

Aeromonas Infections in Patients with Liver Cirrhosis in Japan

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ABSTRACT

Aeromonas species are recognized as opportunistic pathogens that cause serious problems in patients with liver cirrhosis (LC). In this article, 25 case reports of *Aeromonas* infections in patients with LC in Japan are reviewed and summarized. Among the 25 cases, cases of septicemia or skin and soft tissue infections have been relatively well reported. In total, the 1-month mortality rate was 68% (17/25), whereas the overall survival rate was 32% (8/25). In particular, among 16 cases with skin and soft tissue infections, 12 (75%) died within the first 4 days after admission, regardless of the administration of antimicrobial agents and/or lower limb amputation, indicating extremely poor short-term prognosis.

Keywords: *Aeromonas* infections; Liver cirrhosis; Hepatitis

Abbreviations: DM: Diabetes Mellitus; HCV: Hepatitis C Virus; LC: Liver Cirrhosis; SBP: Spontaneous Bacterial Peritonitis

INTRODUCTION

Patients with Liver Cirrhosis (LC) are at a high risk of developing bacterial infections for several reasons, including hypoactivity of phagocytic cells in the hepatic reticuloendothelial system, decreased production of complement, bacterial translocation partially because of impaired intestinal permeability, and bacterial influx into the general circulation through portacaval shunts [1,2]. The most common bacterial infections identified in patients with LC are Spontaneous Bacterial Peritonitis (SBP), which is a life-threatening infection in patients with ascites; urinary tract infections; respiratory infections, particularly pneumonia, skin and soft tissue infections; and bacteremia [1].

Aeromonas species are Gram-negative, rod-shaped bacteria that are proliferative and omnipresent in both fresh water and soils [3,4] and are occasionally isolated from the faeces of healthy individuals [5]. *Aeromonas* infection is most commonly associated with gastroenterocolitis; extra-intestinal infections, such as bacteremia, pneumonia, empyema, arthritis, endocarditis, meningitis, urinary tract infection, biliary tract infection, peritonitis, including SBP; and skin and soft tissue infections [3].

Aeromonas species are recognized as opportunistic pathogens that cause serious problems, especially septicemia in immunocompromised patients with LC, hematological malignancies, diabetes mellitus (DM), severe biliary tract diseases,

and renal failure [4-7]. They also cause life-threatening skin and soft tissue infections [3] in addition to *Vibrio* species, particularly in patients with LC. Moreover, *Aeromonas bacteremia* in patients with LC or malignancy has been found to be associated with a higher mortality rate than bacteremia caused by other organisms [6]. *Aeromonas*-implicated clinical diseases are primarily caused by *Aeromonas hydrophila*, *A. sobria*, and *A. caviae* [5]. Chuang et al. [2] reported that the severity and mortality of bacteremia caused by *A. caviae* were lower than bacteremia caused by *A. hydrophila* or *A. sobria*. They further reported that *A. caviae* was less associated with LC than other species (*A. hydrophila* or *A. sobria*) [2].

Studies of *Aeromonas* infections complicated in patients with LC have been reported primarily in regions of East Asia, notably Taiwan and Korea, partially because of their ubiquitous presence in the environment and high incidence in chronic liver diseases [8]. However, cases of *Aeromonas* infections in patients with LC have only been sporadically reported in Japan. Additionally, to the best of our knowledge, there have been no review articles regarding *Aeromonas* infections in patients with LC in Japan. Therefore, in this article, case reports of *Aeromonas* infections in patients with LC in Japan both in English and Japanese (proceedings were excluded) that were retrieved from the PubMed and Japana Centra Revuo Medicina (Igaku Chuo Zasshi) databases, respectively, are reviewed and summarized. A literature search was performed using the following keywords: (1) “*Aeromonas*” and “liver cirrhosis,” (2)

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“Aeromonas” and “bacteremia,” and (3) “Aeromonas” and “bacterial infection.”

