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Hemorrhagic blisters in fulminant *Aeromonas hydrophila* bacteremia: Case report and literature review

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ABSTRACT

The *Aeromonas* species, belonging to the family Aeromonadaceae, are opportunistic pathogens found in humans with an incidence rate of 76 cases per million inhabitants in Southern Taiwan. The incidence of *Aeromonas* septicemia is relatively low, accounting for less than 15% of cases. Patients diagnosed with *Aeromonas hydrophila* bacteremia who were presented with skin blisters and septic shock have been reported to have a mortality rate of 100%. *Aeromonas* infection must be considered in the differential diagnosis of gangrene-like tissue damage or skin lesions in patients with end-stage renal disease, due to the potential sources of infections. A 49-year-old Taiwanese diabetic woman with end-stage renal disease had underwent regular hemodialysis. She was referred to our hospital due to a one-day course of fever, dyspnea, hypotension, and fulminant hemorrhagic blisters covering her whole body. A physical examination uncovered multiple hemorrhagic blisters, along with a ruptured blister over the lower left leg. Laboratory tests revealed an elevation of liver enzymes, impaired renal function, lactatemia, and high anion-gap metabolic acidosis. Cultures of both blood and hemorrhagic blister fluid grew *Aeromonas hydrophila*. However, she experienced persistent shock despite aggressive intravenous fluid, empiric antibiotics, and inotropic agents with norepinephrine and dopamine. Early diagnosis and prompt management using intravenous fluids, antibiotics and surgical debridement is recommended in order to improve a patient's survival rate.

1. Introduction

The *Aeromonas* species, belonging to the family Aeromonadaceae, are opportunistic pathogens found in humans with an incidence rate of 76 cases per million inhabitants in Southern Taiwan[1-3].

Extra-intestinal *Aeromonas* infections have been reported, with the most common species responsible for human infection being *Aeromonas hydrophila* (*A. hydrophila*)[1,2]. The incidence of *Aeromonas* septicemia is relatively low, accounting for less than 15% of all cases[4]. The overall mortality rate attributed to

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A. hydrophila is approximately 50%. Patients of *A. hydrophila* bacteremia experiencing skin blisters and septic shock have been reported to have a mortality rate of 100% [1,5]. The possibility of obtaining the *A. hydrophila* infection through poor hand hygiene, saline solutions, open skin access due to large bore catheters, contamination of the dialysis catheter by the patient or nurse after contacting with contaminated water supply, must be considered [3,6,7]. *Aeromonas* infection must be considered during the differential diagnosis of gangrene-like tissue damage or skin lesions in patients with end-stage renal failure (ESRD), due to the potential sources of infections.

2. Ethics approval and consent to participate

All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee (No. CE18102A), along with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards. Oral informed consent was obtained from the patients for publication of this case report and any accompanying images.

During their lifetime, patients consented orally to the use of their history and all the related images and information for scientific purposes. Each patient provided written informed consent for publication.

3. Case report

A 49-year-old Taiwanese woman with a medical history of diabetes mellitus (DM) and ESRD, who had been undergoing regular hemodialysis (HD) for 8 years through an arteriovenous fistula over the right forearm at a rural hospital, was admitted to our facility. She was referred to our emergency department (ED) and presented with a one-day course of fever, dyspnea, hypotension, and fulminant hemorrhagic bullae covering her whole body. Upon arrival at the ED, the patient's vital signs showed a respiratory rate of 34 breaths/min, heart rate of 124 beats/min, blood pressure of 76/48 mmHg and body temperature of 39.5 °C. A physical examination revealed cardiopulmonary distress, pale conjunctiva, multiple hemorrhagic blisters, and a ruptured blister over the lower left leg (Figure 1). Endotracheal intubation was implanted for both airway protection and ventilation using 100% oxygen. Laboratory investigations uncovered a white blood cell count of 7 600/mm³ with segmented neutrophils of 92.6%, hemoglobin of 8.2 g/dL, platelet counts of 121 × 10³/mm³, blood urea nitrogen

