A Rare Case Of Cholera In Hawaii

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Cholera is the most fatal of the infectious diarrheas but only rarely encountered in Hawaii. Two cases previously have been documented in the Islands. We describe an elderly patient, without obvious risk factors, who contracted cholera. Early consideration of cholera as a diagnostic possibility is recommended in patients with unexplained, profuse diarrhea. The unique features of this case are discussed in this report.

Case Report

A 77-year-old Japanese man was admitted to a community hospital for weakness and diarrhea. Four days prior to admission he had a sudden onset of loose, watery stools, but denied any other symptoms. Over the next 2 days, the severity of the diarrhea increased progressively and the patient sought medical attention. He was prescribed an antidiarrheal agent with minimal relief. The morning of admission, the volume and frequency of diarrhea had increased dramatically to 15 episodes per hour; this was associated with dizziness, abdominal cramping, and tenesmus.

There had been no recent ingestion of raw seafood or dairy products, and no recent travel or use of an antibiotic. No other family member or personal contact had been ill. The patient, a retired farmer, lived with his wife and family.

The patient's past medical history was remarkable for a partial gastrectomy curative for peptic ulcer disease, and he also had intolerance to lactose. No previous episodes of significant diarrhea were reported.

Physical examination was notable for orthostatic hypotension, poor skin turgor, hypophonia and a dry oral mucosa. Abdominal and rectal examinations were unremarkable. The stool was green, watery and guaiac negative.

Laboratory examination revealed significant metabolic acidosis, hemoconcentration with elevated hematocrit and serum proteins and elevated blood urea nitrogen and serum creatinine. Stool Wright stain was negative. Stool culture performed on MacConkey's medium revealed non-lactose-fermenting colonies identified as *Vibrio cholera* through biochemical analysis. Serogroup confirmation was performed by the State Department of Health.

The patient's hospital course was notable for massive diarrhea production, often exceeding 1 liter per hour, marked hypovolemia, acidosis and acute renal insufficiency. Rehydration, electrolyte and bicarbonate repletion was accomplished intravenously in the intensive care unit and Doxycycline was administered. The patient was subsequently discharged in stable condition on the 6th hospital day.

Discussion

Although, in retrospect, our patient presented with many classic clinical features of cholera, the diagnosis on admission was not immediately obvious. Early differential diagnostic considerations included other infectious agents such as enterotoxigenic *E. coli, Campylobacter, Salmonella, Shigella* and *S. aureus.* The Zollinger-Ellison syndrome was also but less likely a consideration given the patient's previous partial gastrectomy. Other noninfectious causes of secretory diarrhea such as the vasoactive intestinal polypeptide-secreting tumors and the carcinoid syndrome were considered unlikely.

Vibrio cholera was initially considered to be unlikely. Neither the patient nor his family, all reliable historians, could reveal any history of exposure. Moreover, cholera is known to be extremely rare in Hawaii; only 2 previous cases have been documented. As a result, the quantity of stool produced was initially surprising and underestimated, which made adequate fluid resuscitation inadequate in the early hours of hospitalization.

Regardless of etiology, it is possible that the patient's previous partial gastrectomy increased his likelihood for contracting cholera, as patients with that condition or other causes of hypochlorhydria have increased susceptibility to infection[1].

Classification

There are more than 70 serogroups of *Vibrio cholera* classified based on the characteristics of the Somatic O antigen. Only serogroup O-1 is responsible for epidemic cholera; this is further subdivided into 2 biotypes: Classical and El Tor. The El Tor biotype differs from the Classical biotype both biochemically (hemolysin-producing, polymixin B-resistant) and epidemiologically (higher infectivity, causing milder infections, hardier in the external environment)[2]. Each biotype is further subdivided into serotypes based on the presence of additional antigenic determinants.

Epidemiology

Vibrio cholera is endemic to the Ganges delta; however, 7 pandemics have occurred since 1817[3]. The current pandemic of the El Tor biotype began in 1961 and encompasses southeast Asia,

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the Indian subcontinent, the Middle East, Africa and the Gulf Coast of North America[4].

Humans are the only host of *V. cholera*. Transmission occurs through human fecal contamination of water and occasionally of food (raw vegetables and seafood). However, *V. cholera* can survive in the external environment for limited periods of time.

