



Endocarditis with *Aeromonas salmonicida*

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ABSTRACT

Aeromonas salmonicida (*A. salmonicida*) is a facultative Gram-negative bacillus, inhabiting in water. It is a common source of furunculosis and septicemia in fish. Report on the human infection with this organism is rare. A male farmer referred with weakness and intermittent fever. He had cardiac valves' regurgitation due to fever with rheumatic heart disease. He had a history of swimming in well water. Transthoracic echocardiography (TTE) revealed a mobile mass of 1.3 × 0.9 cm attached to the mitral valve chordae, suggestive of a vegetation. *Aeromonas salmonicida* was isolated from the blood. After cardiac surgery and taking ceftriaxone for 4 weeks, he was discharged in good general condition. Five previous case reports of human infection with this organism were found. The patient was the sixth human case, and the first endocarditis, reported with this organism. *A. salmonicida* is a rare agent for human infection. Contact with water is a risk factor for this type of infection. It seems that the use of modern diagnostic methods has been effective in identifying the microorganism.

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Introduction

Members of the genus *Aeromonas* were first reported as a pathogen of vertebrates by Sanerelli in 1891 [1]. The organism is a facultative oxidase positive and Gram-negative low virulence bacillus, commonly found in water and soil. However, in recent years due to the use of improved techniques for isolation and identification of bacteria from biological specimens such as BACT/ALERT and Vitek 2-compact system, there have been numerous reports of various human and animal infections caused by *Aeromonas* spp, mainly from Asian countries [2–4]. The most common manifestations of infection with *Aeromonas* include gastroenteritis, bacteremia, and soft tissue infections [3]. The maximum burden of *Aeromonas* in the water occurs in warm seasons. Most infected cases had been reported in the warm seasons; however bacteremia with these organisms in the cold seasons has also been reported [5]. The four most commonly known species of *Aeromonas* are *hydrophila*, *sobria*, *caviae* and *salmonicida*.

A. hydrophila has been the most common cause of human infection [2]. *Aeromonas salmonicida* (*A. salmonicida*) was isolated from a Bavarian trout- breeding farm by Emmerich and Weibel in 1894 [1]. The outer protein coat and several pili are responsible for the colonization and bacteremia as virulence factors [6]. *A. salmonicida* causes furunculosis and sepsis in the fish. Since the optimum temperature for the growth of this organism is not 37 °C, it is usually not being considered as a human pathogen; therefore, reports of human infections with *A. salmonicida* are very rare [6,7].

Case report

A 20- year-old farmer man was admitted at the Imam Khomeini hospital, Tehran, Iran, in September 2018 with weakness and intermittent fever. There was no nausea, vomiting, loss of weight, chest pain, dyspnea, and dysuria, but he had a history of consuming local dairy and swimming in well water. There was severe mitral regurgitation and moderate to severe tricuspid regurgitation, due to rheumatic fever in his past medical history. The patient had no other comorbidity or risk factor in the medical history. The vital signs were normal at the first visit and the physical examination was unremarkable, except for holosystolic murmur (4/6) in the mitral area. There

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was no Janeway lesions, petechiae or Osler nodes. Laboratory analyses showed white blood cell count of about 9800 per microliter, erythrocyte sedimentation rate 100 mm/h and C-reactive protein 42 mg/dL. Chest x-ray did not show abnormality. Transthoracic echocardiography (TTE) revealed a mobile mass of about 2.2 cm, attached to the tip of the anterior mitral valve leaflet, a possible ruptured chorda, and a mobile mass of about 1.3 × 0.9 cm attached to a MV chorda, suggestive of vegetation and moderately severe left ventricular (LV) dilation with preserved LV systolic function (LVEF = 50.55%). Because of fever, a mobile mass on TEE and a history of local dairy consumption, the *Brucella* profile tests (*Brucella* Ab – Agglutination tests), *Coxiella burnetii* serology and blood cultures were requested. The results of these laboratory tests were negative, except blood cultures.

Two sets of blood cultures, received during the first 8 h of admission before starting antibacterial therapy, were performed in BACTT/ALERT vials, and positive results were obtained one day after cultivation. Positive vial was sub-cultured on blood agar and MacConkey agar media. After the growth, colonies were tested for Gram staining and identification with phenotypic test [2]. *Aeromonas* spp was identified based on biochemical tests, including oxidase (positive), hydrogen sulphide production (negative), indole (negative), urea (negative) and citrate utilization (negative), Methyl Red (negative), Voges Proskauer (positive) (MRVP test), and growth on Triple Sugar Iron Agar (TSI) was K/K, Simmon–citrate (positive), SIM Sulphide (negative), Indole (negative) and motility (negative). Then to identify the species, chromosomal DNA was extracted, using the phenol-chloroform method [8], and subjected to PCR amplification, targeting the 16S rRNA gene as described previously [8]. PCR product was subjected to direct sequencing and the identity was confirmed as *A. salmonicida* (GenBank MK271278). Drug susceptibility testing was performed by Vitek 2 (BioMérieux Clinical Diagnostics, USA) (Table 1).

Antibiotic therapy with ceftriaxone (1 g/twice daily) was started intravenously. Open heart surgery was performed for mitral replacement. The intraoperative findings based on the surgical report were as follows: the mitral valve completely was associated with many vegetations. Excisions and then mitral valve replacement were performed with mechanical valve carbomedics (size 31). At surgery, the mitral valve was affected by vegetations. A mitral valve replacement was performed. Histopathologically, endothelial tissue inflammation and destruction was detected, compatible with infective endocarditis. Four weeks after the surgery and still receiving ceftriaxone, the patient was discharged without fever, in well general conditions and several negative blood cultures. Oral cefixime (400 mg daily) was prescribed for another 4 weeks. Finally, after three months of treatment discontinuation and follow up, no symptom of relapse was found.

