CASE REPORTS

Refer to: Platia E, Vosti KL: Noncholera vibrio septicemia. West J Med 132:354-357, Apr 1980

Noncholera Vibrio Septicemia

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NONCHOLERA VIBRIOS (NCV), sometimes called nonagglutinable vibrios, are classified microbiologically as *Vibrio cholerae,* and are in fact biochemically indistinguishable.[1] They are differentiated by the inability of noncholera vibrios to agglutinate in vibrio group I antiserum;[2] *V parahaemolyticus, V alginolyticus* and other halophilic vibrio species are biochemically distinct. Clinical disease caused by NCV has been reported infrequently. A recent review from the Center for Disease Control compiled a total of 28 cases of patients with isolates, mostly from the stool, identified as noncholera vibrio.[3] Hughes and coworkers noted that the incidence of infection with NCV appeared to be rising in the United States over the past decade, perhaps related to ever increasing foreign travel and other factors.[3] We report the case of a patient with chronic lymphocytic leukemia in whom noncholera vibrio septicemia developed upon return from a trip to the Far East.

Report of a Case

A 67-year-old man with a six-year history of chronic lymphocytic leukemia was admitted to hospital for evaluation of fever, chills and left-sided facial pain. Except for a long history of peptic ulcer disease, with a partial gastrectomy in 1965, he was in good health until 1972, at which time the diagnosis of chronic lymphocytic leukemia was made. Treatment without chemotherapy was begun and the patient did well until 1977, when administration of chlorambucil and prednisone was initiated because of a leukemic, pulmonary infiltrate. The patient's condition improved. In late 1977, he noted the occurrence of frequent furuncles on his trunk and extremities and had one episode of facial cellulitis. Analysis of immunoglobulin disclosed hypogammaglobulinemia, with a substantial decrease in IgG and IgA (γ-globulin 300 mg, IgG 200 mg [normal 800 to 1,800 mg] and IgA 25 mg [normal 90 to 450 mg]). Skin tests with mumps, *Candida, Trichophyton* and tuberculin antigens showed him to be anergic. Monthly intramuscular injections of γ-globulin were begun. In late May 1978, paranasal sinusitis developed with pronounced facial pain and purulent nasal drainage from which *Staphylococcus aureus* was isolated. He was treated with oral administration of dicloxacillin for three weeks with apparent resolution.

In June 1978 the patient received a ten-day cycle of chlorambucil and prednisone before embarking on a three-week pleasure trip to Hong Kong, Taiwan and the Philippines. A month before leaving he received cholera and smallpox immunizations. On June 30, 1978, while in the Philippines, he noted the onset of loose, liquid, brown stools, occurring four to six times per day. He said that he did not eat raw foods but admitted to frequent meals of seafood and ad libitum consumption of local water. His wife, who accompanied him and ate a similar diet, remained well. Left-sided facial pain and tenderness had returned shortly after departing on his trip and continued to grow worse.

Upon his return to California on July 4, 1978, he went directly to the hospital for admission, as he felt that his paranasal sinusitis had returned. Although low-grade diarrhea was still present and unabated, he did not consider it to be a major problem. On admission he appeared chronically ill and emaciated, and frequently complained of pain in the area of the paranasal sinuses. Vital signs were a temperature of 38.3°C (100.9°F), pulse rate of 100 and respiratory rate of 20 per minute and blood pressure of 130/65 mm of mercury. A physical examination disclosed bilateral percussion tenderness over the frontal and maxillary sinuses and bilateral purulent nasal dis-

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Submitted, revised, July 3, 1979.

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charge, the left side being greater than on the right. Lymph nodes in the axillary and inguinal regions were moderately enlarged. Examination of the chest and heart showed no abnormalities. The abdomen was soft and not tender, with audible bowel sounds and a palpable spleen 5 cm below the left costal margin. On neurological examination the patient gave sluggish responses but he was oriented and without focal signs.

Laboratory studies on admission included a hematocrit of 33 percent, and a leukocyte count of 10,000 per cu mm with 3 percent bands, 25 percent polymorphonuclear cells and 72 percent lymphocytes. Automated SMA-6 and SMA-12 profiles were within normal limits. Analysis of urine, an x-ray study of the chest and an electrocardiogram were similarly unremarkable. Sinus x-ray studies showed opacification of both maxillary sinuses with air-fluid levels. Gram stain of the nasal discharge showed many polymorphonuclear cells and Gram-positive cocci in clumps. The stool was liquid, brown and guaiac-negative, fecal leukocytes were absent, and no ova or parasites were seen.

