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# Case Report

## Non O1 Vibrio cholera: An emerging pathogen in blood? - A review and report of cases from a regional laboratory at the Eastern Province in Saudi Arabia

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**ABSTRACT:**
We present our experiences with non O1 Vibrio cholerae bacteremia cases from a single centre without prior history of consumption of sea food or contact with marine environment. The importance of its emerging nature as a pathogen and the course of infection with this unexpected organism has been reviewed and discussed.
**Key words:** Non O1 Vibrio cholera, bacteremia

**INTRODUCTION:**
Vibrios were prevalent in coastal areas and many studies were published from such areas.[1,2,3] Vibrio cholerae non O1 serotypes with the exception of O139 are considered less pathogenic and cause only sporadic diarrheal illness. Nevertheless the increasing number of immune compromised patients is changing the scenario of the pathogenic potential of many innocuous bacteria and non O1 vibrios are no exception. We present our experiences with non O1 Vibrio cholerae bacteremia from the regional laboratory in the Eastern province of Saudi Arabia over a period of 2 years.

**CASE 1:**
An 85 year old Saudi male, a known case of cholangio-carcinoma with metastasis, presented to the emergency room with a complaint of pain abdomen, fever of 39.6 °C of one day duration and mild diarrhea. He had hemiparesis 4 months prior to this admission. The patient was a farmer from the South and was a vegetarian. The patient was admitted and blood, urine and stool were sent to the microbiology laboratory for culture and started on injection gentamicin 60 mg intravenous BD and aztreonam intravenous BD. Stool and urine cultures revealed no significant findings. Blood culture grew Klebsiella pneumoniae which was sensitive to both the antibiotics the patient was receiving. After an initial improvement, the condition deteriorated and a repeat blood culture was sent. The patient expired shortly after. The second specimen of blood grew Klebsiella pneumoniae and a second Gram negative bacillus which was a non lactosefermentor on MacConkey agar plate. This was oxidase positive and identified biochemically as Vibrio cholerae by API 20E. Serotyping identified the strain as Vibrio cholerae non O1. The strain was sensitive in vitro to tetracycline, chloramphenicol, trimethoprim- sulfamethoxazole, gentamicin, ciprofloxacin and polymyxin B. He had no travel history, exposure to sea water or food and any fresh wounds.

**CASE 2:**
A 50 year old Egyptian presented to the emergency room with a complaint of pain and distension of the abdomen, fever of 1 day duration and drowsiness. The patient was diabetic since 15 years, had a history of Bilharziasis 8 years prior to the present illness and underwent cholycystectomy 4 years prior to the current admission. After clinical examination the patient was admitted with a diagnosis of chronic liver disease with stage 1 encephalitis. The blood chemistry supported the clinical diagnosis. The ascitic fluid showed pus cells but culture showed no growth. The patients serum was positive for HCV antibodies. Blood culture grew Gram negative rods which were identified as Vibrio cholerae by API 20E. It was non motile and confirmed by motility indole urease method as well as the hanging drop. Serologically it was identified as non O1 by failing to agglutinate with Vibrio cholerae O1 polyvalent antiserum and 0139 antiserum. Antimicrobial susceptibility testing showed susceptibility to tetracycline, trimethoprim-sulfamethoxazole, cephalexin, ceftriaxone, gentamicin and ciprofloxacin. The patient was administered ceftriaxone 1 gm IV BD empirically and the same was continued after the culture result was known. Follow up cultures were negative. Stool cultures were negative for Vibrio cholerae. The patients condition improved and was discharged.

