V. cholerae,* some authors recommend monotherapy with tetracyclines, third-generation cephalosporins and quinolones, or their combinations, with dual antibiotic therapy recommended in complicated infections or immunocompromised patients. The duration of therapy varies between two weeks to more than two months. Resistance to ciprofloxacin, tetracyclines and cefotaxime has also been described with some strains reported to be multidrug resistant [5,9,10]. We recommend that antibiotic choice and duration should be based on local susceptibility patterns, clinical presentation and severity of illness.

NOVC bacteraemia has been associated with mortality ranging between 24 and 62% [9–11]. The high mortality is attributed to delayed or under-diagnosis and inappropriate antimicrobial therapy.[5] With the increasing incidence of vibrio species in the environment due to climate change and associated global warming, awareness regarding invasive NOVC infections should be enhanced [9,10]. While further research is warranted to ascertain virulence factors, optimal antibiotics for treatment, and duration of therapy, clinicians need to be aware of this entity. This will ensure that a relevant patient history is obtained, appropriate specimens are collected for laboratory testing, and treatment is instituted timeously.

CRediT authorship contribution statement

Vinitha Alex: Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **Mahavishnu Moodley:** Writing – review & editing, Writing – original draft.

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.

Ethical consideration

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References

[1] Harris JB, LaRocque RC, Qadri F, Ryan ET. Calderwood SB. cholera. Lancet 2012; 379(9835):2466–76. Jun.
[2] Tamason CC, Tulsiani SM, Siddique AK, Hoque BA, Mackie Jensen PK. What is cholera? a preliminary study on caretakers' knowledge in Bangladesh. J Health Popul Nutr 2016;35(1):3. Dec.
[3] Ojeda Rodriguez JA, Hashmi MF, Kahwaji CI. Vibrio cholerae Infection. [Updated 2024 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526099.
[4] Montero DA, Vidal RM, Velasco J, George S, Lucero Y, Gómez LA, et al. Vibrio cholerae, classification, pathogenesis, immune response, and trends in vaccine development. Front Med 2023;10:1155751. May 5.
[5] Deshayes S, Daurel C, Cattoir V, Parienti JJ, Quilici ML, De La, Blanchardière A. Non-O1, non-O139 vibrio cholerae bacteraemia: case report and literature review. Springerplus 2015;4(1):575. Oct 5.
[6] Zhang Q, Alter T, Fleischmann S. Non-O1/Non-O139 vibrio cholerae—an underestimated foodborne pathogen? an overview of its virulence genes and regulatory systems involved in pathogenesis. Microorganisms 2024;12(4):818. Apr 18.
[7] Smith AM, Sekwadi P, Erasmus LK, Lee CC, Stroika SG, Ndzabandzaba S, et al. Imported cholera cases, South Africa. Volume 29, Number 8—August 2023 Emerging Infect Diseases J - CDC 2023 [cited 2023 Nov 24]; Available from: https://wwwnc.cdc.gov/eid/article/29/8/23-0750_article.
[8] AFRO-cholera monthly bulletin-July 2024. pdf.
[9] Marek A, Inkster T, Anderson E, Jenkins C, Boyd J, Kerr S, et al. Non-toxigenic vibrio cholerae bacteraemia: case report and review of the literature. J Med Microbiol 2013;62(9):1357–9. Sep 1.
[10] Petsaris O, Nousbaum JB, Quilici ML, Le Coadou G, Payan C, Abalain ML. Non-O1, non-O139 vibrio cholerae bacteraemia in a cirrhotic patient. J Med Microbiol 2010;59(10):1260–2. Oct 1.
[11] Drozd M, Garland E, Walker AMN, Slater TA, Koshy A, Straw S, et al. Infection-related hospitalization in heart failure with reduced ejection fraction: a prospective observational cohort study. Circ Heart Fail 2020;13(5):e006746. May.
[12] Zhang X, Lu Y, Qian H, Liu G, Mei Y, Jin F, Xia W, Ni F. Non-O1, Non-O139 *vibrio cholerae* (NOVC) bacteremia: ccase report and Literature review, 2015-2019. Infect Drug Resist 2020;13:1009–16. https://doi.org/10.2147/IDR.S245806. Apr 7PMID: 32308442; PMCID: PMC7156264.
[13] Wayne PA. Clinical and Laboratory Standards Institute. CLSI. Abbreviated Identification of Bacteria and Yeast. Approved guideline- Second edition. CLSI document M35-A2; 2008.
[14] https://www.eucast.org/clinical_breakpoints.