Aeromonas infections in patients with LC in Japan

The detection frequency of *Aeromonas* species in blood culture has been reported to be higher in patients with LC than in the general hospitalized population [9]. In our previous study of a single facility in Japan, the detection frequency of *Aeromonas* species was 5.8% (7/120) among the total organisms detected in blood cultures of patients with LC [7], whereas another study of a single facility in Japan reported a rate of 6.8% (3/44) [10], whereas the rate among general hospitalized populations in Japan is reportedly 0%-1.9% [7]. Frequencies of *A. hydrophila septicemia* are reportedly 14%-58% among all patients with LC and *Aeromonas septicemia* in Japan [11]. Furthermore, we reported that the severity of liver dysfunction in *Aeromonas*-induced bacteremia is greater than that

in Enterobacteria-induced bacteremia in Japanese patients with LC [12].

Case reports of Aeromonas infections in Japan

The clinical characteristics and prognoses of 25 reported cases of *Aeromonas* infections in patients with LC in Japan reported from 1992 to 2016 are summarized in Table 1. Among the 25 cases, three were reported in English [4,13,14] and the remaining 22 in Japanese [9,11,15-31]. The age at diagnosis of *Aeromonas* infection ranged between 40 and 78 years, and 19 patients were male and five were female with one case unknown. The etiology of LC was as follows: hepatitis C virus (HCV) infection in six cases [13,21,22,25,29], hepatitis B virus infection in six [9,11,16,26,27,30], alcohol-related in nine [4,14,15,17,20,21,23,28,31] HCV infection plus alcohol-related in one [22], and unknown in three [18,19,24]. The Child-Pugh classification of underlying liver dysfunction was as follows; Child C in nine, Child B in one, and unknown in 15 cases.

Table 1: Clinical characteristics and outcomes in the 25 reported cases of *Aeromonas* infections in patients with liver cirrhosis in Japan.

Case	Age (years)	Isolated species	Types of infection	Child-Pugh classification	Underlying diseases	Treatments	Outcomes	Reference
1	55	<i>A. sobria</i>	Necrotizing fasciitis	C	DM	Ceftizoxime, Minocycline	Death within 2 days	[17]
2	55	<i>A. hydrophila</i>	Septicemia, Necrotizing fasciitis	Uncertain	DM	Benzylpenicillin	Death within 2 days	[18]
3	60	<i>A. sobria</i>	Septicemia, Necrotizing fasciitis	Uncertain	DM	Antimicrobial agents	Death within a day	[19]
4	54	<i>A. hydrophila</i>	Septicemia	C	-	Ampicillin, Gentamicin	Death within 2 days	[20]
5	52	<i>A. sobria</i>	Septicemia, Necrotizing fasciitis	Uncertain	-	Lower limb amputation	Death within a day	[21]
6	58	<i>A. hydrophila</i>	Septicemia, Skin and soft tissue infections	Uncertain	-	Antimicrobial agents	Death within a day	[21]
7	55	<i>A. hydrophila</i>	Septicemia	Uncertain	-	Fosfomycin, Amikacin	Alive	[22]
8	62	<i>A. hydrophila</i>	Septicemia, Empyema	C	-	Ceftizoxime	Alive	[22]
9	54	<i>A. hydrophila</i>	Septicemia	C	DM, Iliac artery aneurysm	Imipenem/Cilastatin	Alive	[22]
10	49	<i>A. sobria</i>	Septicemia, Necrotizing fasciitis	Uncertain	-	Imipenem, Minocycline	Death within 2 days	[4]
11	49	<i>A. sobria</i>	Septicemia, Skin and soft tissue infections	Uncertain	-	Imipenem, Minocycline	Death within 2 days	[23]
12	40	<i>A. hydrophila</i>	Pneumonia	Uncertain	Chronic renal failure	Panipenem/Betamipron	Death within 2 days	[13]
13	57	<i>A. hydrophila</i>	Septicemia, Skin and soft tissue infections	Uncertain	DM	Imipenem/Cilastatin, Clindamycin	Alive	[24]
14	69	<i>A. hydrophila</i>	Septicemia, Skin and soft tissue infections	Uncertain	-	Cefpirome, Minocycline	Death within 2 days	[25]
15	67	<i>A. hydrophila</i>	Bacterascites?	Uncertain	-	Uncertain	Death within 2 days	[15]
16	59	<i>A. hydrophila</i>	Septicemia, Necrotizing fasciitis	Uncertain	-	Cefditoren Pivoxil	Death within 2 days	[11]
17	66	<i>A. hydrophila</i>	Septicemia, Necrotizing fasciitis	C	-	Ceftriaxone, Lower limb amputation	Death within 4 days	[26]
18	53	<i>A. hydrophila</i>	Septicemia, Skin and soft tissue infections, Bacterascites?	C	-	Antimicrobial agents (-)	Death within a day	[16]
19	54	<i>A. hydrophila</i>	Septicemia, Skin and soft tissue infections	C	-	Imipenem/Cilastatin, Amikacin	Death within 4 weeks	[27]
20	50	<i>A. hydrophila</i>	Septicemia	C	DM	Imipenem/Cilastatin	Alive	[9]
21	63	<i>A. sobria</i>	Septicemia, Necrotizing fasciitis	Uncertain	DM	Meropenem	Death within 2 days	[28]
22	63	<i>A. hydrophila</i>	Septicemia, Necrotizing fasciitis	C	-	Levofloxacin, Ceftazidime, Lower limb amputation	Alive	[29]
23	71	<i>A. hydrophila</i>	Septicemia	B	-	Meropenem, Teicoplanin	Alive	[14]
24	78	<i>A. hydrophila</i>	Septicemia	Uncertain	Malignant lymphoma	Tazobactam/Piperacillin	Death within 3 weeks	[30]
25	61	<i>A. hydrophila</i>	Septicemia, Necrotizing fasciitis	Uncertain	-	New quinolone, Lower limb amputation	Alive	[31]

