

Original Article

Report and literature review on six patients with agranulocytosis accompanied by *aeromonas hydrophila* septicemia

Heping Shen, Yongmin Tang, Xiaodan Chen, Shilong Yang

Department of Hematology, Children's Hospital of Zhejiang University School of Medicine, China

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Abstract: *Aeromonas hydrophila* (*A. hydrophila*) belongs to the species of *Aeromonas* of the family Vibrionaceae, which are commonly present in fresh water, sewage, sludge, soil and human's feces; and is pathogenic to aquatic livestock, livestock and humans. It is a typical kind of pathogenic bacteria in human, livestock and fish. This kind of bacteria is a conditioned pathogen that can cause infection inside and outside the intestinal tract. Infection in humans is mainly caused by contact with polluted water or drinking of polluted water, and sick livestock is likely the source of infection. This kind of bacteria may generate multiple kinds of virulence factors such as hemotoxin, enterotoxin, and so on; which may cause food poisoning in people, as well as symptoms of acute gastroenteritis, diarrhea-like cholera, septicemia, phlegmon and so on. In recent years, a number of literatures have been reported on the extra-intestinal infection of *A. hydrophila* such bacteria detected in fester after cerebral injury and in ascites and blood of patients with liver cirrhosis. It is rare to see extra-intestinal infection of *A. hydrophila* during myelosuppression. Six patients with blood infection were admitted at our hospital from January 2008 to December 2013, and all patients were sick children with myelosuppression. This report aims to probe into the characteristics of the occurrence and development of this disease by reviewing the clinical manifestations of these six patients combined with literature reviews.

Keywords: Agranulocytosis, *aeromonas hydrophila* septicemia

Introduction

From January 2008 to December 2013, blood cultures of six patients in the Children's Hospital of Zhejiang University School of Medicine were found with *aeromonas* infection (**Table 1**). Among these patients, four were female and the remaining two were male; and average age of the patients was 9.4 years old (range, 4.3-15.3). Cytokines and procalcitonin were detected in five of six patients. Results of the analysis of the blood cultures of the six patients are as follows.

Data and method

Case 1

A seven year and four month old female patient was hospitalized for epistaxis accompanied by skin hemorrhagic spot for 10 days and fever for one day on February 4, 2012. She was diag-

nosed as aplastic anemia (severe) through bone marrow examination after being hospitalized. Anti-infection treatment was performed, and her fever subsided on February 11. ATG treatment was performed on February 15. On February 17, her fever recurred; and she was given tienam for anti-infection treatment. Her fever subsided the next day. Then, her fever recurred again on February 22, and her hemogram results continued to stay below normal levels (WBC, $0.37 \times 10^9/L$; N, $0.12 \times 10^9/L$; Hb, 88 g/L; Plt, $40 \times 10^9/L$). On February 27, the patient complained of stomachache; and linezolid and tazocin were administered to the patient. Abdominal ache on the right side became obvious on February 28, and G-bacteria were orally reported by blood culture. Abrosiao was performed and mepem was adopted instead of tienam. Abdominal distension occurred and the stomachache continued to become obvious on March 1. On March 3, chest

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Table 1. Basic information of six patients with acute lymphoblastic leukemia

Item	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Gender	Female	Male	Female	Female	Female	Male
Age	7.4	11.1	15.3	4.3	7.1	11
Underlying disease	AA severe	ALL medium risk	ALL medium risk	HLH	ALL high risk	ALL high risk
Previous Therapy	ATG therapy	VALD therapy	VALD therapy	CSA, vp16	VALD therapy	VALD therapy
Neutropenia in fever ($\times 10^9/L$)	0.12	0.34	1	0	0	0.08
Symptom of digestive tract	Yes, abdominal pain and distension	Yes, abdominal pain, vomit, and diarrhea	Abdominal pain and vomit	No	Yes, abdominal pain and distension	Yes, abdominal pain
Shock	Yes	Yes	No	No	No	Yes
Pneumonia	Yes, blood-stained sputum	Yes	No	No	Yes, blood-stained sputum	No
Bubbler	Yes	Yes	No	No	Yes	Yes
Hyperglycemia	No	Yes	Yes	No	Yes	Yes
IL-6	642	More than 5,000	312.4	4,020	3,638	
IL-10: pg/ml						Not done
Cytokines IL-6	1,143.3	1,621	74.5	118	2,981	
IL-10: pg/ml						
PCT: pg/ml	0.234	Not done	0.54	0.28	3.56	Not done
CRP: mg/L	More than 160	More than 160	130	134	More than 160	More than 160
Recovery of neutropenia	Not recovered yet at the twelfth day	Neutropenia was 0.86 at the sixth day	Neutropenia is normal at the eighth day	Neutropenia is normal at the fourth day	Neutropenia is 0.04 at the fourth day	Not recovered yet at the fourth day
Prognosis	Dead	Survival	Survival	Survival	Dead	Dead

