

## CASE REPORT

# *Aeromonas hydrophila* Sepsis Mimicking *Vibrio vulnificus* Infection

Se Young Park, M.D.<sup>1</sup>, Hyun Min Nam, M.D.<sup>1</sup>, Kun Park, M.D., Ph.D.<sup>1</sup>,  
Seok Don Park, M.D., Ph.D.<sup>1,2</sup>

<sup>1</sup>Department of Dermatology, and <sup>2</sup>Institute of Wonkwang Medical Science, Wonkwang University School of Medicine, Iksan, Korea

*Aeromonas hydrophila* is a facultatively anaerobic, asporogenous gram-negative rod that has often been regarded as an opportunistic pathogen in hosts with impairment of a local or general defense mechanism. A 68-year-old alcoholic woman presented with shock and gangrene on the right arm. At first, her clinical presentations were severe painful erythematous swelling that worsened within a few hours with development of gangrene, edema, and blisters. Bullous fluid and blood cultures yielded *A. hydrophila*. Histopathological findings of sections obtained from the vesicle revealed subepidermal vesicles; necrosis of the epidermis, papillary dermis, and subcutaneous fat; and massive hemorrhage in the subcutis. Despite all efforts to save the patient, she died 8 hours after admission. Clinical features of *A. hydrophila* sepsis resemble those of *Vibrio vulnificus* sepsis. Therefore, in addition to the case report, we compared the cultural, biochemical, and morphological differences between *A. hydrophila* and *V. vulnificus* for facilitation of early and accurate identification of the causative agent. (Ann Dermatol 23(S1) S25 ~ S29, 2011)

**-Keywords-**

*Aeromonas hydrophila*, Microbiological techniques, *Vibrio vulnificus*

Received July 1, 2010, Revised August 25, 2010, Accepted for publication August 25, 2010

\*This paper was supported by Wonkwang University in 2011.

\*This paper was presented at the 6th Japan-Korea Joint Meeting of Dermatology.

**Corresponding author:** Seok Don Park, M.D., Ph.D., Department of Dermatology, Wonkwang University Hospital, 344-2 Shinyong-dong, Iksan 570-711, Korea. Tel: 82-63-859-1601, Fax: 82-63-842-1895, E-mail: sdpark@wonkwang.ac.kr

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## INTRODUCTION

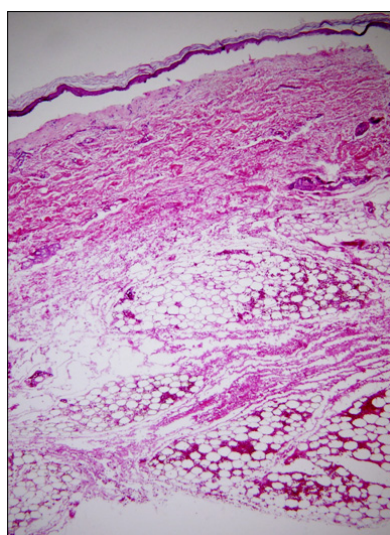
*Aeromonas* species are widely distributed in stagnant and flowing fresh waters, at the interface of sea water and fresh water, and in sewage. They have also been isolated from soil and foodstuffs<sup>1</sup>. *Aeromonas hydrophila* (*A. hydrophila*) has often been recognized as an opportunistic pathogen in hosts with impairment of a local or general defense mechanism. According to the literature, the following 4 categories of infection have been described: cellulitis, acute diarrheal disease, sepsis, and other infections<sup>2,3</sup>. Here, we report on a clinical syndrome resulting from infection with *A. hydrophila*, which was indistinguishable from the one usually associated with infection due to *Vibrio vulnificus* (*V. vulnificus*). *V. vulnificus* sepsis is a primary sepsis syndrome that can develop in individuals with preexisting chronic hepatic disease after consumption of raw seafood. It usually occurs during the summer, and, in Korea, it is characterized by high mortality (62.4%)<sup>4</sup>. We conducted a brief comparison of cultural, biochemical, and morphological characteristics between *A. hydrophila* and *V. vulnificus* sepsis for early and accurate identification of the causative pathogen.