A. hydrophila was isolated in 19 (76%) cases [9,11,13-16,18,20-22,24-27,29-31] and *A. sobria* in 6 (24%) [4,17,19,21,23,28]; no cases involving *A. caviae* was found. Consumption of Japanese cuisine, such as sashimi and sushi, were the cause of infection in 9 (36%) cases [11,17,21-23,27-29,31] and complications of DM in 7 cases (28%) [9,17-19,22,24,28]. Cases of bacteremia (and septicemia) or skin and soft tissue infections caused by *Aeromonas* species in patients with LC have been relatively well reported. Although two cases of patients with LC with ascites positive for *Aeromonas* species have been reported [15,16], there was no diagnosis of SBP caused by *Aeromonas* species in these cases because the polymorphonuclear cell count in the ascites was uncertain. One case of pneumonia caused by *A. hydrophila* infection of the lung tissues was found [13]. Meanwhile, septic shock and disseminated intravascular coagulation were confirmed in 18 [4,9,11,13-16,18-20,23-27,29-31] and 11 cases [9,15-18,23,24,26,28-30], respectively.

In total, 15 (60%) patients died within 4 days after admission and an additional 2 (8%) within 3-4 weeks after admission. The 1-month mortality rate was 68% (17/25), whereas the overall survival rate was 32% (8/25). In particular, among 16 cases with skin and soft tissue infections [4,11,16-19,21,23-29,31], 13 (81.3%) died within one month, which included 12 (75%) within the first 4 days after admission [4,11,16-19,21,23,25,26,28], regardless of the administration of antimicrobial agents and/or lower limb amputation, indicating extremely poor short-term prognoses. The Child-Pugh classification was Child C in four cases and unknown in 11 cases among 15 death cases within the first 4 days after admission and Child C in four cases, Child B in one case, and unknown in three cases among 8 survival cases. Therefore, there were apparent correlations between short-term mortality and Child-Pugh classification, although the number of cases was limited in this article.

CONCLUSION

In many cases of reported *Aeromonas* infections, skin and soft tissue infections in patients with LC were observed to rapidly progress, leading to poor prognoses, regardless of the administration of antimicrobial agents. Moreover, the consumption of sushi and sashimi is suspected to be a source of *Aeromonas* infections in patients with LC in Japan. Therefore, patients with LC should be advised to avoid raw seafood as much as possible to prevent infections due to *Aeromonas* as well as *Vibrio*, species.

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