

Received: 2012.03.14
Accepted: 2012.05.10
Published: 2012.05.17

Fatal septicemia and endotoxic shock due to *Aeromonas hydrophila*

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Summary

Background:

Although rare, bloodstream infections caused by *Aeromonas* tend to be very severe and progress rapidly.

Case Report:

We report a case of an 81-year-old man with fatal septicemia and endotoxin shock caused by *Aeromonas hydrophila*. The patient had dilated cardiomyopathy, paroxysmal atrial fibrillation, interstitial pneumonitis and renal dysfunction was admitted to our hospital with chest pain and dyspnea. Transthoracic echocardiography demonstrated impaired left ventricular wall motion and severe mitral regurgitation due to tethering. Cardiac catheterization revealed severe stenotic lesions in the left anterior descending artery and the right coronary artery. Surgery for coronary artery bypass grafts and mitral annuloplasty were performed. However, 2 days after surgery, he suddenly developed a high-grade fever and his hemodynamics deteriorated rapidly. His blood cultures revealed *gram-negative Bacillus* and the endotoxin concentration in the blood was elevated. Despite intensive support efforts, the patient died 1 day after the sudden change. His blood culture revealed *A. hydrophila*.

Conclusions:

Whenever *Aeromonas* is found in a patient's bloodstream, clinicians should start appropriate and intensive treatment immediately.

key words:

Aeromonas hydrophila • septicemia • endotoxin

Full-text PDF:

<http://www.amjcaserep.com/fulltxt.php?ICID=882773>

Word count:

1186

Tables:

1

Figures:

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References:

9

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BACKGROUND

Aeromonas is an anaerobic gram-negative bacillus that commonly inhabits soil and fresh or brackish water. *Aeromonas* has been rarely identified as a human pathogen, except in immunologically compromised hosts. There are 3 common motile *Aeromonas* strain pathogens related to humans, namely, *A. caviae*, *A. sobria* and *A. hydrophila*. *A. hydrophila* is the most common *Aeromonas* strain in humans. While the overall frequency of *Aeromonas* as a cause of gram-negative bacteremia is low, *Aeromonas* bacteremia has a high fatality rate [1].

In this report, we present a patient with fulminant *A. hydrophila* septicemia and endotoxin shock after surgery for coronary artery bypass grafts and mitral annuloplasty. Clinicians should be aware of the virulence of this rare organism.

CASE REPORT

In February 2010, an 81-year-old man was admitted to our hospital with complaints of exertional chest pain and dyspnea. In 1998, he was diagnosed with dilated cardiomyopathy and chronic renal dysfunction. Beta-adrenergic antagonist therapy was initiated. In 2002, he was diagnosed with paroxysmal atrial fibrillation and oral amiodarone was started. In 2009, he was diagnosed with interstitial pneumonitis and steroid therapy was started. In that period, cardiac echocardiography showed left ventricular generalized hypokinesis and the ejection fraction was 45%.

On admission, his heart rate was 92 bpm, blood pressure was 78/59 mmHg, and body temperature was 36.5°C. He took oral steroids 15 mg/day. The electrocardiogram showed sinus rhythm at 80 bpm and ST depression in leads II, III, aVF, V4, 5, 6. His chest radiograph showed cardiomegaly (cardiothoracic ratio 65%) and pulmonary congestion. His laboratory findings on admission were as follows: white blood cell count, 7,520/mm³, C-reactive protein level, 0.08 mg/dL, hemoglobin was 9.6 g/dL, and liver functions, normal. Serum creatine phosphokinase level, 34 IU/L (normal, <216 IU/L). Blood urea nitrogen level 58.7 mg/dL, creatinine level, 2.48 mg/dL, estimated glomerular filtration rate, 20.3 mL/min/1.73 m² and sialylated carbohydrate antigen KL-6 level, 163 U/mL (normal, <500 U/mL). Brain natriuretic peptide (BNP) levels were remarkably elevated at 1989.7 pg/mL (normal, <20 pg/mL). Cardiac echocardiography showed left ventricular severe hypokinesis, ejection fraction of 29%, and severe mitral regurgitation due to tethering.

The patient received initial treatment with bed rest, oxygen administration, salt restriction, increase in diuretics, and continuous infusion of low-dose carperitide.

Although his symptoms and BNP improved gradually, he still experienced chest pain during bathroom walking. The coronary angiogram by cardiac catheterization showed very severe stenotic lesions in the left anterior descending artery and the right coronary artery.

In March 2010, surgery for coronary artery bypass grafts and mitral annuloplasty were performed. He received intravenous administration of ampicillin-sulbactam as

Table 1. Susceptibility profiles of *Aeromonas hydrophila*.