**CASE 3:**
A 2 year old Saudi male child, known case of Wiscott Aldrich syndrome was admitted through our emergency with high fever (39.6 °C), cough and skin eruptions of 2 days duration. The child had prior repeated admissions to the hospital with intercurrent infections. After the appropriate investigations the patient was given cefuroxime 250 mg IV 8$^{th}$ hourly in view of his chest infection. Initial cultures were not significant. 3 days after admission, the patient had

spiking fever and the blood culture was repeated which grew gram negative bacilli and was identified as vibrio cholerae by API20E. The organism failed to agglutinate with polyvalent O1 antiserum or 0139 antiserum and so was identified as non O1 serotype. The stool specimens were repeatedly negative for Vibrio cholerae. The strain was sensitive to trimethoprim-sulfamethoxazole, augmentin, tetracycline, gentamicin, chloramphenicol, ciprofloxacin, imipenem, ceftriaxone. The child was discharged, but expired 5 months later with bronchopneumonia.

## CASE 4:

A 26 year old Saudi woman, known case of SLE and chronic renal failure visited the hospital complaining of high fever (39.8 °C). On examination she was febrile. Blood cultures were taken and she was placed on an empiric therapy of oral ciprofloxacin. Blood culture grew Gram negative rods and was identified by API 20E as Vibrio cholerae and serology as non O1 serotype sensitive to chloramphenicol, trimethoprim-sulfamethoxazole, cefotaxime, aztreonam, ciprofloxacin, cefixime, gentamicin, doxycycline, and imipenem. Ciprofloxacin was given and the patient was discharged. Her condition improved clinically. Stool cultures done after blood culture was negative for Vibrio cholerae.

## CASE 5:

A 45 year old female, known case of end stage renal disease on continuous ambulatory peritoneal dialysis since 2 years presented to the emergency room with a tender distended abdomen, fever and a blood pressure of 80/60 mmHg. She was admitted to the ward with a diagnosis of peritonitis. A peritoneal lavage was performed and intra peritoneal cephalexin and gentamicin were given. The BP further dropped to 60/30 mmHg and the patient was shifted to the ICU and was started on intravenous vancomycin. 16 hours after admission the patient expired. The blood and peritoneal fluid grew Vibrio cholerae identified by API 20E. The strain was sensitive to cephalexin, ceftriaxone, tetracycline, gentamicin, and ciprofloxacin. It was identified as non O1 by Vibrio cholerae antisera. Stool culture was not done as the patient died before the blood and peritoneal fluid grew the organism.

## DISCUSSION:

Vibrio cholerae can be divided into three main sub-types: O1 toxigenic, 01 non toxigenic and non-01 strain. [4] Vibrio cholerae consists of over 193 serotypes [5] and the common epidemic diarrhea producing serotypes belong to O1 and 0139[6]. The other strains which do not show agglutination with O1 and O139 antisera are known as Non O1 vibrios. Vibrio cholerae non-01 is found in water sources worldwide.

Biochemically they are indistinguishable from Vibrio cholera 01 or 0139. Unlike the serotypes 01 and 0139, they cause only sporadic diarrheal illness with occasional strains causing febrile enteritis with bloody diarrhea [7].They have been isolated from the hepatobiliary system and can occasionally cause extra intestinal infections like bacteremia, peritonitis [8], infections of the skin [2], soft tissue and ear [9.10]. They do not produce cholera toxin but they do elaborate a heat stable enterotoxin (NAG-ST) [11], dermonecrotic factor, capsule, hemagglutinin / hemolysins, cytotoxin [2, 5] exotoxin [12] and can be enteroinvasive. [5, 13] This may explain its pathogenicity. One of the proposed route by which viable Vibrio cholerae may in some circumstances cause bacteremic illness is by translocation across the mucosa by the intestinal M cells which are enterocytes adapted to sample enteric organisms. These organisms are then translocated to the gut lymphoid tissue, where a specific lgA response is generated. Thus the probable transmural migration via the intestinal mucosa and Porto systemic shunting into the blood stream, explains its role in septicemia and death with or without diarrhea [14]. It was also shown that pathogenic strains of non O1 Vibrio cholera are capsulated, produce translucent colonies and are protected from serum bactericidal activity [12, 15].Molecular studies suggest that these strains may be closely related to the distinctive toxigenic Vibrio cholerae O1. [16]