## CASE REPORT

In September, a 68-year-old woman visited our emergency department with a 1-day history of tense necrotic vesicobullous lesions over the cyanotic skin of the right arm. On the morning of the admission day, the patient experienced sudden severe pain in the right upper extremity. Over the next several hours, she developed painful erythematous swelling and vesicles, which showed gradual progression to hemorrhagic bullae and ecchymoses. Her medical history was not remarkable; however, she had not undergone regular health checkups. In addition, she had a



**Fig. 1.** Edema, cyanosis, and dusky purplish discoloration with necrotic tense blisters on the right upper extremity.



**Fig. 2.** Biopsy specimen obtained from the vesicle revealed subepidermal vesicle, necrosis of the epidermis, papillary dermis and subcutaneous fat, and massive hemorrhages in the subcutis (H&E,  $\times 40$ ).

20-year history of alcohol abuse (750 ml of Korean rice wine per day). However, whether or not she had eaten raw fish was not certain.

Physical examination revealed slightly icteric sclera and edema, cyanosis, and dusky purplish discoloration with necrotic tense vesicobullous lesions on the right arm (Fig. 1). She became comatose while being transferred from a private clinic to our hospital. Her pupils were completely dilated, and her blood pressure could not be checked because of low pressure. She was in a state of cardio-

**Table 1.** Cultural characteristics of *Aeromonas hydrophila* and *Vibrio vulnificus*

Medium	Color of colonies	
	<i>A. hydrophila</i>	<i>V. vulnificus</i>
Blood agar	Greenish gray	Greenish gray
TCBS agar	Yellow	Deep green
BEA agar	Black	No growth
MacConkey agar	Colorless	No growth
EMB agar	Black	No growth
HE agar	Yellow	Deep green
SS agar	Colorless	No growth
Endo agar	Red	Pink

TCBS: thiosulfate-citrate-bile salts-sucrose, BEA: bile esculin azide, EMB: eosin methylene blue, HE: Hektoen enteric, SS: Salmonella-Shigella.

pulmonary arrest. After approximately 30 minutes of active cardiopulmonary resuscitation and medical therapy for treatment of shock, her vital signs became stabilized. After 40 minutes, we started intravenous injection of ampicillin and cephalosporin. However, she died at 1 hour after administration of antibiotic therapy.

Her white blood cell count was  $4,000/\mu\text{l}$  with 50% neutrophils, hemoglobin level was 12.8 g/dl, and platelet count was  $350,000/\mu\text{l}$ . Levels of serum alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase were 326 IU/L, 528 IU/L, and 208 IU/L, respectively. Total serum protein level was 2.9 g/dl, with an albumin level of 1.4 g/dl. Bacterial cultures obtained from blood and bullous fluid were positive for *A. hydrophila*.

A skin biopsy specimen obtained from a vesicle revealed a subepidermal vesicle; necrosis of the epidermis, papillary dermis, and subcutaneous fat; and massive hemorrhage in the subcutis (Fig. 2).

## Bacteriological studies

### 1) Cultural characteristics of *A. hydrophila* and *V. vulnificus*

Using 16 strains of *V. vulnificus* and 1 strain of *A. hydrophila* isolated from blood and/or bullous fluid of patients with primary sepsis, we studied the culture characteristics of the strains on 8 types of media that are commonly used in clinical laboratories. Media used were blood and thiosulfate-citrate-bile salts-sucrose (TCBS) for *Vibrionaceae*, bile esculin azide (BEA) for Group D *Streptococci*, and selective isolation media for *Enterobacteriaceae*, such as MacConkey, eosin methylene blue (EMB), Hektoen enteric (HE), Salmonella-Shigella (SS), and Endo agars. All strains were cultured at  $37^{\circ}\text{C}$  for 24 hours at. Culture results are summarized in Table 1.

## 2) Differences in biochemical characteristics between *A. hydrophila* and *V. vulnificus*

In all, 33 tests were performed for obtaining differential data. We tested 1 *A. hydrophila* strain and 16 *V. vulnificus* strains. Results are summarized in Table 2.