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CT examination revealed pneumonia accompanied by hydrops in the pleuroperitoneal cavity. Abdomen B ultrasound indicated hepatomegaly, intrahepatic cystic echo, rough gallbladder wall, and the quantity of hydrops in the entero-coelia; and echocardiography hinted few hydrops in the pericardium. She was likely to suffer from aspergillus infection in the lung. Thus, voriconazole was added to fight against fungus. On March 4, her heart rate rapidly increased. She suffered from chest congestion, blood was found in sputum, oxygen saturation was 70% under mask oxygen inhalation, moist crackles (bubble sounds) were heard in both lungs, her breathing was 60 to 70 times per minutes, and her left upper extremity swelled slightly. Tracheal cannula was performed on the patient. On March 5, the patient had low blood pressure (88/37 mmHg). Swelling occurred on the left upper arm, which was obviously accompanied by blisters. Dilatation and epinephrine were applied; however, the patient's blood pressure remained low and urine volume decreased. On March 6, at 5:30, ventricular arrhythmias and cardiac arrest occurred, and the patient died. *Aeromonas hydrophila* (*A. hydrophila*) was found in sputum, vein catheterization and blood culture, which are allergic to imipenem, piperacillin plus tazobactam, ceftriaxone, aztreonam and ceftazidime. The patient was finally diagnosed as: (1) aplastic anemia (severe), (2) septicemia (*A. hydrophila*), (3) acute pneumonia accompanied by pleural effusion, (4) peritonitis, (5) respiratory failure, and (6) pneumorrhagia.

Case 2

An 11 year and one month old male patient was hospitalized due to six-month acute lymphoblastic leukemia on September 17, 2009. VALD scheme chemotherapy was performed on the patient after examination. His blood glucose increased after chemotherapy, diagnosed as secondary diabetes mellitus, and was given a diabetes diet and injection of insulin. On September 30, agranulocytosis was observed on the patient. On October 1, the patient suffered from fever accompanied by waist soreness, chest congestion and vomiting; and the patient released jelly-like diarrhea feces once. The patient's blood pressure fell to 96/46 mmHg, and his hemogram examination revealed the following: WBC, $0.58 \times 10^9/L$; N,

$0.34 \times 10^9/L$; Hb, 138 g/L; Plt, $7 \times 10^9/L$. The patient's hypersensitivity CRP was more than 160 mg/L; and he was given mepem, vancomycin and fluconazole for anti-infection, methylprednisolone for anti-inflammation, and dopamine and dobutamine for cardiostimulant and blood pressure elevation treatment. On October 2, the patient suffered from stomachache, vomiting, anhelation and cyanosis; and his blood pressure decreased to 87/41 mmHg. On October 4, a tracheal cannula was inserted since oxygen saturation decreased to 68% under masked oxygen inhalation. A blister approximately 4×4 cm appeared on his right thigh; and blood culture report hinted *A. hydrophila*, which indicated allergy to imipenem, ceftazidime, piperacillin plus tazobactam. On October 7, *A. hydrophila* became more obvious on the patient, and urine volume decreased. The patient was given CRRT treatment. On October 8, the patient's cytokine (IL-6) levels were high, which was >5,000 pg/ml; as well as IL-10 (1,621 pg/ml) and TNF (82.9 pg/ml). Blood perfusion was performed once on the patient, and re-examination revealed the following: IL-6, 82 pg/ml; IL-10, 22.2 pg/ml. Afterwards, *Pseudomonas aeruginosa* was found in his blood culture and aurum culture was found with *Acinetobacter baumannii* infection, which was only allergic to levofloxacin. The patient was given aztreonam, levofloxacin, erythrocin, voriconazole, tigecycline and amikacin for anti-infection treatment. On October 6, neutrophil granulocyte increased to $0.83 \times 10^9/L$. On October 15, his body temperature was normal. On October 16, his tracheal cannula was removed and his symptoms improved. Final diagnosis were as follows: (1) acute lymphoblastic leukemia (common, intermediate risk group), (2) septicemia (*A. hydrophila*), (3) septicemia (*pseudomonas aeruginosa*), (4) ventilator-associated pneumonia (*Acinetobacter baumannii*), (4) deep vein catheterization (*enterococcus faecium*), and (5) secondary diabetes mellitus.