Discussion

A. salmonicida belongs to the genus *Aeromonas*, a common source of furunculosis and septicemia in fish especially salmonids cold-blooded vertebrates, especially salmonid fish, [9]. The true prevalence of this Gram-negative bacillus around the world is unknown, because in many countries, there are no proper isolation techniques, and positive cases are not accurately diagnosed [5].

In this report, while we have reported a case of endocarditis caused by *A. salmonicida*, a literature search was performed through the end of 2018 to find the reports that are compatible with *A. salmonicida* infection in human. Based on this search of the literature, using PubMed/MEDLINE for *A. salmonicida* infection/human, five reports were found. To the best of knowledge, this subject is the sixth human cases, and the first report of *A. salmonicida* endocarditis, which has been documented so far (Table 2). Human infections with *Aeromonas* usually occur after trauma, drinking or contact with contaminated water [2]. In our case, there was a recent history of swimming in well water. In five other reported cases, contact with the similar water sources was clearly identified in three patients. Most *Aeromonas* infections are seen in people with cancer, cirrhosis or subjects with immunodeficiency, although there are reports of serious infections with this Gram-negative bacillus in immunocompetent individuals [3,5]. In this patient, the most important risk factor was cardiac valve dysfunction due to rheumatic fever, which was also reported in Bora *et.al* report in 2016, although the reported patient had no evidence of endocarditis [9]. In four other reports, there have been several underlying diseases that have not been documented, but it can be said that almost all of the reported cases had at least one underlying disease (Table 2).

There are reports of the infections by these microorganisms related to drinking contaminated water, which usually cause gastroenteritis, but the most common symptoms of *Aeromonas* septicemia are fever, chills, hypotension and jaundice [5]. Similar to previous reports on patients infected with *A. salmonicida*, our young patient had also intermittent fever and weakness. Based on the positivity of culture result from valve sample, the patient's endocarditis is definite, according to the Duke Criterion for diagnosis of endocarditis [10].

The causative agent of these infections has been erroneously reported as *A. hydrophilia* in a number of cases, and this disturbance somewhat interferes with the detection of clinical infections of other species. Based on these problems, it is recommended that infections due to *Aeromonas* species, should be sent to the reference laboratories for determining the species before reporting [3]. In our report and other human studies related to *A. salmonicida*, the use of new diagnostic methods, such as the Vitek 2 compact system, has been effective in detecting this microorganism.

Table 1
Drug susceptibility test results for *A. salmonicida*.

Susceptibility information	Analysis time: 17.75 hours		Status: final	
Antimicrobials	MIC	interpretation	antimicrobials	
Amikacin	≤2	S	piperacillin	≤4 S
Cefepime	≤1	S	piperacillin/tazobactam	≤4 S
Ceftazidime	4	S	rifampin	n ¹ n
Ciprofloxacin	0.5	S	ticarcilin	≤8 S
Gentamicin	≤1	S	tobramycin	2 S
L	2	S		
evofloxacin				

n: No data.

Table 2Six *A. salmonicida* human infections which have been reported so far.

outcome	well water or fish ingestion	Treatment /period	Susceptible pattern	Culture Site/ diagnosis	Chief complaint	Underlying Disease	Sex	Age	Author/ Year
Survived	No	cefexime/ no data	all the drugs	Blood/ septicemia	low grade fever, weakness and malaise	recurrent miscarriage	f	34y	R.TewaRi ¹ / 2014
No data	No data	No data	all the drugs	purulent discharge/ soft tissue infection	Furuncles fever	no	m	67y	R.Kamble ⁷ / /2015
	yes		resistant to ampicillin &tetracycline	Blood/ septicemia	low grade fever,abdominal pain, weakness&malaise	Rheumatic heart disease	f	12y	Archana Bora ⁹ / 2016
survived	yes	cefepime/14 days	Only intermediate to cefazolin and susceptible to others	Blood/ pneumonia	congestion and muscle soreness, productive cough&blood-streaked sputum	Sarcoidosis, DM& CKD	m	67	C. Ann Moore ⁶ / 2017
Survived (poor visual)	yes	amikacin 125 µg/0.1 ml/ intravitreal injections	sensitive for amikacin, gentamicin and colistin	Aqueous humor and vitreous aspirate/ Endophthalmitis	ocular pain, discharge, and gradual decrease of vision	cataract surgery	f	55y	A. Varshney ⁴ / 2017
Survived	yes	ceftriaxone 1 g/BD/IV for 4 weeks and then cefexim 400 mg /daily for 4 weeks	all the drugs	Blood and valve vegetation	weakness and intermittent fever	rheumatic heart disease	m	20y	M.Salehi/ 2019

Fluoroquinolones are the first line treatment for *Aeromonas* infections, although the several reports of quinolone resistance for *Aeromonas spp.* exist and for this reason ceftriaxone before the results of antimicrobial susceptibility testing and then, due to microorganism susceptibility test and proper clinical response, ceftriaxone continued [3]. There is a report of resistance to ampicillin and tetracycline in a patient with *A. salmonicida* septicemia [9]. In a report by Moore et al., the use of broad-spectrum cephalosporins has been recommended for treatment of *A. salmonicida* infections, while *Aeromonas* isolated from this patient had intermediate resistance to cefazolin [6]. In our case and most of the patients who had accurate information about their treatment, broad- spectrum cephalosporins, such as cefpime and ceftriaxone were successful in treatment.

Conclusion

A. salmonicida is a rare agent for human infections. Contact with water is an important risk factor for the infection. It seems that the use of modern microbial diagnostic methods has been effective in detecting the microorganism in recent years.

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