Antibiotic	MIC (µg/ml)
Cefazolin	16.0
Cefmetazole	<1.0
Ceftriaxone	<1.0
Amikacin	<2.0
Gentamicin	<1.0
Tobramycin	<1.0
Ampicillin-sulbactam	>32.0
Piperacillin-tazobactam	<4.0
Imipenem/cilastatin	<1.0
Meropenem	<0.25
Aztronam	<1.0
Ampicillin	>32.0
Piperacillin	8.0
Levofloxacin	<0.12
Ciprofloxacin	<0.25
Sulfamethoxazole-trimethoprim	>320.0
Minocycline	<1.0
Ceftazidime	<1.0
Cefepime	<1.0

prophylaxis against postoperative infection (3 g/day, twice a day). However, 2 days after surgery, he suddenly developed a high-grade fever, and his hemodynamics deteriorated rapidly. The endotoxin concentration of his blood was elevated to 408 pg/mL (normal, <5 pg/mL). Septic and endotoxin shock were strongly suspected, 4 blood cultures were obtained immediately. All of 4 blood cultures revealed gram-negative coccobacilli. Ciprofloxacin (600 mg/day) and human immunoglobulin (5.0 g) were started. Resuscitative efforts, including endotoxin adsorption therapy with a column of polymyxin B-immobilized fibers, intra-aortic balloon pumps, and percutaneous cardiopulmonary support were performed.

Despite intensive support efforts, the patient died 1 day after the sudden change. Another 2 days later, the bacterium was identified as *A. hydrophila*. This bacterium was not susceptible to ampicillin-sulbactam (Table 1).

DISCUSSION

Aeromonas are gram-negative, non-spore forming rods. *Aeromonas* are ubiquitous bacteria that are native to aquatic environments, and have been found in fresh, brackish, estuarine, marine, chlorinated, and unchlorinated water supplies worldwide.

Miles and Halnan were the first to report the isolation of an *Aeromonas* strain from the feces of a patient [2]. There

are 3 common motile *Aeromonas* strain pathogens related to humans, namely, *A. caviae*, *A. sobria* and *A. hydrophila*. *A. hydrophila* is the most common *Aeromonas* in humans. In a normal human host, infection with *Aeromonas* may produce mild diarrhea and, occasionally, cellulites. However, severe *Aeromonas* infection occurs when the host defense is compromised. *Aeromonas* causes a variety of systemic infections. By far the most serious and life-threatening complication of systemic *Aeromonas* infection is *Aeromonas* septicemia. The 3 species (*A. caviae*, *A. sobria* and *A. hydrophila*) account for >95% of *Aeromonas* septicemia [1]. The majority of patients with *Aeromonas* septicemia have a history of leukemia [3], other malignant diseases, or hepatobiliary disease [4]. In our patient, some predisposing factors have been identified. Just after surgery for coronary artery bypass grafts and mitral annuloplasty, the renal failure and oral administration of steroids might be adversely affected.

While the overall frequency of *Aeromonas* as a cause of gram-negative septicemia is exceedingly low (<0.15%) in one previous survey [5], the fatality rate for *Aeromonas* septicemia is very high. In 1988, Janda et al. reported that the fatality rate for *Aeromonas* septicemia has exceeded 50% [1]. Lau et al. reported that the overall mortality rate among 42 *Aeromonas* septicemia was 64%, and nineteen patients (70%) died within 7 days after the *Aeromonas* bacteremia [4]. Ko et al. reported that the overall fatality rate at 14 days among 104 *Aeromonas* septicemia cases was 32%, and two-thirds of the deaths occurred within 72 h after the patients' arrival at the hospital [6]. In a recent report, Kang et al. evaluated the clinical significance of *Aeromonas* septicemia in 182 patients. The mortality directly related to *Aeromonas* septicemia was still 24.1% [7].

Aeromonas species produce beta-lactamase, and they are often reported to be resistant to penicillin, ampicillin, first-generation cephalosporin, carbenicillin, vancomycin, and clindamycin. Antibiotics include third-generation cephalosporins, aztreonam and imipenem, or a fluoroquinolone is consistently effective against *Aeromonas* species [4]. A recent report demonstrated that either ciprofloxacin or azithromycin is recommended as first-line drug in patients with *Aeromonas* infection [8]. In our patient, 1 day after cardiac surgery, cultures of sputum grew *A. hydrophila*. The patient did not have symptoms of either abdominal pain or diarrhea, the primary portal of entry might have been the respiratory tract. Unfortunately, like the blood culture, the organism from sputum was resistant to ampicillin-sulbactam, which was administered as prophylaxis against postoperative infection.

Aeromonas produce an array of virulence factors that include endotoxin. Endotoxin is one of the principal components on the outer membrane of gram-negative bacteria. Endotoxin causes the release of cytokines such as interleukin-1 and tumor necrosis factor-alpha and activates complements and coagulation factors. Endotoxin is considered one of the principal biological substances that cause gram-negative septic shock. In this case, the endotoxin concentration of the patient's blood was elevated to 408 pg/mL (normal, <5 pg/ml), thus the patient's condition might have been adversely affected by endotoxin. The polymyxin B-immobilized fiber column is a medical device that aims to remove circulating endotoxin by absorption [9]. In patients with *Aeromonas* septic shock, the use of polymyxin B-immobilized fiber column should be considered without hesitation.

CONCLUSIONS

Clinicians should be aware of the virulence of *Aeromonas*.

Although rare, bloodstream infections caused by *Aeromonas* tend to be very severe and progress rapidly. Therefore, when *Aeromonas* is found in a patient's bloodstream, clinicians should start appropriate and intensive treatment immediately, including vigorous pulmonary and cardiovascular support.

Conflict of interest

All authors declare that they have no conflict of interest.

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