Case 3

A fifteen year and three month old female patient was hospitalized due to her two-year acute lymphoblastic leukemia on July 8, 2010. VDLD scheme chemotherapy was performed on the patient from July 12 to July 25. On July 20, fear of cold, fever, vomiting, and abdominal

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discomfort occurred on the patient. Routine blood examination revealed: WBC, $1.75 \times 10^9/L$; N, 60%; Hb, 143 g/L; Plt, $89 \times 10^9/L$. Blood gas analysis revealed hyponatremia. Sodium supplement through the vein (Na^+ , 123 mmol/L) was adopted and tienam was adopted for anti-infection. Her fever subsided the next day. Blood culture indicated *A. hydrophila*. On July 28, her hemogram was normal, blood culture was positive, and she was discharged from the hospital because she was better. Final diagnosis were: (1) acute lymphoblastic leukemia (common, intermediate risk group), (2) septicemia (*A. hydrophila*), and (3) secondary hyperglycemia.

Case 4

A four year and three month old female patient was hospitalized on October 1, 2010, because she suffered from fever for eight days. Her examination revealed the following: WBC, $1.81 \times 10^9/L$; N, 60%; Hb, 94 g/L; Plt, $8 \times 10^9/L$; CRP, 7 mg/L. Abdominal B ultrasound hinted hepatosplenomegaly, marrow hinted hemophagocytosis, Epstein-Barr (EB) virus DNA was positive at 1×10^3 copies, and she was diagnosed as EB virus-associated hemophagocytic syndrome. Dexamethasone, VP-16 and cyclosporine were adopted for anti-infection. Her fever subsided on October 9. However, her fever recurred again on October 20. Blood routine examination revealed the following: WBC, $0.58 \times 10^9/L$; N, 0%; CRP, 134 mg/L. Blood culture was found with *A. hydrophila*, which was allergic to imipenem, meropenem, piperacillin plus tazobactam, ceftriaxone, aztreonam and ceftazidime. Meropenem, piperacillin plus tazobactam were successively adopted for treatment. On October 24, her hemogram results returned to normal. On October 27, her body temperature was normal, her blood culture was positive, and she was released from the hospital because she felt better. Final diagnosis were: (1) hemophagocytic syndrome, (2) septicemia (*A. hydrophila*).

Case 5

A seven year and ten month old female patient was admitted to our hospital on December 3, 2012, who was diagnosed with acute lymphocytic leukemia for more than seven months. The patient had a history of aspergillus pneumonia. After admission on December 5, the

patient was treated with VILD chemotherapy; however, high levels of blood glucose were observed during the course of the chemotherapy. Thus, the patient was treated with a diabetic diet and subcutaneous insulin injection. On December 20, the patient had agranulocytosis. On December 23, the patient had fever, erosion in the angle of mouth, as well as lower limb and lumbar ache; and was treated with tienam to fight infection. Then, the patient suffered from sustained fever with a progressive increase in CRP, and the patient continued to have agranulocytosis with $2-25 \times 10^9/L$ of blood platelet. Blood platelet was injected to the patient, but had a minimal effect. On December 25, swelling and pain occurred on the patient's limbs, scalp, and multiple soft tissue mass of the scapular region, as well as in the limbs. Vancomycin was administered to the patient. On December 26, the patient started to have symptoms of anhelation, cough with blood-stained sputum, as well as bubbles in the limbs, scalp and scapular region at night. On December 27, the patient had right limb pain, babble and oliguria; and was treated with sulperazone. On the early morning of December 28, the patient had pain in the stomach, vomiting with blood fluid, melena for one time, clear pain in the right neck and limbs, as well as bands of babble in the right neck, in which some were ulcerated with tasteless blood fluid and high levels of lactic acid upon inspection of the flesh. At 2:30 A.M., the patient had paroxysmal abdominal pain in the whole abdomen and vomited with blood fluid. At 2:33 A.M., the patient did not respond to calls, and her heart rate was 46 BPM with a low and slow heart sound. The patient was treated with epinephrine and cardio-pulmonary resuscitation, tracheal intubation as administered, had no response, and was pronounced dead. As suggested by the blood culture report: *A. hydrophila* is sensitive to imipenem, piperacillin and tazobactam, ceftriaxone, cefoperazone and sulbactam, aztreonam, and ceftazidime. Final diagnosis: (1) acute lymphoblastic leukemia (T cellular type, high risk), (2) sepsis (*A. hydrophila*), (3) possible DIC, (4) aspergillus pneumonia, (5) multiple organ failure.

