Yonsei Medical Journal
Vol. 23, No. 2, 1982

Vibrio vulnificus Septicemia in a Patient with Liver Cirrhosis

Yunsop Chong*, Mi Young Park*, Samuel Y. Lee*
Kwan Sik Kim and Sang In Lee****

Departments of Clinical pathology and Internal Medicine**,*
Yonsei University College of Medicine, Seoul, Korea

Vibrio vulnificus was isolated from a blood culture of a 41-year-old male patient with liver cirrhosis. He had eaten raw fish one day prior to the onset of clinical symptoms which included fever, chills, diarrhea and hypotension. He also developed cellulitis of the right leg which developed into a necrotic ulcer.

The isolate was a slightly curved gram-negative bacillus and the colony morphology on a TCBS plate was similar to that of *V. parahaemolyticus.* Acid production from lactose was detected after 2 days of incubation. Other biochemical tests showed typical reactions of *V. vulnificus.* The isolate was susceptible to all of the tested antibiotics except to clindamycin, colistin and penicillin G.

Key Words : Septicemia, *V. vulnificus* infection.

Vibrio vulnificus is a recently recognized species of halophilic gram-negative bacilli found in marine organism and in sea water. This organism is known to cause two forms of clinical infection, septicemia and wound infection (Hollis *et al.*, 1976).

The literature on these infections is sparse (Blake *et al.*, 1979). In Korea, Goo *et al.* (1983) isolated the organism from five septicemic patients during the period of 1980 to 1981. In August 1982, we isolated the organism from a blood culture of a patient with liver cirrhosis who had eaten raw fish.

Most of the reported cases were related to raw oyster consumption, crab bites or contamination of wound with sea water. The source of infection was not ascertained in the cases of Goo *et al.* (1983). In our case the source was considered to be the raw fish.

In this report the clinical presentation of the patient and microbiological characteristics of the isolate are presented.

Received November 5, 1982

CASE REPORT

A 41-year-old male (unit no. A1091964) was transfered to our hospital from a private hospital on August 9, 1982 because of hypotension and hematemesis. The past history of the patient included an admission due to liver cirrhosis 2 years previously. He was an inhabitant of Seoul city and had traveled to the east coast

of Korea in July, but had no contact with sea water at that time. The present illness started with eating raw fish at a restaurant in Seoul two days prior to admission.

One day prior to admission at this hospital, he was admitted to a private hospital because of chills, fever, diarrhea and gum bleeding. He had watery and yellowish diarrhea five times on this day. Because of a blood pressure of 60/40 mm Hg and hematemesis he was transfered to our hopital on August 9, 1982.

On admission, physical examination revealed minimal ascites and mild abdominal tenderness, both direct and rebound. Spider angioma were noted on the upper chest wall. The blood pressure was 75/45 mm Hg with a heart rate of 108/min. The skin was warm and dry. Body temperature was 39.3°C. A chest X-ray showed moderate splenomegaly and a possible mass in the left upper abdomen.

On admission, peripheral blood findings were hemoglobin 13 g/100 ml, hematocrit 30%, WBC count 13,300/μl with differential count of 62% segmented neutrophils, 28% bands, 7% lymphocytes and 3% immature granulocytes. Platelet count was 53,000/μl. Some of the abnormal blood chemistries were total protein 6.3 g/100 ml with 1.6 g albumin, total bilirubin 4.0 mg/100 ml, alkaline phosphatase 50 IU/l, aspartate transpeptidase 190 IU/1, alanine transpeptidase 86 IU/1 and creatinine 4.4 mg/100 ml. Prothrombin times were between 18.3 to 16.9 seconds (28-34% of normal) during the period of August 10 to 21.

A stool culture done on admission did not yield *Salmonella, Shigella, Yersinia, Campylobacter* or *Vibrio*. Two blood cultures were taken on the fourth hospital day. After 24 hours incubation one bottle yielded a gram-negative bacillus which was later identified as *V. vulnificus*.