A preliminary diagnosis of staphylococcal sinusitis was made. After cultures of blood, stool and nasal discharge were obtained, the patient received nafcillin intravenously, 12 grams per day in six divided doses. Bilateral lavage of the maxillary sinuses was done, with drainage of much purulent material. Cultures of the sinus drainage grew *S aureus,* blood cultures were negative and stool cultures were reported as negative for enteric pathogens. Within 24 hours his fever defervesced, and after several lavages of his sinuses he felt much improved. The low-grade diarrhea persisted in hospital, and on hospital day 4 the patient again began to have a low-grade fever. An x-ray study of the abdomen was remarkable only for several calcified gallstones, and several stool cultures were again reported as negative for enteric pathogens. On the ninth hospital day he became febrile with a temperature of 39.5°C (103.1°F) and pronounced chills, rigors and diffuse abdominal cramps. Chloramphenicol was added to his regimen of intravenous administration of nafcillin, after several blood cultures were drawn and a spinal puncture done. Examination of the spinal fluid gave normal values and a culture was sterile. The following day, both blood cultures grew a vibrio species biochemically identical to *Vibrio cholerae,* but nonagglutinable in 0:1 antiserum.[6] These results were confirmed by the county and state laboratories. The organism was sensitive to clindamycin, ampicillin, chloramphenicol, tetracycline, gentamicin and tobramycin. Within 24 hours of the initiation of therapy with chloramphenicol, the patient became afebrile, without abdominal pain and with resolution of his diarrhea. Shortly thereafter, numerous stool cultures were taken again in repeated attempts to isolate noncholera vibrios. These were unsuccessful. Nafcillin therapy was discontinued after a 14-day course, and chloramphenicol was administered for two weeks. Tetracycline was not given because of a reported allergic reaction in the past. The patient remained free of symptoms for several days after discontinuation of antibiotics, and was discharged. At a one-month follow-up visit to the clinic, he was doing well.

Discussion

Dutta and co-workers[4] first reviewed the choleragenic nature of certain nonagglutinable strains of *V cholerae* (NCV) in 1963, and were able to induce a cholera-like disease with them in infant

TABLE 1.—*Clinical Features of Patients With Noncholera Vibrio Septicemia*

	Patient (Reference)			
	1 (Present Report)	*2 (Hughes[3])*	*3 (Hughes[3])*	*4 (Hughes[3])*
Age/sex	67/M	72/M	64/M	56/M
Residence	California	Kentucky	North Carolina	Texas
Exposure to NCV	Travel to Philippines	Salt water	Salt water	Unknown
Diagnosis	Diarrhea, fever	Pneumonia, Gram-negative sepsis	Cellulitis, meningitis, Gram-negative sepsis	Gram-negative sepsis
Associated diseases	Chronic lymphocytic leukemia	Acute monocytic leukemia	Severe peripheral vascular disease	Cirrhosis
Treatment	Antibiotics	Antibiotics, steroids	Antibiotics, steroids	Unknown
Outcome	Survived	Died	Died	Died

NCV = noncholera vibrios

rabbits. McIntyre and colleagues[5] in 1965 reported a series of 19 patients at the Cholera Research Laboratory in Pakistan with NCV isolated from their stools. Some patients presented with a syndrome of fulminant diarrhea, some with a cholera-like illness with voluminous, watery stools, requiring intravenous fluid replacement therapy, and others presented with a mild illness requiring no therapy. Similarly, in the report by Hughes and co-workers[3] on isolates of NCV which had been referred to the Center for Disease Control, most of the patients had an acute diarrheal illness with positive stool cultures, and survived. However, three of their patients had positive blood cultures for NCV and all died; one of these patients was reported previously in 1974. Of interest, all three of the patients with bacteremia had a significant and chronic associated disease, including one man with acute monocytic leukemia. The clinical features of these three patients are compared with those of our patient in Table 1.

Our patient, too, presented with an acute diarrheal syndrome of low-grade nature of a week's duration though his primary complaint was facial pain referable to an apparent paranasal sinusitis. Treatment directed toward the *S aureus* that had been obtained from his sinus discharge was followed by improvement of the sinusitis. However, the low-grade diarrhea and crampy abdominal pain continued in hospital, though not particularly impressive in nature. However, a week later, after multiple negative stool cultures, the patient appeared clinically septic, with high fever and rigors, and NCV was grown from several blood cultures. It is difficult to explain why the NCV organism could not be isolated from the patient's stool at any time throughout his illness. One possibility is that NCV was indeed present in the stool but was not identified in the laboratory. Most strains grow on MacConkey agar in 18 to 24 hours, but form minute, colorless colonies which can be overlooked.[6] After the NCV was isolated from the patient's blood, special efforts were made with selective thiosulfate-citrate-bile salts-sucrose media to culture the organism from the stool, but without success—perhaps because antibiotics had been administered previously. It should be noted that the organism might have been harbored in the patient's diseased gall bladder. Some evidence exists that in chronic carriers of *Vibrio cholerae,* the organism may be sequestered in a diseased gall bladder with stones.[7]