Case 6

An eleven year old male patient was admitted to our hospital for abdominal pain for one day. He was diagnosed as acute lymphoblastic leu-

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Table 2. Analysis of the clinical characteristics of patients with *Aeromonas hydrophila* sepsis

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Underlying disease	Multiple myeloma	Leukemia	Diabetes	Gastric ulcer	Leukemia	Cirrhosis	Chronic hepatitis	Cirrhosis	No
Age (Years old)	46	59	54	23	4	38	49	63	30
Gender	Female	Female	Female	Male	Female	Male	Male	Male	Male
Neutrophil granulocyte ($\times 10^9/L$)	1.24	1.6	Normal	WBC 6.2	0.48	5	3.1	2.4	3.6
Bubble	Bubble in low limbs	No	Yes, together with ecchymosis	No	Yes	Yes	No	Yes	Yes
Abdominal symptoms	No	No	Abdominal pain and obvious abdominal distension	No	Abdominal pain, vomit, and diarrhea	Vomit	Diarrhea	Diarrhea	No
Shock	No	No	Yes	No	No	Yes	No	Yes	No descriptions
Previous Therapy	VTD and aspirin	Chemotherapy	oral hypoglycemic drugs	No	Chemotherapy	No	No	No	No
Hyperglycemia	No	No	Yes	No	No	No	No	No	No
Inducement	Unknown	Unknown	Applying un-sterilized needles of insulin injector	Dive for fish	Unknown	A right foot sprain and eat barbecue	Unknown	Unknown	Unknown
Fever	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Other symptoms	Right popliteal vein embolism and slight inflammation on both lungs	Sleepiness	Atrial fibrillation	Headache, yellow urine, severe anemia, coma	Pharyngalgia	Right leg aches, anhelation and hypoxia, coagulation disorders	No	Ache on both legs and coagulation disorders	Right upper extremity swelling and necrosis
PCT	Not done	Not done	Not done	Not done	Not done	11.84	Not done	100 ug/l	Not done
Bacterial sensitivity	Sensitive	Sensitive	Sensitive	Unknown	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Prognosis	Dead	Survival	Dead	Dead	Dead	Dead	Improve	Dead	Dead
	Case 10	Case 11	Case 12	Case 13	Case 14	Case 15	Case 16	Case 17	Case 18
Underlying disease	No	Chronic kidney disease	Chronic liver disease	Cardiomyopathy, atrial fibrillation, interstitial pneumonia, and renal failure	Drink	Rheumatoid arthritis	Chronic kidney disease	Thalassemia	ALL
Age	47 years old	55 years old	77 years old	81 years old	68 years old	72 years old	49 years old	16 years old	Two years old and half
Gender	Male	Male	Male	Male	Female	Female	Female	Male	Female
Neutrophil granulocyte ($\times 10^9/L$)	6	WBC4.7	Regular	Regular	2	7	Regular	Regular	0.1, recovered within five days
Bubble	Yes	No	No	No	Yes	No	Yes	Yes	No
Abdominal symptoms	Diarrhea	No	No	No	No	Gallstone and cholangitis	No	Nausea and vomiting, abdominal pain	No
Shock	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes

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Previous Therapy	No	Take hormone and do dialysis	Treat liver cirrhosis	Use steroid hormone	No	Take hormone	Take hormone and do dialysis	Nonstandard deferoxamine treatment	Inducing chemotherapy
Incentive	Unknown	Applying polluted dialysis catheters	Eat raw fish and drink too much wine	Two days after intake of cardiac catheterization	Unknown	Unknown	Unknown	Fracture	Eat fish and self-made cheese
Fever	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Other symptoms	Ache on lower limbs and been black, oozing, coagulation disorder dysfunction, and liver or kidney function failure	Cough and a slight effusion in pleural	Weakness, mental disorientation, and dyspnea	Chest pain and dyspnea	Right upper arm pain with gangrene and dysfunction of liver	No	Necrosis and gas gangrene, and dyspnea	Spleen embolization, pericarditis, hepatomegaly together with fibrosis, lung consolidation	Fasciitis and gangrene surgery
Bacterial sensitivity	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Prognosis	Dead	Survival	Dead	Dead	Dead	Survival	Dead	Dead	Survival

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kemia (T cellular type, high risk) after bone marrow examination. After hospitalization, he was in complete remission for treatment with induction chemotherapy for half a month, and was treated with regular chemotherapy in our hospital. The patient was treated with VILD chemotherapy on June 23, 2005. Then, he suffered from abdominal discomfort, vomiting, and so on. On July 2, the patient's abdominal discomfort became worse. He had fever with fear of cold, a low blood pressure of 85/45 mmHg, and his current hemogram was: WBC, $0.4 \times 10^9/L$ and N, 20%. The patient was treated with ornidazole and tienam for infection, dexamethasone to treat against inflammation, and plasma volume expansion using normal saline. Then, the patient's blood pressure temporarily improved. On July 3, the patient had pain in the left shank and his blood pressure decreased to 70/49 mmHg. The patient was treated with Tazocin, and his blood pressure slightly improved after treatment with plasma volume expansion. On July 4, the patient's left lower limb swelled with obvious blood bubbles, which was considered as an obvious partial phlegmon, and instable blood pressure that decreased to 78/45 mmHg. The patient was treated with Vancocin and plasma volume expansion using normal saline. On July 5, blood pressure of the patient continued to be instable and decreased to 68/40 mmHg. Swelling on the lower limbs of the patient was obvious, and his bubbles were obviously bigger and extended to the inguinal region. The patient had brown bloody vomitus with anhelation. Upon examination, APTT was 64.5 seconds, PT was 19.2 seconds, and blood platelet level decreased to $14 \times 10^9/L$. Parents of the patient decided to abandon therapy and the patient dead on that very day. Blood culture and liquid of the bubble culture were *A. hydrophila*, suggesting that it was sensitive to imipenem, ceftazidime, and piperacillin+tazobactam. Final diagnosis: (1) acute lymphoblastic leukemia (T cellular type, high risk), (2) sepsis (*A. hydrophila*), and (3) septic shock.

Results

A total of six patients had *A. hydrophila*, as determined by blood culture in our hospital from January 2008 to December 2013. Three patients are died and the other three patients survived, and mortality was 50%. The patient with bubbles, severe septic shock symptoms,

and 1,000 pg/ml or more of cytokine IL-10 was examined; and neutrophil granulocyte recovered slowly, and has a higher death rate.

Clinical characteristics of several patients with sepsis caused by *A. hydrophila* infection from domestic and overseas locations were analyzed as shown in **Table 2** [1-18].

Discussion

A variety of pathogenic aeromonas have been discovered sequentially since the 1980s, in which some bacteria have been proven to cause diarrhea, acute gastroenteritis, infections, cellulitis, peritonitis in patients with low immunity, and septicemia by case reports and clinical studies. Moreover, multiple patient deaths have been caused by acute infection with aeromonas [19]. The fatality rate for cases with serious nosocomial infections such as cirrhosis and malignant tumor in patients with low immunity, peritonitis and sepsis in immunocompromised patients is high; which can reach up to 50% [20, 21]. Aeromonas infection in hospitals is significantly higher than outside the hospital. This germ is a conditioned pathogen that has a low probability of blood infection occurrence, and is likely to occur in individuals with low immunity. *A. hydrophila* sepsis occurred in six patients in this study, and all patients were infected under circumstances of decreased immunity and IV myelosuppression. Among these patients, mortality rate was 50%; indicating that sepsis caused by the strain has a high mortality, which is similar to previous reports. Four patients had high blood sugar before infection. However, whether this high sugar environment is conducive to *A. hydrophila* remains unclear. Furthermore, according to a report, the deaths of two diabetic patients at home and abroad were caused by *A. hydrophila* infection [22].

