

A fatal non-O1 *Vibrio cholerae* septicemia in a patient with liver cirrhosis

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Vibrio Cholerae (*V. cholerae*) strains are usually divided into O1 and non-O1 serogroups according to the different antigens that they synthesize.¹ *Vibrio cholerae* species cause gastrointestinal infections (especially O1), or extra intestinal infection (particularly non-O1). There has been several reports of bacteremia and other septic conditions associated with non-O1 *V. cholerae*, many of these infections have followed a fatal course, presenting as a fulminant septicemia in patients with liver diseases, who had ingested raw or undercooked seafood.² In this report, we present the case of a Saudi male with Lawrence Moon Biedl syndrome, cirrhosis and diabetes mellitus (DM), who developed fatal septicemia caused by non-O1 *V. cholerae*.

A 34-year-old Saudi male, known patient of Lawrence Moon Biedl syndrome, DM, liver cirrhosis and positive hepatitis B virus, was admitted through the Emergency Room to the medical unit of King Abdul-Aziz University Hospital with diarrhea, abdominal pain and distention of 10 days duration. On physical examination, he was alert, icteric, with a temperature of 36.3°C, heart rate of 84 beats/minute, and blood pressure of 129/71mm Hg. Ascites was present with abdominal tenderness. The patient was treated with osteocare one tablet po od, essential one tab po od, legolon 70mg tid, motilium 10mg tab po tid, pentazole 20mg one tablet bid and ceftriaxone one gram intravenously (IV) bid. A specimen of stool was sent for culture. The patient was stable until 2 weeks after admission when he became febrile with a temperature of 38.6°C. A blood was obtained for culture. Upon questioning, the family of the patient revealed that he had eaten uncooked seafood when he spent the weekend at home with the family with permission from the hospital. The patient started vomiting a coffee-ground vomitus, an urgent endoscopy was carried out where a first degree not bleeding esophageal varices was found, in addition to severe gastritis and duodenitis and multiple gastric erosions. He was then treated with amoxil one-gram po bid and clarithromycin 500mg po bid in addition to the pentazole he was already taking. The patient developed a progressive abdominal swelling, abdominal and epigastric pain over the next 2 days, with difficulty in breathing. A spontaneous bacterial peritonitis was diagnosed clinically, and diagnostic paracentesis was carried out and yielded 3100/mm³ of a yellowish turbid

fluid, the leukocyte count was 2400/mm³ with 80% polymorphonuclear cells. The laboratory investigations showed a high blood leucocyte count of 15.6/ul (normal 3-11000/ul) with 85% neutrophils, lymphocytes 3.4%, monocytes 9.7% and eosinophils 2%. Hemoglobin level was 11.5g/dl (normal 13-17g/dl). His sodium serum level was 129mmol/L (normal 135-148mmol/L), potassium 5.4mmol/L (normal 3.5-5.5mmol/L), serum creatinine was 281umol/L (normal 40-120umol/L), total protein 49g/L (normal 60-87g/L), albumin 12g/L (normal 34-50g/L), aspartate aminotransferase 732 iu/L (normal 5-50 iu/L), alanine aminotransferase 249 iu/L (normal 5-65 iu/L), total bilirubin 593 μmol/L (normal 0-17 μmol/L) and direct bilirubin 457 μmol/L (normal 0-7 μmol/L). Despite treatment, the patient's condition quickly worsened, a septic shock was developed, blood pressure dropped to 88/53mm Hg, the patient was moved to the intensive care unit and was given intravenous life support therapies and piperacillin/tazobactam 4.5g IV every 6 hours, but 24 hours later he died.

Blood culture was performed using the automated blood culture system BacT-Alert [Organon Teknika, United States of America (USA)]. Ten milliliter of the patient's blood was inoculated into each bottle of blood culture, one for aerobic and the other for anaerobic growth. Both bottles were positive after 10 hours incubation, the gram-stained smears of the bottles showed gram-negative curved rods. Subculture of the positive blood culture was carried out onto sheep blood agar and chocolate agar that were incubated in an atmosphere of 5% CO₂ at 37°C for 24 hours. The isolated colonies were beta-hemolytic on blood agar, oxidase positive were identified as *V. cholerae* with the use of API 20E (Analytab, Inc.) and the growth on thiosulfate-citrate-bile-salt-sucrose agar (TCBS), as large raised shiny yellow colonies (Figure 1). Further identification as *V. cholerae* was carried out by using the Vitek-2 System (bioMerieux Inc., Hazelwood, MO, USA). The susceptibility testing of the isolate was performed by both the Vitek-2 System, and by Kirby-Bauer disk diffusion method, according to the National Committee for Clinical Laboratory Standards guidelines,³ and showed it to be sensitive to all the antibiotic tested including ampicillin, amoxicillin/clavulanic acid, gentamicin, amikacin, cefuroxime, piperacillin, piperacillin/tazobactam, ciprofloxacin, meropenem and ceftriaxone. The organism was identified as non-O1 *V. cholerae* as it failed to agglutinate with the *V. cholerae* O1 antiserum (Difco Laboratories, USA). Ascitic fluid was processed in blood culture bottles, which were directly inoculated with 10ml of ascitic fluid at the bedside at the time of paracentesis. The ascitic fluid culture was negative for any organisms after 7 days of incubation in the BacT-Alert.