In addition to supportive care, the patient was on ampicillin for the first 2 hospital days and then on erythromycin and chloramphenicol. On the second hospital day the blood pressure returned to 120/90 mm Hg. On the third hospital day the diarrhea stopped. Body temperature returned to normal on the fifth hospital day (Table 1). On the fifth hospital day both of his legs were found to be edematous and the right leg later developed a necrotic ulcer.

On the 12th hospital day he ruptured an esophageal varix and had profound bleeding. Despite aggressive therapy, including blood transfusions, he expired on the 15th hospital day.

Table 1. Summary of Clinical findings during the first week of illness

Date	Aug 7	8	9	10	11	12	13
Fish consumption	+						
Diarrhea (times)		5	5	4			
Fever (°C)		+	39.3	38	37.8	39.2	37
Chills		+	+				
Bleeding from gums		+					
Blood pressure (mm Hg)		60/40	75/45	120/90			
Blood culture						+	
Leg skin lesion							+

MATERIALS AND METHODS

Two blood samples were taken on the fourth hospital day. Our procedure of blood culture is to draw 10 ml samples, divide them into two equal portions and inoculate each of 50 ml of Tryptic soy broth (TSB, Difco) and 50 ml of Brewer thioglycollate medium (Difco). The cultures were incubated at 35°C and daily inspections were made. Identification of the isolate was made by means of both conventional tests (Lennette *et al.*, 1980) and the API 20E system (Analytab Products, Plainview, N.Y.). The conventional media were supplemented with 1% salt. The inoculum for the API system was suspended in saline. Antimicrobial susceptibility was tested by the Kirby-Bauer disk diffusion method (NCCLS, 1979).

RESULT

After an overnight incubation of the blood cultures one of the TSB bottles showed turbidity and the subculture on a blood agar plate yielded large greenish moist colonies with hemolysis. Colonies on TCBS were green indicating no acid production from sucrose. Colonies on MacConkey agar were colorless. The organism did not grow on mannitol salt agar or on SS agar. The isolate was a slightly curved gram-negative bacillus. Electron microscopy showed a curved bacillus with a long polar flagellum (Fig. 1).

TSI reaction after a 24-hour incubation showed an alkaline slant and acid butt. Motility, indole, and ornithine decarboxylase were all positive on Motility indole ornithine medium. The result of other biochemical tests, observed for up to one week of incubation, were