Acutely ill patients may excrete up to 60 liters of stool over the course of their illness with 10^7 organisms per milliliter present in the stool[2]. Direct contamination of the environment by improper handling of sewage is the major route of epidemic dissemination. Additionally, it is speculated that mildly symptomatic and asymptomatic patients play an important role in epidemics[5].

In endemic areas, children are affected more frequently than are adults; however, it is less common in infants under 2 years of age because of passive immunity[6]. In non-endemic areas, children and adults are affected equally.

Pathogenesis

Ingestion of approximately 10^4 organisms is required to produce clinical infection[7]. The ability of *V. cholera* to colonize the lining epithelium of the small intestine is determined by adhesion factors, chemotaxis, and motility[8]. The cholera enterotoxin, responsible for clinical symptomatology, is composed of 5 binding subunits and a single activating subunit[5]. Interaction with nicotinamide adenine dinucleotide (NAD) results in increased intracellular 3',5' adenosine monophosphate (cAMP) and subsequent inhibition of the sodium-chloride transport mechanisms. As a result, active chloride secretion occurs throughout the intestine. The accumulation of isotonic fluid in the small intestine exceeds the absorptive capacity of the large intestine, producing the characteristic isotonic, bicarbonate-rich stool[9].

Clinical Manifestations

The incubation period may vary from a few hours to as long as 5 days, but is typically 48 to 72 hours[2]. Most cases are mild and clinically indistinguishable from other causes of gastroenteritis[4]. Severe cases are associated with the production of massive quantities of watery diarrhea often exceeding one liter per hour.

The degree of dehydration determines the severity of clinical symptoms. Severe sequelae include cardiac arrhythmias, acute renal failure, and cardiovascular collapse.

Physical findings reflect loss of intravascular fluid and include orthostasis, poor skin turgor, hypotension, tachycardia and Kussmaul respirations.

Laboratory abnormalities include hemoconcentration, hyponatremia, hypokalemia, metabolic acidosis, elevated blood urea nitrogen, creatinine and plasma protein concentration.

Diagnosis

The diagnosis of cholera is suspected with the acute onset of profuse, watery diarrhea associated with marked dehydration. The simplest technique of the direct stool examination with dark-field microscopy reveals *Vibrios* with characteristic helical motility patterns.

Immobilization by adding Group 0-1 antisera is confirmatory, if available[6]. Leukocytes are not seen on methylene blue stain. Stool culture is best performed on selective media such as MacConkey's, Monsur's, or TCBS (thiosulfate-citrate-bile salt-sucrose) agar. Following incubation, suspected *Vibrio* colonies are confirmed by adding Group 0-1 type specific antisera. Differentiation between El Tor and Classical biotypes requires further tests for phage-suceptibility, hemolysin-production, and Polymyxin B-sensitivity.

Acute infection leads to a rise in vibriocidal and antitoxin antibody titers. Titers are elevated by the 5th day of infection, peak near the 10th day, and decline over a 6-month period[2]. A marked rise in antibody titer in acute and convalescent serum is highly indicative of cholera[6].

In non-epidemic settings, the differential diagnosis of choleraic diarrhea includes other pathogens such as enterotoxigenic *E. coli*, rotavirus and non-01 *V. cholera*. Rarely, vasoactive, intestinal, polypeptide-secreting tumors (VIPomas) produce choleraic diarrhea.

Treatment and Prognosis

Prompt replacement of intravascular volume and electrolytes is the primary goal of therapy. In severely hypovolemic patients, intravenous rehydration is necessary.

Electrolyte replacement, including potassium and bicarbonate, should parallel stool electrolyte losses. Oral tetracycline therapy should be instituted following rehydration to shorten disease course. Prophylaxis, however, is not recommended.

Promptly treated, cholera has a mortality rate of less than 1%[5]. Mortality of untreated cases, however, may approach 50% which emphasizes the significance of early recognition and treatment.

Conclusion

Although rare in Hawaii, cholera should be considered as a diagnostic possibility in the setting of acute, profuse secretory diarrhea, regardless of risk factors. At the time of this writing, the source of this isolated case of cholera remains obscure, and only one additional, unrelated case has been reported.

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