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Monomicrobial Necrotizing Fasciitis Caused by *Aeromonas hydrophila* and *Klebsiella pneumoniae*

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Key Words
Necrotizing fasciitis · *Aeromonas hydrophila* · *Klebsiella pneumoniae*

Abstract
Objective: To compare specific characteristics and clinical outcomes of monomicrobial necrotizing fasciitis caused by *Aeromonas hydrophila* and *Klebsiella pneumoniae*. ***Material and Methods:*** Cases of monomicrobial necrotizing fasciitis caused by *A. hydrophila* (n = 11) and *K. pneumoniae* (n = 7) over an 8-year period were retrospectively reviewed. Differences in mortality, patient characteristics, clinical presentations, and laboratory data were compared between the *A. hydrophila* and the *K. pneumoniae* groups. ***Results:*** The clinical signs and symptoms at the time of presentation did not differ significantly ($p > 0.05$) between the two groups. The *A. hydrophila* group had a significantly shorter interval between contact and admission (1.55 ± 0.52 vs. 5.14 ± 2.12 days, $p < 0.001$) and significant lower total white blood cell counts (10,245 ± 5,828 vs. 19,014 ± 11,370 cells/mm^3, $p < 0.045$) than the *K. pneumoniae* group in the emergency room. Hepatic dysfunction was associated with mortality in patients with *A. hydrophila* infection, while diabetes mellitus was associated with mortality in patients with *K. pneumoniae* infection. Overall, 5 (45.5%) patients in the *A. hydrophila* group and 3 (42.8%) in the *K. pneumoniae* group died. ***Conclusion:*** The initial clinical course of *A. hydrophila* monomicrobial necrotizing fasciitis was characterized by more rapidly progressive disease than that of the *K. pneumoniae* infection. Patients with hepatic dysfunction and necrotizing fasciitis should be suspected of having *A. hydrophila* infection, and diabetic patients with necrotizing fasciitis should be suspected of having *K. pneumoniae* infection initially.

Introduction

Necrotizing fasciitis is a rapidly progressive, life-threatening soft-tissue infection that is a true medical and surgical emergency needing early diagnosis, emergent surgical debridement, and broad-spectrum antibiotic therapy when patients present to the emergency department [1–4]. Although necrotizing fasciitis is often caused by polymicrobial infection, the prevalence of monomicrobial necrotizing fasciitis has recently been reported to be as high as 60–80% [4–7]. Our previous study revealed that the clinical course of necrotizing fasciitis caused by Gram-negative microorganisms was more rapid and fulminant than that of Gram-positive infection, and Gram-negative aerobic pathogens, such as

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Vibrio vulnificus, Klebsiella pneumoniae, Aeromonas hydrophila, and *Escherichia coli,* were the most frequently isolated microorganisms causing necrotizing fasciitis [4].

Aeromonas spp. are Gram-negative bacilli that thrive in aquatic environments, especially in sewage, fresh or brackish water, soil, tap water, and nonfecal organic materials [8–11]. Necrotizing fasciitis caused by *A. hydrophila* often occurs after soft-tissue trauma with associated exposure to contaminated water or nonfecal organic materials and can produce skin lesions similar to those observed in necrotizing fasciitis caused by *Vibrio* species [8–12]. *A. hydrophila* is frequently associated with polymicrobial infections and can cause synergistic necrotizing fasciitis in patients coinfected with *Clostridium* species or Gram-negative bacilli, of which *Klebsiella* spp. have recently been reported to be the most common copathogens [11–14].

K. pneumoniae, a member of the Enterobacteriaceae, is a common cause of Gram-negative bacteremia and has frequently been described as a facultative organism in polymicrobial necrotizing fasciitis [15, 16]. Monomicrobial necrotizing fasciitis caused by *K. pneumoniae* is extremely rare in the Western hemisphere [16], but community-acquired infections have been increasingly reported in the past decade, especially in the Asian regions, including Taiwan, Hong Kong, Japan, Singapore, and Malaysia, with fatality rates of nearly 50% [16–21].