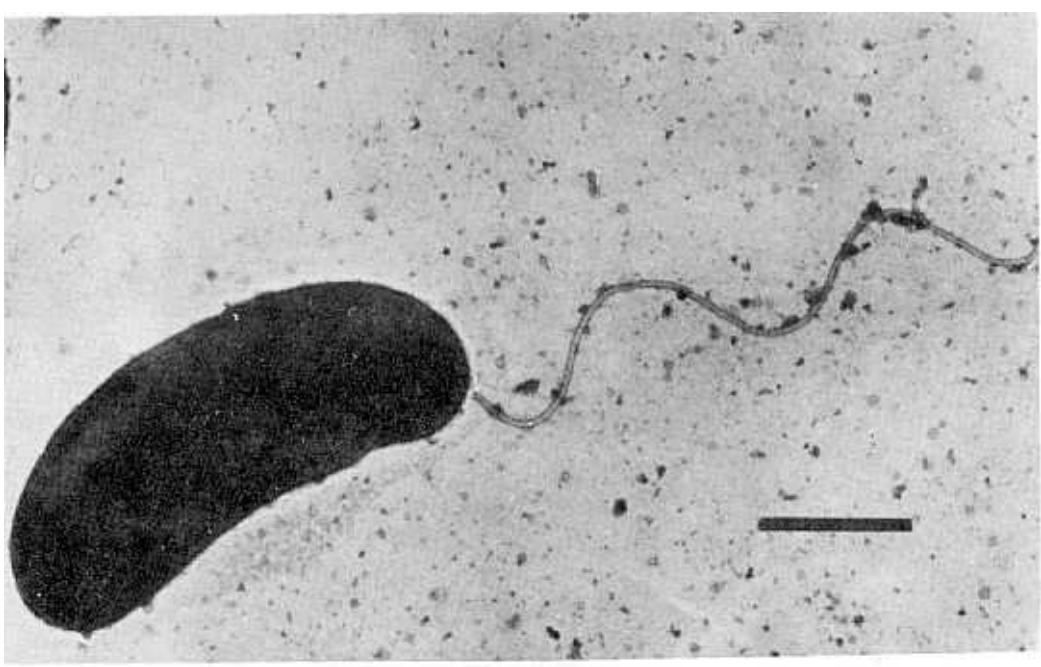

Fig. 1. Electron micrograph of the isolate. Bar equals 1μm.

Table 2. Cultural and biochemical characteristics of *V. vulnificus* isolate

Characteristic	*V. vulnificus*[a]	Isolate 82-8-5033	Characteristic	*V. vulnificus*[a]	Isolate 82-8-5033
H_2S (TSI)	–[b]	–	Lactose	+	+[c]
Urease	–	–	Maltose	+	+
Indole	+	+	Mannitol	d	+
Voges-Proskauer	–	–	Mannose	+	+
Simmons citrate	+	+	Melibiose	d	–
Motility	+	+	Salicin	+	+
Gelatin liquefaction	+	+	Sucrose	–	–
LDC	+	+	Trehalose	+	+
ODC	+	+	Xylose	–	–
ADH	–	–	ONPG		
Gas from glucose	–	–	Catalase	+	+
Acid from	+	+	Nitrate reduction	+	+
Arabinose	–	–	Oxidase	+	+
Cellobiose	+	+	Glucose fermentation	+	+
Dextrin	+	+	NaCl tolerance	+	+
Fructose	+	+	0%	–	–
Galactose	+	+	6%	+	+
Glucose	+	+	8%	–	–
Glycerol	d	+			

[a] Adapted from Hollis et al., 1976 and Lennette et al., 1980.

[b] +, 90% or more positive; –, 90% or more negative; d, + or –.

[c] After 2 days incubation.

as shown in table 2. Based on these findings, the isolate was identified as *V. vulnificus*. This identification was later confirmed by Dr. George K. Morris of the Center for Disease Control, USA.

The isolate was susceptible to ampicillin, carbenicillin, cephalothin, cefamandole, cefoxitin, chloramphenicol, erythromycin, tetracycline, amikacin, kanamycin, tobramycin, and co-trimoxazole. It was resistant to clindamycin, colistin and penicillin G (19mm).

DISCUSSION

Besides *V. cholerae*, *V. parahaemolyticus* is the only other well known vibrio to cause gastroenteritis. Other recognized vibrio infections are wound infection and septicemia caused by *V. parahaemolyticus* (Roland, 1970; Zide *et al.*, 1974; Porres & Fuchs, 1975) and *V. alginolyticus* (Ryan, 1976; Pezzlo *et al.*, 1977; Hiratsuka *et al.*, 1980), bacteremia by *V. metschenikovi* (Jenn-Jaques *et al.*, 1981) and gastroenteritis by *V. mimicus* (Davies *et al.*, 1981) and *V. hollisae* (Hickman *et al.*, 1982).

It was Hollis *et al.*(1976) who first studied the previously unnamed *V. vulnificus*. It was first called lactose-positive (Lac +) vibrio and later it was named *V. vulnificus* (Farmer, 1979). The fact that the CDC received only 48 isolates during the period of 1964 to June 1977, suggests that *V. vulnificus* infections are not very common (Blake *et al.*, 1979). This infection has also

been reported in Japan and Belgium (Martens *et al.*, 1979; Blake *et al.*, 1980). In Korea, Goo *et al.* reported 5 cases in 2 years, and our case is probably the sixth.