There were some case reports in literature of non O1 V cholerae septicemia from patients with chronic liver disease [2, 17, and 18], gastrectomy [18] acquired immune deficiency syndrome [6, 7] cholecystitis [12] nephrotic syndrome [8], hematological malignancies [8], meningitis [9, 19] and immunodeficiency. Some cases may manifest with cellulitis [20] and another case was reported in burns. [21]

Primary septicemia has often been associated with travel, consuming raw oysters, shell fish or exposure of damaged skin to contaminated sea water or fresh water. [2, 3] But the potential for infection in patients as with our experience without risk factors does exist. [22] In a retrospective study of infections caused by non O1 Vibrio cholerae in Taiwan, it was found that out of 30 isolates 15 patients had bacteremia of which without exception had hepatic cirrhosis. [3] Therefore bacteremia was the most common presentation. In our study, 2 patients were with liver disease, one each of immunodeficiency, renal failure and SLE. One of our cases had concomitant Klebsiella pneumoniae bacteremia. In majority of the cases in literature and in our cases, the patients did not have contact with sea water, shellfish or any other sea food which are known sources of vibrios. Similarly most of the patients stool cultures were consistently negative for these pathogens. Few cases had prior mild diarrhea which might have cleared these bacteria from the intestine. Nevertheless it is presumed that the portal of entry is through intestines.

The mortality rates in these cases vary and are probably related to the virulence of the strain or biotype of the organism and also a number of host factors. In the present report only in one case mortality was directly attributable to infection. Hypotension as seen in our case 5, within twelve hours of admission, has a high mortality rate as reported by Klontz [23] and Farina et al. [6]

The presence of plasmids in a few strains of non O1 vibrio although do not correlate with antibiotic resistance or influence ribotype patterns and rather than being regarded as a heterogeneous group of lesser consequence, the non O1 vibrio cholerae are perhaps more properly viewed as strains with the underlying potential to cause epidemic disease if the appropriate component of virulence genes is acquired. This may be probably due to gene transfer between a non O1 and an O1 strain whereby the acquired DNA alters the antigenic properties of the recipient O1 strain, providing a selective advantage causing an early aggressive spread in a region where a large part of the population is immune to O1 strains. [11, 24, 25]

The frequency with which non O1 vibrios are being isolated from stool specimens of both symptomatic and asymptomatic persons from our laboratory exemplifies that non O1 vibrios are prevalent in this region, which is a coastal area. During the past 2 years out of 22 strains of vibrios 23% were non O1 serotypes. The reasons for the sudden emergence of this pathogen in septicemias (5 cases in 2 years) are not known. The cases reported to our knowledge are the first of its kind from the Eastern province.

The biochemical identification of V cholerae might sometimes be confused with Aeromonas species. Apart from Arginine hydrogenase, other tests that support the identification are its morphology, growth in the presence of vibriostatic compound 0/129, string test, growth in the presence of 6% NaCI, and production of gas in TSI. [24] Further serotyping of these strainsmay not is clinically useful but different serotypes may exhibit different virulence characters or properties e.g. a non motile strain was observed in one of our cases as well as in a case report from Kuwait. [17]

Regarding the choice of antibiotic there are no specific guidelines about the most effective antibiotic to use in case of vibrio septicemias and most of the non O1 vibrios are multi drug resistant. [11] Conventional antibiotics like tetracycline, erythromycin, trimethoprim-sulfamethoxazole or fluroquinolones were used to treat the enteric infection. One research group demonstrated a combination regimen (Cefotaxime with minocycline) showed synergistic effect in vitro. [3] Though there were no prospective studies, third generation cephalosporins and fluroquinolones or a combination of these antibiotics may be a good choice for treating invasive infections.

Vibrio cholerae non O1 has been identified as able to exist in water bodies of the world and this experience emphasizes the emergence of this otherwise uncommon pathogen in patients with underlying chronic medical disorders or immuno-suppression which requires a thorough clinical examination, prompt identification and institution of appropriate antibiotic therapy given the high fatality rate of this organism.

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