of 78 mg/dL, creatinine of 6.4 mg/dL, sodium of 138 mEq/L, potassium of 4.9 mEq/L, chloride of 98.0 mEq/L, calcium of 8.2 mg/dL, albumin of 2.1 g/dL, glutamic-oxaloacetic transaminase of 108.0 U/L, glutamic-pyruvic transaminase of 72.0 U/L, alkaline phosphatase of 232.0 U/L, lactate dehydrogenase of 413.0 U/L, lactate 77.5 mg/dL, C-reactive protein of 32.3 mg/dL, blood glucose of 23.0 mg/dL, prothrombin time of 16.2 s, and activated partial prothrombin time of 42.3 s. Arterial blood gas revealed a pH level of 7.061, PaO₂ of 88 mmHg, PaCO₂ of 30.2 mmHg, and an HCO₃⁻ of 15.3 mmol/L at 100% oxygen. The laboratory data is summarized in Table 1. A supine chest X-ray demonstrated cardiomegaly and an infiltration of both lower lung fields (Figure 2). However, the patient exhibited persistent shock (systolic blood pressure of around 60 mmHg) and expired in the ED despite an aggressive treatment of intravenous fluid, glucose water, ceftriaxone at 2 000 mg once daily, plus vancomycin at 1 000 mg twice daily, and inotropic agents with both norepinephrine and dopamine. Cultures of blood and blister fluid grew *A. hydrophila* three days later.

Table 1

Summary of laboratory investigations.

	Items	Result	Reference range (units)
Complete blood cells	White blood cells	7 600.000	4 000-11 000 (counts/mm ³)
	Segmented neutrophils	92.000	40%-74%
	Hemoglobin	8.200	12-14 (g/dL)
	Platelet	121.000	140-400 (× 10 ³ counts mm ³)
Biochemistry	Blood urea nitrogen	78.000	5-25 (mg/dL)
	Creatinine	6.400	0.7-1.4 (mg/dL)
	Sodium	138.000	137-153 (mEq/L)
	Potassium	4.900	3.5-5.3 (mEq/L)
	Chloride	98.000	95-105 (mEq/L)
	Calcium	8.200	8-10 (mg/dL)
	Albumin	2.100	3.5-5.0 (g/dL)
	Glutamic-oxaloacetic transaminase	108.000	8-38 (U/L)
	Glutamic-pyruvic transaminase	72.000	10-50 (U/L)
	Alkaline phosphatase	232.000	50-190 (U/L)
	Lactate dehydrogenase	413.000	120-240 (U/L)
	Lactate	77.500	3-12 (mg/dL)
	C-reactive protein	32.300	<0.3 (mg/dL)
Coagulation profiles	Glucose	23.000	70-99 (mg/dL)
	Prothrombin time	16.200	9.5-11.7 (s)
Arterial blood gas	Activated partial prothrombin time	42.300	24.3-32.7 (s)
	pH	7.061	7.35-7.45
	PaO ₂	88.000	80-100 (mmHg)
	PaCO ₂	30.200	35-45 (mmHg)
	HCO ₃ ⁻	15.300	22-26 (mmol/L)



Figure 1. Multiple hemorrhagic blisters, along with a ruptured blister over the lower left leg.



Figure 2. Chest X-ray revealing a tracheal intubation, cardiomegaly, and infiltration over both lower lungs.

4. Discussion

Species of the genus *Aeromonas*, which are halophilic, non-acid fast, non-spore forming, gram-negative, and facultative aerobic bacteria, belong to the family Aeromonadaceae. They are opportunistic pathogens in humans with an incidence of 76 cases per million inhabitants occurring between 2008 and 2010 in Southern Taiwan[1-3,7,8]. It is noticeable that infection from the species of the genus *Aeromonas* has been reported during the summer months[9]. The incidence of *Aeromonas* bacteremia in Taiwan was 50-143 folds higher than those appearing in Western countries[10].

Four categories of *Aeromonas* infection have been described including cellulitis, acute diarrheal disease, sepsis, and other types of infections. There have been reports on extra-intestinal infections such as empyema, lower respiratory tract infections,

meningitis, necrotizing fasciitis, osteomyelitis, peritonitis, septic arthritis, urinary tract infections, and traumatic wound infections; particularly in immunocompromised patients, such as those suffering from DM, liver cirrhosis, and chronic kidney disease[1,2,11-14]. Two well-known predisposing conditions associated with *Aeromonas* bacteremia in Korea are cancer (42.3%) and liver cirrhosis (39.3%)[15]. Incidences of DM and chronic kidney disease regarding patients on dialysis for *Aeromonas* bacteremia in Taiwan have been reported at rates of 23.5% and 5.0%, respectively[16]. The major focus of *Aeromonas* bacteremia is hepatobiliary tract infections (50.6%), with the others being primary bacteremia (17.9%), skin and soft tissue infection (4.2%), and catheter related infection (3.0%)[15]. The incidence of skin and soft tissue infection progressing to myonecrosis and gangrene of the involved soft tissue has been reported to be 62.5% in India[14].