It is known that this organism causes two types of infection. The septicemic form is mostly seen in males over 40 years of age with a history of excessive alcohol consumption and an underlying hepatic disease such a cirrhosis or hepatitis. These are conditions which reduce host resistance to bacterial infections (Tisdale, 1961; Anderson, 1975). Most of the infections are related to raw oyster consumption. The second form is wound infection caused by a crab bite or by sea water contamination of wound in an otherwise normal young person (Blake *et al.*, 1979). Castillo *et al.* (1981) reported secondary septicemia in two aged persons with underlying illnesses.

Our patient was typical in that he was a 41-year-old male and had liver cirrhosis. The infections occur in summer, as in our case. The source of infection was uncertain in the 5 cases of Goo *et al.*, (1983). In our case, the epidemiological history was obtained from the patient. He had no recent sea water contact or oyster ingestion, but he had taken raw fish one day prior to the onset of his illness. We do not know of any other case which was caused by eating raw fish. In Korea, raw oyster is a popular dish and raw fish is increasing in popularity. Alcohol consumers are particularly fond of these dishes when they drink even at inland cities like Seoul. In such a setting, together with the prevalence of hepatic diseases in Korea, it can be expected that more of these infections could exist in this country. Therefore our clinicians should be aware of this infections, while our microbiologists should be prepared for the identification of this organism.

V. vulnificus has been isolated from the sea water of Guam (Blake *et al.*, 1980). Kelly and Avery (1980) isolated this organism from 36% of sea water samples in the Gulf of Mexico. The organism seems as prevalent as *V. parahaemolyticus* in sea water. *V. parahaemolyticus* infection is very prevalent in Japan and in Korea. This infection usually occurs following eating raw fish, but we have experienced an outbreak which followed eating soy sauce dressed crab. If *V. vulnificus* is as prevalent as *V. parahaemolyticus*, then raw oyster, fish and crab might well be a source of infection .

In our patient, diarrhea started 12 hours after eating raw fish. The diarrhea occured 4 to 5 times a day and lasted for 3 days. Fever of up to 39.3°C continued for 5 days. According to Blake *et al.* (1979), frequently observed clinical features are fever (92%), chills (82%), and hypotention (systolic pressure $\leqslant$80 mm Hg). In our patient systolic pressure of 60 to 75 mm Hg continued for 2 days. He had gum bleeding and hematemesis. His platelet count was 53,000/μl. Decreased platelet count in the septicemic form of *V. vulnificus* infection is thought to be due to disseminated intravascular coagulation (Blake *et al.*, 1979). In our case the prothrombin time remained prolonged throughout the hospitalization, but further studies on the coagulation problem were not done. Death was apparently due to bleeding from ruptured esophageal varices.

Blood cultures were taken on the fifth day of the illness. Among the 4 bottles only one yielded growth. The growth was detected after one day of incubation. Because of the hemolytic greenish large colonies on subculture blood agar, we at first suspected *Aeromonas hydrophila*. Because of poor growth on biochemical media without added salt it became apparent that it was not *Aeromonas*. It is reported that *V. vulnificus* is frequently mistaken for *V. parahaemolyticus*, *A. hydrophila*, *Pseudomonas*, *Pleisiomonas shigelloides* and

Serratia (Blake *et al.*, 1979).

Besides green colonies on TCBS, our isolate produced an alkaline slant on TSI which is characteristics of *V. parahaemolyticus*. Another difficulty in the idenification was that the N/F system (Flow Laboratories Inc., McLeen) and Oxi/Ferm system (Roche Diagnostics, Nutley) did not list this organism. Previous misidentifications were considered due to unsettled classification (Fernandez and Pankey, 1975). We were able to differentiate the isolate from other vibrios by demonstrating lactose fermentation, failure to ferment sucrose and slightly lower salt tolerance than *V. parahaemolyticus*.

Antimicrobial susceptibility of our isolate was quite similar to the reports from America. The susceptibility of the isolates of Goo *et al.* (1983) was slightly different from ours in that theirs were resistant to carbenicillin, cephalothin, and gentamicin.