## 3) Morphological differences between *A. hydrophila* and *V. vulnificus*

### Microscopic findings

*A. hydrophila* were gram-negative straight bacilli, whereas

**Table 2.** Biochemical characteristics for differentiation between *Aeromonas hydrophila* and *Vibrio vulnificus*

Test	<i>A. hydrophila</i> *	<i>V. vulnificus</i> (%) <sup>†</sup>
Triple sugar iron		
Butt	Acid	Acid (100)
Slant	Alkali	Alkali (81)
Gas	+	— (0)
Growth in nutrient broth		
0% NaCl	+	— (0)
6.5% NaCl	—	+
Voges-Proskauer reaction	+	(66/34) <sup>‡</sup>
(+1% NaCl, 37°C)		
Arginine dihydrolase	+	— (0)
Ornithine decarboxylase	—	+
Catalase	+	(81)
Acid production from		
Sucrose	+	— (0)
Melibiose	—	+
Lactose	—	(75/12)
		+
		(88)

\*Data from 1 strain, <sup>†</sup>Data from 16 strains, <sup>‡</sup>Numbers in parenthesis show the percentage of strains positive for 1~2 days/percentage of strains positive for ≥3 days.

*V. vulnificus* were gram-negative curved bacilli (Fig. 3).

### Electron microscopic findings

In general, the size of *A. hydrophila* was smaller than that of *V. vulnificus*. *A. hydrophila* had a rough cell wall and a relatively wide periplasmic space, compared with *V. vulnificus* (Fig. 4).

### Antibiotic susceptibility

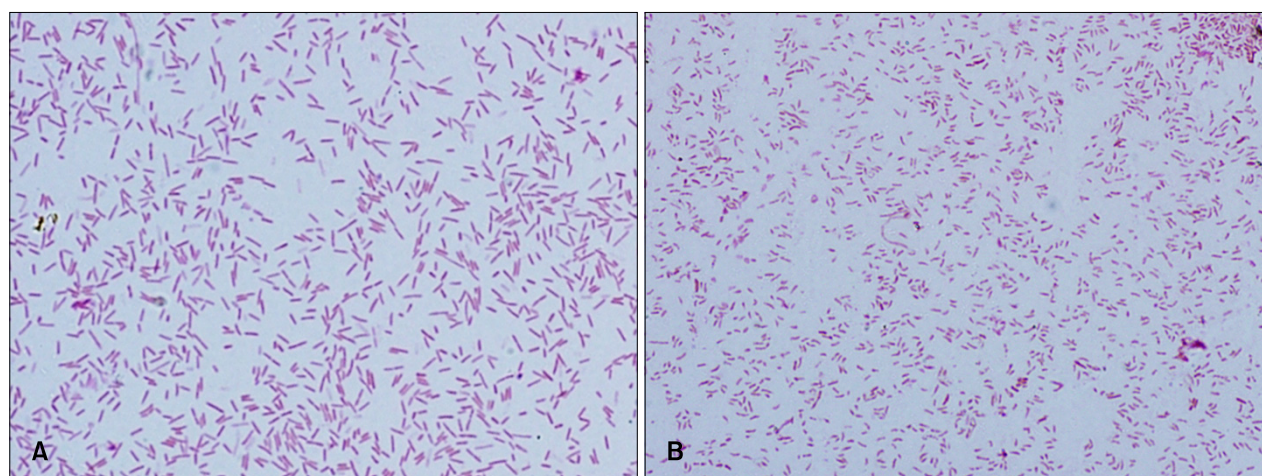
*A. hydrophila* was sensitive to chloramphenicol, cefamandole nafate, netilmicin sulfate, gentamicin, amikacin sulfate, and ceftriaxone sodium and was resistant to ampicillin, carbenicillin, and cephalothin.

*V. vulnificus* (all 16 strains) were sensitive to ampicillin, tobramycin, erythromycin, piperacillin, chloramphenicol, and cephalosporins (third generation).