Three species of the genus *Aeromonas*, *A. hydrophila*, *Aeromonas caviae*, and *Aeromonas veronii* biovar *sobria*, are responsible for more than 85% of human infections. The most common species responsible for human infection is *A. hydrophila*[8,9]. Gram-negative microorganisms account for 21%-30% of bloodstream infections in patients who received regular HD[3]. The incidence of *Aeromonas* septicemia is relatively low, accounting for less than 15% of cases[4,8].

ESRD is associated with an alternation in the primary host defense system. *A. hydrophila* infections and presentations in patients with ESRD tend to vary depending upon dialysis modalities. Systemic infections appear to be more common in patients undergoing HD, due to dissemination of bacteria through the open skin access of the large bore catheters. Alternatively, contamination of the dialysis catheter by the patient or dialysis nurse, after contact with a contaminated water supply or dialysis solution, may result in this type of infection. Contamination of the dialysis solution, along with contamination through touch, may be potential sources of infections[3,6,7]. We could not exclude the possibility of *A. hydrophila* infection occurring through poor hand hygiene, saline solutions, the open skin access of the large bore catheters, or contamination of the dialysis catheter by either the patient or dialysis nurse after coming in contact with a contaminated water supply[3].

The overall mortality rate attributed to *A. hydrophila* is approximately 50%. Several factors are associated with a poor prognosis, including old age, altered consciousness, skin and soft tissue infection, a rapidly progressing infection concomitant with septic shock, pneumonia, alcoholic cirrhosis, and prolonged HD[3,7,8,17]. Patients presented with skin blisters and septic shock have been reported to have a mortality rate of 100%[1]. The mean interval between the onset of *Aeromonas* bacteremia to sepsis-related mortality is 8.2-10.0 days[10,15]. Among the patients, 3.6% were diagnosed with *Aeromonas* bacteremia progress to the clinical condition and expire within 72 h after arrival at the hospital. Risk factors of mortality associated with *Aeromonas* bacteremia are metastatic cancer, shock, delayed use of appropriate antibiotics, a prolonged prothrombin time, and an elevated creatinine level. All

of the non-survivors experienced evidence of shock[15].

Aeromonas infection must always be considered during the differential diagnosis of gangrene-like tissue damage or a skin lesion, in patients with an immunosuppressed status, such as DM and malignancy[9]. The most active empirical treatment interventions against *Aeromonas* should consist of third-generation cephalosporins, combined with gentamicin or amikacin, imipenem, and fluoroquinolone in cases of severe infection, where the duration of therapy depends on the site of infection and the patient's response to antibiotics[5,8-10]. Combination therapy involving antibiotics has been prescribed in 49.4% of *Aeromonas* bacteremia patients. The median duration of antibiotics use is 10 days. Initiation of antibiotics within 6 hours of clinical presentations, such as fever, alerted consciousness, hypotension, and shock, has been observed in 81.0% of patients experiencing *Aeromonas* bacteremia. Ceftriaxone-susceptibility and ceftriaxone-resistance has been found in 84.5% and 15.5% of patients with *Aeromonas* bacteremia, respectively[15]. Timely surgical debridement for removal of the focus of the infection is essential for any infection control to be life-saving[5,8-10].

4. Conclusions

A. hydrophila is an opportunistic pathogen in humans, particularly those with an immunocompromised status. Clinicians should keep in mind that hemorrhagic blistering is a severe clinical manifestation of *A. hydrophila* bacteremia. The mortality rate is associated with old age, skin and soft tissue infection, septic shock, and altered consciousness. Early diagnosis and prompt management using intravenous fluids, antibiotics, and surgical debridement if necessary, are strongly recommended due to the high mortality rate of 50%-100% in patients experiencing *A. hydrophila* bacteremia, who are presented with skin blisters and septic shock.

Conflict of interest statement

The authors declare that they have no competing interests.

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