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Unusual Non-Serogroup O1 *Vibrio cholerae* Bacteremia Associated with Liver Disease

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A 50-year-old woman and a 31-year-old man with underlying liver disease presented with fever and signs of liver failure. The blood cultures in both cases yielded non-serogroup O1 *Vibrio cholerae* strains which were biochemically identical except that one strain was nonmotile. Despite treatment with antibiotics, the older patient died; the other patient survived. Both strains were found to be susceptible to most antibiotics tested in vitro. No apparent source of infection could be identified in either case.

Vibrio cholerae serogroup O1 is generally regarded as a noninvasive enterotoxigenic organism causing gastroenteritis of various severities (6). In contrast, *V. cholerae* non-O1, although biochemically indistinguishable from *V. cholerae* O1, has been often associated with extraintestinal infection (7). During the 3-year period from 1977 through 1979, only 12 strains of non-O1 *V. cholerae* isolated from blood and 22 isolated from other nonenteric sources (wound, ear, sputum, nasotracheal suction, bile, etc.) were submitted to the Centers for Disease Control for confirmation of identity and serotyping (16).

We report here two cases of bacteremia caused by non-serogroup O1 *V. cholerae* in patients with underlying liver disease.

Case 1. A 50-year-old woman, previously diagnosed with hypertension, diabetes mellitus, duodenal ulcer, and postviral chronic hepatitis, was admitted with fever and deteriorating level of consciousness to Al-Adan Hospital on 23 December 1988. Her temperature was 40°C; her blood pressure was 140/90 mm Hg; her heart rate was 120 beats per min. She was obese, deeply jaundiced, and comatose. She had urinary and fecal incontinence and edema of the lower legs. Abdominal examination revealed an irreducible umbilical hernia. There were no meningeal signs, and the chest was clear. Two days after admission, the patient developed hematemesis. A complete blood analysis showed a hemoglobin of 110 g/liter; and a leukocyte count of 20.8×10^9/liter, with 90% polymorphonuclear leukocytes, 5% band forms, 4% lymphocytes, and 1% monocytes. The platelet count was 103×10^9/liter, the prothrombin time was 34 s, and the activated partial thromboplastin time was >3 min. Blood chemistry findings were as follows: glucose, 7.5 mmol/liter; urea, 13.4 mmol/liter; serum creatinine, 135 μmol/liter; total serum protein, 70 g/liter; serum albumin, 13 g/liter; total bilirubin, 211 μmol/liter; alanine transaminase, 59 U/liter; and aspartate transaminase, 132 U/liter.

The patient had been hospitalized before on at least two occasions (December 1987 and January 1988) with similar complaints. Following symptomatic treatment and subsequent recovery, she was discharged each time. In January 1988 her blood was found to be positive for hepatitis B core antibody but negative for hepatitis B surface antigen and hepatitis B surface antibody. During follow-up in August 1988, Tc-99 tin colloid liver scan findings were compatible with chronic parenchymatous liver disease such as cirrhosis, with signs of portal hypertension. Endoscopy of the upper gastrointestinal tract showed small varices involving the distal one third of the esophagus and a deep ulcer crater on the anterior wall of the bulb in the duodenum.

She now received treatment for liver failure, hypertension, and duodenal ulcer. After blood was drawn for culture, antibiotic therapy was initiated with a parenteral ampicillin-cloxacillin combination (Ampiclox) (4 g) and gentamicin (80 mg). However, the condition of the patient deteriorated and she died on hospital day 3.

All three blood cultures yielded growth of a gram-negative rod on blood agar plates after 18 h of incubation at 37°C. Although the organism was identified as *V. cholerae* by conventional biochemical methods and by its profile in the API 20E system (API-system S.A., Montalieu-Vercieu, France) (analytical profile 5147127), it was consistently found to be nonmotile. By using the standard Kirby-Bauer disk diffusion method, the organism was found to be susceptible to tetracycline, ampicillin, cephalothin, cefotaxime, gentamicin, chloramphenicol, and amikacin; it was resistant to colistin.

Case 2. A 31-year-old man was admitted to Al-Farwania Hospital in October 1988 with fever and jaundice. He had cirrhosis resulting from bilharziasis which was diagnosed on the basis of histopathological findings in liver biopsy. The patient was investigated for liver functions. Since he was transferred to another hospital, his file could not be reviewed for detailed clinical information. The laboratory records yielded the following data: hemoglobin, 119 g/liter; leukocyte count, 29.8×10^9/liter, with 93% polymorphonuclear leukocytes and 7% lymphocytes; erythrocyte sedimentation rate, 26 mm/h; platelets, 185×10^9/liter; blood glucose, 3.7 mmol/liter; urea, 6.6 mmol/liter; sodium, 135 mmol/liter; potassium, 2.6 mmol/liter; chloride, 109 mmol/liter; total bilirubin, 114 μmol/liter; aspartate transaminase, 105 U/liter; and alanine transaminase, 58 U/liter. Two of three blood cultures and one ascitic fluid yielded growth of a gram-negative rod which was identified as *V. cholerae* by API 20E. The API profile index, as well as the antibiotic susceptibility pattern, was similar to that of the isolate from case 1. The only difference was in motility, the strain from case 2 being motile. The isolates were sent to J. Vandepitte, Universitair Ziekenhuis St. Rafael, Leuven, Belgium, and