## DISCUSSION

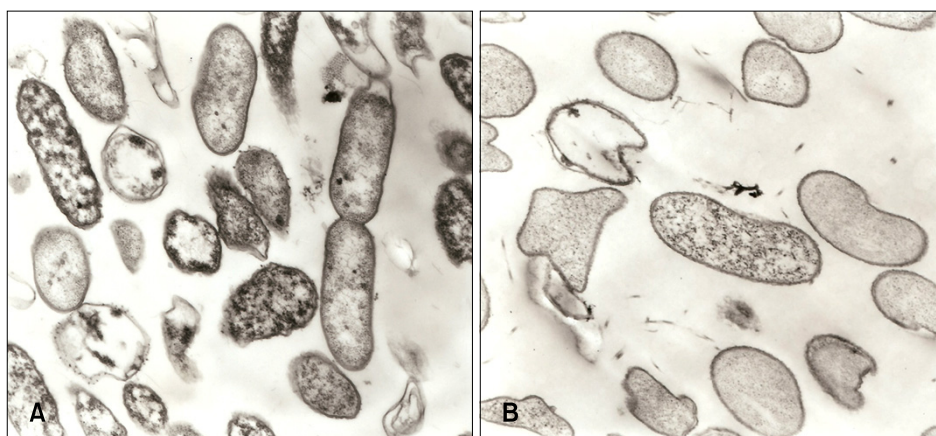
Primary sources of clinical isolates of *Aeromonas* species include stool, wound, abscess, cellulitis, and blood<sup>5</sup>. In a normal human host, infection with *A. hydrophila* may produce mild diarrhea and, occasionally, cellulitis. However, severe *Aeromonas* infection occurs when host defenses are compromised. The majority of patients with *A. hydrophila* sepsis have a history of leukemia, other malignant diseases, or hepatobiliary diseases<sup>6</sup>.

Among the many bacteria responsible for causing sepsis with skin lesions, *V. vulnificus* and *A. hydrophila* have the capacity to cause illness and skin lesions in compromised hosts; the infections caused by these 2 strains are clinically indistinguishable from one another. The clinical features of our patient were similar to those observed in



**Fig. 3.** Gram staining of culture smears of *Aeromonas hydrophila* (A) and *Vibrio Vulnificus* (B) showing gram-negative straight rods and gram-negative curved rods, respectively (Gram stain, ×1,000).





**Fig. 4.** Electron micrograph of *Aeromonas hydrophila* (A) stained with ruthenium red showing straight rods and division septum, compared with the morphology of *Vibrio vulnificus* (B) showing curved bacilli ( $\times 13,000$ ).

patients with *V. vulnificus* sepsis.

In Korea, most patients with *V. vulnificus* infection have preexisting hepatic disease or history of alcohol abuse, and *V. vulnificus* sepsis almost always occurs during the summer (between July and September)<sup>4</sup>. Therefore, because the patient was severely alcoholic and had visited our hospital in September, we diagnosed this patient as having sepsis due to *V. vulnificus*.

Of the many exotoxins produced by *A. hydrophila*, endotoxin and  $\beta$ -hemolysin have been known to contribute to pathologic and cutaneous findings<sup>7,8</sup>. Sepsis caused by *A. hydrophila* and by *V. vulnificus*, despite the many morphological, cultural, and biochemical dissimilarities between the 2 bacterial strains, show clinical similarities with regard to cutaneous lesions, such as hemorrhagic necrosis, edema, blisters, and a fulminant fatal course in patients with a history of alcohol abuse, hepatic disease, and malignant disease.

Gram stain, culture, and biochemical tests are used for identification of *A. hydrophila*. Use of these methods is the best way to confirm diagnosis; however, they are fastidious and time consuming. A polymerase chain reaction (PCR) method that is convenient, rapid, and specific for identification of pathogens has recently been developed<sup>9</sup>. However, due to lack of facilities, this method was not used for our case.

Results of our antibiotic sensitivity test on *A. hydrophila* were consistent with those reported by other researchers<sup>6,10</sup>. Gentamicin, chloramphenicol, and tetracycline would appear to be the treatment of choice. Unlike *V. vulnificus*, *A. hydrophila* is known to be resistant to ampicillin and erythromycin. Since the antibiotic susceptibility patterns of the 2 bacterial strains differ, we recommend the use of chloramphenicol or third generation cephalosporins as the first drug of choice for patients in whom infection caused by one of these two bacteria is suspected.