It was found that the levels of cytokines IL-6 and IL-10 of the six patients that died were high, especially in children with IL-10 levels that have significantly increased and whose mortality rate increased to two-thirds; thus, IL-10 is closely related to organism damage. Mortality rate due to septic shock during the early stage of infection is 3/4, especially when blisters occur; while mortality rate of pulmonary infection is 2/3. Differences between super-sensitivity CRP and PCT levels in the death and sur-

vival of children are not significant. Most children with *A. hydrophila* sepsis have abdominal symptoms such as abdominal pain, vomiting, etc. This accounts for five in six patients, which may be related to poor body resistance after chemotherapy, gastrointestinal mucosa damage, and *A. hydrophila* in the bowel that easily entered into the blood as parasites. Immuno-compromised patients can have severe and fatal infections including muscle necrosis and gangrene deep pustules [23, 24]. Sepsis caused mainly by *A. hydrophila* and mild aeromonas has a mortality rate of up to 30-70% [25]. Prognosis would be relatively good when neutrophil can rapidly be recovered. The death of the patients all resulted from aggravation and agranulocytosis. The patient in the second case survived under the circumstance of pulmonary infection, high cytokine storm and local blisters. This had a certain relationship with neutrophil recovery after six days of infection, reducing the cytokine storm by hemoperfusion. Therefore, we believe that having a high cytokine storm by hemoperfusion may improve survival rate. It was puzzling that the conditions of these three patients continued to progress in antibiotic-sensitive applications, suggesting a certain relationship with strong bacterial strain virulence and pathogenicity.

Based on the collected reports of *A. hydrophila* sepsis patients, symptoms found in 18 patients [26-43] were as follows: fever rate accounts for 17/18, skin blisters rate accounts for 10/18, shock rate accounts for 9/18, abdominal symptoms rate accounts for 8/18, and hyperglycemia rate accounts for 1/18. Overall mortality rate was 13/18; while mortality rate of skin blisters and shock was 100% and 7/9 respectively. The mortality rate of two patients with *A. hydrophila* was 50%, indicating that mortality rate is high for a normal population or a normal immunity population. Hence, sepsis caused by *A. hydrophila* infections can result in serious infections and death not only for neutropenic patients, but also for normal immune people. However, this mostly occurs in patients who have underlying diseases. For the 18 patients, one of the drug-sensitive patients is unknown; while other strains were sensitive to antibiotics, which are similar with patients admitted to our hospital. We analyzed the pathogenesis of *A. hydrophila* for reasons that the patients still died after using sensitive drugs.

The *A. hydrophila* strain is invasive. Virulence factors have exotoxins, proteases, S-layer, fimbria and transferrin; in which, exotoxin and extracellular enzymes are major causative factors. Exotoxin, which has been previously determined, includes aerolysin, hemolysin, hemolytic toxin, cytolytic enterotoxin, and so on [44]. Several features of extracellular enzymes include hemolysin, enterotoxin and protease [45-47]. Exotoxin is a component of extracellular enzymes and a component of extracellular products of aeromonas. In this study, we found that heat-resistant metalloproteinases have a direct pathogenic effect on infection [48]. Its pathogenic mechanism may undermine the body's immune system, prompting the breeding of aeromonas in body tissues, releasing proteases that directly affect tissues, and resulting in the dissolution of necrosis. In addition, immunogenic extracellular enzymes have immunogenicity, which can have similar clinical symptoms with sepsis caused by infective strains [49, 50]. Studies have shown that high elastase secreted by *A. hydrophila* should be considered as a risk factor [51].

In summary, attention should be given to *A. hydrophila*, which is an opportunistic pathogen that has strong virulence of some bacterial strain; causing high mortality in immunocompromised people. Antibiotics should be timely and reasonably used when patients with sepsis have symptoms such as skin blisters and shock combined with other infected parts, as well as the high mortality rate of cytokines. When necessary, damage to the body should be studied and researched to reduce cytokine by hemoperfusion.

Disclosure of conflict of interest

None.

Address correspondence to: Shilong Yang, Department of Hematology, Children's Hospital of Zhejiang University School of Medicine, No. 57, Zhuganxiang, Hangzhou 310000, China. Tel: 86-0571-88873611; 86-0571-86753591; E-mail: yangshilong_y@126.com

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