Figure 1 - Thiosulfate citrate bile salt sucrose agar medium showing large raised shiny yellow colonies of *Vibrio cholerae*.

The stool specimen received from the patient was processed for common enteric pathogens including *Salmonella*, *Shigella* and *Campylobacter* species, by inoculation into MacConkey agar, desoxycholate agar, and xylose-lysine-desoxycholate agar (Saudi Prepared Media Company, Saudi Arabia) as well as TCBS agar for *V. Cholerae*. No pathogens were isolated from the stool specimen. To assess the clinical features and susceptibility of cirrhotic patients to non-O1 *V. cholerae* bacteremia, 21 patients with underlying cirrhosis and the aforementioned bacteremia were retrospectively reviewed by Lin et al.² seafood ingestion (7 cases), seawater exposure (2 cases), were risk factors, but nosocomial infections were also noted in 6 cases. Presenting symptoms and signs included ascites (95.2%), fever (81%), abdominal pain (52%), diarrhea (33%) and cellulitis and bullae formation (19%). The over-all case-fatality rate was 23.8%, 75% of the deaths were observed in patients with skin manifestations. Our study is consistent with these findings, where our patient had a history of seafood ingestion 2 days before his illness, and the main presenting symptoms and signs were ascites, fever, abdominal pain and diarrhea. Another study in septicemia with non-O1 *V. cholerae* was conducted in the National Cheng Kung University Hospital in Taiwan,⁴ and reported 30 episodes of non-O1 *V. cholerae* infections. The major clinical presentation was bacteremia with concurrent spontaneous bacterial peritonitis, or invasive soft tissue infections, occurred solely in cirrhotic patients. The study's recommendation was to include infection due to non-O1 *V. cholerae* among the differential diagnosis of invasive infections in cirrhotic patients, and to use third-generation cephalosporin and tetracycline analogue, or a fluoroquinolone alone for the treatment of severe *Vibrio* infections. Non-O1 *V. cholerae* systemic illness is a life-threatening infection, up to 61.5% of patient presenting with bacteremia died, despite adequate antibiotic treatment.⁴ A high degree of

suspicion and prompt administration of antibiotics may reduce the mortality rate.² The majority of cases of non-O1 *V. cholerae* systemic illness have been reported from endemic areas (Gulf Coast of USA, Mexico, Southern Asia). Non-O1 *V. cholerae* infection is associated with ingestion of contaminated seafood and its common presentation is gastroenteritis. Septicemia may be found in immunocompromised hosts, the majority of known cases have occurred in patients with liver cirrhosis, or hematologic malignancy. Until now 29 patients with non-O1 *V. cholerae* septicemia have been reported, 11 (38%) had chronic liver disease.⁴ Liver cirrhosis, malignancy and steroid use were independent risk factors for fatality in patients with invasive *V. cholerae* non-O1 infection.⁵ Given the high fatality rate of this infection, it is important for physicians to consider this diagnosis in patients who have underlying risk factors and appropriate epidemiologic exposures. Physicians should advise cirrhotic patients to avoid eating raw seafood, and these patients should be specifically questioned regarding recent seafood ingestion.

Numerous broad-spectrum antibiotics have been used to treat severe non-O1 *V. cholerae* infection,² but recently there are non-conclusive recommendation regarding the drug of choice and the duration of therapy. Tetracycline, which demonstrates an excellent in-vitro activity against *vibrio* strains, appears to be the drug of choice in documented *vibrio* infections, but a third generation cephalosporins or a fluoroquinolone drug, may be a better choice for patients with cirrhosis.

Received 7th March 2004. Accepted for publication in final form 21st June 2004.

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