Also of interest was the continued low-grade diarrhea for two weeks before our patient's episode of sepsis, rather than an acute, short bout of voluminous diarrhea. This may have been related to the patient's status as a compromised host, as discussed below. He did appear to respond adequately to antibiotic therapy with chloramphenicol, with defervescence and gradual resolution of his diarrhea. The role of antibiotics in the treatment of noncholera vibrio infections remains to be established clearly; however, appropriate antibiotics, particularly tetracycline, have been shown to decrease the severity and duration of symptoms in patients with cholera, and it has been suggested that they may have some effect on intestinal infections caused by NCV.[3,8]

Several factors might have contributed to our patient's status as a compromised host. First, his general nutritional state was poor, with chronic anorexia and weight loss. Second, the patient showed evidence of depressed T cell and B cell function, exhibiting anergy to all skin tests and hypogammaglobulinemia, with substantially depressed IgA and IgG. Secretory IgA coproantibody is thought by some to be involved in local antibacterial immunity in infections with *Vibrio cholerae.*[7] It seems reasonable to assume that our patient's secretory antibody might have been quite low. The effectiveness of the cholera vaccine is uncertain, however, because of his hypoglobulinemia it is likely that he may not have responded to the vaccine anyway. Finally, the patient's previous partial gastric resection for peptic ulcer disease and his continued chronic use of antacids may have increased his predisposition to enteric bacterial diseases. The potential importance of the antibacterial effect of gastric acid in the prevention of enteric bacterial diseases, including cholera, has been observed in volunteers in whom a decrease in the size of the inoculum required for infection followed a decrease in gastric acidity with sodium bicarbonate.[8]

Summary

We report a case of noncholera vibrio septicemia of presumed gastrointestinal origin in a man with chronic lymphocytic leukemia who became ill while on a trip to the Far East. His illness was characterized by low-grade diarrhea and abdominal cramps, and septicemia with sudden high fever, chills, and rigors developed two weeks after the onset of symptoms. The occurrence and presentation of his disease may have been related to his leukemia and its treatment, poor nutritional

state, depressed T cell and B cell function, or previous partial gastrectomy. He responded well to antibiotic therapy with chloramphenicol and general supportive measures. To our knowledge, he represents only the fourth reported case of noncholera vibrio septicemia, and is the only such case to have survived.

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Refer to: Machina T, Marcus R, Levin SR: Inhibition of glucagon secretion by diphenylhydantoin in a patient with glucagonoma. West J Med 132:357-360, Apr 1980

Inhibition of Glucagon Secretion by Diphenylhydantoin in a Patient With Glucagonoma

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DIPHENYLHYDANTOIN (Dilantin, phenytoin, DPH) has been shown to inhibit glucagon secretion in vitro.[1] The drug also inhibits insulin secretion in vitro and in humans.[2-7] The glucagonoma syndrome is characterized by dermatitis, stomatitis, elevated plasma glucagon levels, abnormal glucose tolerance, weight loss and anemia.[8,9] The effects of DPH therapy were investigated in a patient with surgically documented glucagon-producing tumors and substantially elevated levels of glucagon in serum.

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Supported by grants from the Veterans Administration, the American Diabetes Association, Southern California Affiliate, and National Institutes of Health, grant AM 21031.

Submitted, revised, August 28, 1979.

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ABBREVIATIONS USED IN TEXT

DPH = diphenylhydantoin
GLI = glucagon-like immunoreactive

Report of a Case

A 49-year-old woman entered the hospital with a six-week history of extensive exfoliative, migratory dermatitis on the lateral aspects of her extremities, buttocks, back and face. She had lost weight, her mental status had deteriorated, and intermittent diarrhea, generalized weakness and stomatitis had occurred. A glucose tolerance test at another hospital showed a fasting plasma glucose level of 130 mg per dl and a two-hour postprandial value of 200 mg per dl. There was no family history of diabetes or endocrine disorders.

The physical examination showed a normotensive, afebrile, ill-looking woman with an extensive, coalescing, erythematous rash characterized by hyperpigmentation, scaliness and areas in various stages of healing. Results of a fundoscopic examination were normal. There were oral fissures and moderately severe glossitis. There were no abdominal masses. The legs were slightly edematous.

Findings of initial laboratory studies included a fasting plasma glucose level of 137 mg per dl, normochromic anemia and levels of serum lipids within normal range. The urine was positive for ketones but showed no glycosuria. Findings of baseline endocrine studies, including thyroid and adrenal functions, were normal. Biopsy of a skin lesion from the forearm showed a nonspecific perivascular, lymphocytic infiltrate with edema and hyperkeratosis. Fasting plasma glucagon level was 3,612 pg per dl (basal measurement in six normal subjects was 162 ± 21 pg per dl [mean $\pm$ SD]), using a pancreatic glucagon-specific antibody,