Some papers have reported on *A. hydrophila* sepsis in the Korean literature<sup>11-13</sup>. Kang et al.<sup>11</sup> evaluated the clinical significance of *Aeromonas* bacteremia in 182 patients. Most cases (75.8%) developed during summer and autumn, and half of the patients (48.9%) suffered from liver cirrhosis. Mortality directly related to *Aeromonas* sepsis was 24.1% and was associated with old age, skin and soft tissue infection, septic shock, and altered consciousness. Ha et al.<sup>12</sup> reported on a patient with alcoholic cirrhosis, and Park et al.<sup>13</sup> reported one who had undergone prolonged hemodialysis. In our case, a 68-year-old patient with a heavy alcoholic history showed skin lesion, sepsis, and comatous mental status, and finally died. Impairment of defense mechanisms, such as lack of significant opsonizing activity against the autologous infecting strain may serve to explain some of the pathogenesis of *Aeromonas* infection on immunocompromised patients<sup>14</sup>.

In conclusion, we have presented a case of an alcoholic woman with sepsis and gangrene caused by *A. hydrophila*, often confused with *V. vulnificus*. Despite clinical similarities between the two strains, distinction of the type of strain responsible for the infection is important. Due to different antibiotic susceptibilities, early and accurate identification of the causative pathogen is essential to achievement of better outcomes.

## REFERENCES

1. Abbott SL. *Aeromonas*. In: Murray PR, Baron EJ, Jorgensen JH, Pfaller MA, Tenover FC, editors. Manual of clinical microbiology. 8th ed. Washington DC: ASM Press, 2003: 701-705.
2. Davis WA 2nd, Kane JG, Garagusi VF. Human *Aeromonas* infections: a review of the literature and a case report of endocarditis. *Medicine (Baltimore)* 1978;57:267-277.
3. Janda JM, Abbott SL. The genus *Aeromonas*: taxonomy, pathogenicity, and infection. *Clin Microbiol Rev* 2010;

- 23:35-73.
4. Park SD, Lee JY, Kim HD, Yoon NH. Clinical study of *vibrio vulnificus* sepsis. Korean J Dermatol 2006;44:696-707.
  5. McCracken AW, Barkley R. Isolation of *Aeromonas* species from clinical sources. J Clin Pathol 1972;25:970-975.
  6. Trust TJ, Chipman DC. Clinical involvement of *Aeromonas hydrophila*. Can Med Assoc J 1979;120:942-946.
  7. Thelestam M, Ljungh A. Membrane-damaging and cytotoxic effects on human fibroblasts of alpha- and beta-hemolysins from *Aeromonas hydrophila*. Infect Immun 1981;34:949-956.
  8. Brenden RA, Huizinga HW. Pathophysiology of experimental *Aeromonas hydrophila* infection in mice. J Med Microbiol 1986;21:311-317.
  9. Trakhna F, Harf-Monteil C, Abdelnour A, Maaroufi A, Gadonna-Widehem P. Rapid *Aeromonas hydrophila* identification by TaqMan PCR assay: comparison with a phenotypic method. Lett Appl Microbiol 2009;49:186-190.
  10. Von Graevenitz A, Mensch AH. The genus *Aeromonas* in human bacteriology report of 30 cases and review of the literature. N Engl J Med 1968;278:245-249.
  11. Kang JM, Kim BN, Choi SH, Kim NJ, Woo JH, Ryu JS, et al. Clinical features and prognostic factors of *Aeromonas bacteremia*. Infect Chemother 2005;37:161-166.
  12. Ha BS, Won YH, Chun IK, Kim YP. Haemorrhagic gangrene of skin caused by *Aeromonas hydrophila*. Ann Dermatol 1989;1:98-101.
  13. Park HJ, Kim HY, Uh Y, Kwon OG, Oh JR. A case of *Aeromonas hydrophila* necrotizing fasciitis in patient on hemodialysis. Infect Chemother 2007;39:218-221.
  14. Ketover BP, Young LS, Armstrong D. Septicemia due to *Aeromonas hydrophila*: clinical and immunologic aspects. J Infect Dis 1973;127:284-290.
-