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TABLE 1. Biochemical characteristics of two isolates of non-serogroup O1 *V. cholerae* reported by the reference laboratory

Test	Result for non-O1 *V. cholerae* isolate from:	
	Case 1	Case 2
ONPG[a]	+	+
Urease	−	−
Indole	+	+
Voges-Proskauer	+	+
H_2S	−	−
Citrate (Simmons)	+	+
Motility	−	+[b]
Gelatin	+	+
Lysine decarboxylase	+	+
Arginine dehydrolase	−	−
Ornithine decarboxylase	+	+
Tryptophan deaminase	−	−
Glucose		
Acid	+	+
Gas	−	−
Lactose	+	+
Arabinose	−	−
Mannitol	+	+
Dulcitol	−	−
Salicin	−	−
Adonitol	−	−
Inositol	−	−
Sorbitol	−	−
Raffinose	−	−
Rhamnose	−	−
Saccharose	+	+
Maltose	+	+
Xylose	−	−
Trehalose	+	+
Cellobiose	−	−
Sorbose	−	−
Glycerol	+	+
Melibiose	−	−
Mannose	+	NI[c]
Malonate	−	−
Mucate	−	−
Nitrate	+	+
Oxidase	+	+
DNase	+	+
Tween 80 esterase	+	+

[a] ONPG, *o*-Nitrophenyl-β-D-galactopyranoside.
[b] Single-polar flagellum.
[c] NI, Not indicated.

C. Richard, Cholera Reference Center, Pasteur Institute, Paris, France, for confirmation of identification and serotyping. Both were identified as *V. cholerae* non-serogroup O1 susceptible to O:129. The biochemical characteristics for both strains obtained by the reference laboratory are listed in Table 1.

Discussion. Although previous reports have documented the association of non-serogroup O1 *V. cholerae* and extra-intestinal infections such as wounds (3, 7, 11), cholecystitis (7, 9, 12), and meningitis (4, 7, 15), septicemia caused by this organism remains a rarity (16). It has been shown, albeit in a small number of cases, that non-O1 *V. cholerae* septicemia occurs in patients with underlying chronic disease, particularly hepatic cirrhosis and hematological malignancy (4, 7, 8, 13). In 23 previously reported cases, the fatality rate was found to be 61.5% (16).

There are studies to show that besides a cholera-like toxin other extracellular toxins and hemolysins are produced by non-serogroup O1 *V. cholerae* (1, 17). This may help explain the severity of diarrheal disease in patients from whom toxigenic strains are isolated compared with that in patients with nontoxigenic fecal isolates (2). Wound and ear infections are generally acquired by exposure to seawater (7, 11). However, the development of septicemia has been more difficult to identify because the organism has only rarely been isolated from stools of septicemic patients with or without diarrhea. In our first case, fecal cultures were not done because the patient died before the blood cultures grew the organism. Stool cultures were negative for vibrios and other enteric pathogens in the second case.

There are reports indicating acquisition of non-serogroup O1 *V. cholerae* enteritis by people living in the Texas-Louisiana Gulf Coast region (10) and Cancun, Mexico (5). Since Kuwait is located in the Arabian Gulf Coast, a study was initiated in the Al-Adan Hospital laboratory in 1986 to determine the occurrence of vibrios in the diarrheal stools of the local population. In addition to other routine media, thiosulfate-citrate-bile salt-sucrose agar medium was inoculated to screen all diarrheal stools submitted for culture. Of 4,987 specimens cultured, none was found to be positive for vibrios, and the study was shelved. In the summer of 1988 many cases of non-O1 *V. cholerae* enteritis were imported by people returning to Kuwait after spending their vacations in endemic areas such as India and Bangladesh. Five cases were identified in the Al-Adan Hospital laboratory. No history of foreign travel could be elicited from our two patients, and it is probable that they became infected from a contact in Kuwait. An association between cases of non-O1 *V. cholerae* gastroenteritis acquired in the United States and the consumption of raw oysters has also been reported (10). Whatever the source of infection, the organism needs to possess invasive properties to cause septicemia (14). Further investigations are required on the pathogenicity of non-O1 *V. cholerae* in normal and compromised hosts. Non-O1 *V. cholerae* has been found to be susceptible to a wide range of antimicrobial agents in vitro. Although both our strains were susceptible to ampicillin and gentamicin, there are reports suggesting variable susceptibilities of non-O1 *V. cholerae* strains to these two antibiotics (16). There are not enough data to indicate the clinical efficacies of various antimicrobial agents used in the treatment of non-O1 *V. cholerae* bacteremia. Despite in vitro susceptibility, ampicillin has not been found to be efficacious in clinical use (16).

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