ACKNOWLEDGEMENTS

We thank Dr. George K. Morris, CDC for his confirmation of our identification of the isolate.

REFERENCES

Anderson BR: *Host factors causing increased susceptibility to infection in patients with Laennec's cirrhosis. Ann. NY Acad Sci 252-348-352, 1975*

Blake PA, Merson MH, Weaver RE, Hollis DG, Heublein PC: *Disease caused by a marine vibrio. Clinical characteristics and epidemiology. N Engl J Med 300:15, 1979*

Blake PA, Weaver RE, Hollis DG,: *Diseasesof humans (other than cholera) caused by vibrios. Ann Rev Microbiol 34:341-367, 1980*

Castillo LE, Winslow DL, Pankey GA: *Wound infection and septic shock due to Vibrio vulnificus. Am J Trop Med Hyg 30:844-848, 1981*

Davis BR, Fanning GR, Madden JM et al: *Characterization of biochemically atypical Vibrio cholerae strains and designation of a new pathogenic species, Vibrio mimicus. J Clin Microbiol 14:631-639, 1981*

Farmer JJ III: *Vibrio (Beneckea) vulnificus, the bacterium associated with sepsis, septicemia, and the sea. Lancet 2:903, 1979*

Fernandez CR, Pankey GA: *Tissue invasion by unnamed marine vibrios. JAMA 233:1173-1176, 1975*

Goo JS, Kim DW, Suk JS et al: *Lactose fermenting Vibrio (Vibrio vulnificus) septicemia-Report of five cases-. J Kor Soc Pathol 16: 463-469, 1983*

Hickman FW, Farmer JJ, Hollis DG et al: *Identification Vibrio hollisae sp. nov. from patients with diarrhea. J Clin Microbiol 15:395-401, 1982*

Hiratsuka M, Saitoh Y, Yamane N: *The isolation of Vibrio alginolyticus from a patient with acute enterocolitis. Tohoku J Exp Med 132: 469-472, 1980*

Hollis DG, Weaver RE, Baker CN et al: *Halophilic Vibrio species isolated from blood cultures. J Clin Microbiol 3:425-431, 1976*

Jenn-Jacques W, Rajashekaraiah KR, Farmer JJ et al: *Vibrio metschenikovii bacteremia in a patient with cholecystitis. J Clin Microbiol 14:711-712, 1981*

Kelly MT, Avery DM: *Lactose-positive Vibrios in sea water a cause of pneumonia and septicemia in a drowing victim. J. Clin Microbiol 11:278-280, 1980*

Martens A, Nagler J. Hansen W et al: *Halophilic, lactose-positive Vibrio in a case of fatal septicemia. J Clin Microbiol 9:233-235, 1979*

Lennette EH, Balows A, Hausler WJ Jr et al: *Manual of clinical microbiology. 3rd ed, Am Soc Microbiol, Washington, 1980*

NCCLS: *Performance standards for antimicrobic susceptibility test. 2nd ed, National Committee for Clinical Laboratory Standards, Villanova, 1979*

Pezzlo M, Valter PJ, Burns MJ: *Wound infection associated with Vibrio alginolyticus. Am J Clin Pathol 71:476-478, 1979*

Porres JM, Fuchs LA: *Isolation of Vibrio parahaemolyticus from a knee wound. Clin Orthopaedics Related Res 106:245-247, 1975*

Roland FP: *Leg gangrene and endotoxin shock due to Vibrio parahaemolyticus-an infection acquired in New England coastal waters. N Engl J Med 282:1306,1970*

Ryan WJ: *Marine vibrios associated with superficial septic lesions. J Clin Pathol 29:1014-1015, 1976*

Tisdale WA: *Spontaneous colon bacillus bacteremia in Laennec's cirrhosis. Gastroenterology 40:141-148, 1961*

Zide N, Davis J, Ehrenkranz NJ: *Fulminating Vibrio parahaemolyticus septicemia. A syndrom of erythema multiforme, hemolytic anaemia, and hypotension. Arch Intern Med 133:479-481, 1974*