Our previous studies [4, 8, 22, 23] revealed that mortality rates in patients with *Vibrio* necrotizing fasciitis have decreased from 38 to 13% due to an effective program that includes early recognition, application of a treatment algorithm for emergency fasciotomy or amputation, treatment with a third-generation cephalosporin plus tetracycline or gentamicin, and an intensive unit care. Patients with *Vibrio* necrotizing fasciitis can be identified early because of a history of contact with seawater or raw seafood. However, patients with *A. hydrophila* and *K. pneumoniae* necrotizing fasciitis still have the highest mortality rates (50 and 60%, respectively) even after early diagnosis and surgical intervention in the emergency room [4]. Monomicrobial necrotizing fasciitis caused by *A. hydrophila* and *K. pneumoniae* are rarely reported [12, 17, 18]. To our knowledge, no publication or literature review has to date described or compared these two causative pathogens of fatal monomicrobial necrotizing fasciitis. Therefore, the purpose of this study was to compare the initial clinical features of *A. hydrophila* and *K. pneumoniae* necrotizing fasciitis, and the risk factors related to the outcomes.

Subjects and Methods

Study Design and Patient Selection

We reviewed the medical records of 33 patients with surgically confirmed necrotizing fasciitis caused by *A. hydrophila* and *K. pneumoniae* who were admitted to the emergency department of our hospital from June 2004 to December 2012. The enrolled patients were categorized into 2 groups: an *A. hydrophila* group and a *K. pneumoniae* group. Eight patients with *A. hydrophila* and 7 patients with *K. pneumoniae* infection who had confirmed polymicrobial necrotizing fasciitis were excluded (these patients survived after surgery).

Broad-spectrum antibiotics were initially administered to all patients, and excisional debridement of the necrotic fascia or immediate limb amputation was performed in all 33 patients diagnosed with necrotizing fasciitis.

Microbiology Laboratory Procedures

The identification of *A. hydrophila* and *K. pneumoniae* was based on standard phenotypic tests used in clinical microbiology laboratories, and the identification of *A. hydrophila* was further confirmed using the Api20E test (BioMerieux, Marcy l'Etoile, France). The antimicrobial susceptibility of *A. hydrophila* and *K. pneumoniae* was evaluated in the hospital microbiology laboratory using the standard disk diffusion technique at our institute. The susceptibility interpretative criteria for Enterobacteriaceae and *Aeromonas* spp. in our microbiological laboratory were established as recommended by the Clinical and Laboratory Standards Institute [24].

Clinical Assessment

Age, gender, comorbidities, signs and symptoms, infection site, results of bacteriological tests, predisposing factors, laboratory findings at the time of admission, interval between contact and admission, interval between diagnosis and first surgery, length of stay, and clinical outcomes were reviewed for each patient.

Differences in mortality, patient characteristics, clinical presentation, underlying chronic diseases, infection site, first operative procedure, laboratory data and hospital course were compared between the *A. hydrophila* group and the *K. pneumoniae* group.

Statistical Analysis

Statistical analyses were performed using SPSS version 12.0 statistical software (SPSS, Chicago, Ill., USA). Student's t test was used for continuous variables and Fisher's exact test was used for categorical variables to examine significant relationships between risk factors and outcomes in the two groups. $p < 0.05$ was considered statistically significant.

Results

Of the 18 patients, 15 were men and 3 were women, and the mean age was 63.6 ± 14.9 years (range 40–90). The most common complaints of patients with necrotizing fasciitis were hypotension and pain and swelling of the involved limbs with edematous, patchy, erythema-

Table 1. Characteristics of patients with monomicrobial necrotizing fasciitis caused by *A. hydrophila*

Patient No.	Age, years	Gender	Chronic underlying diseases	Site	Interval A, days	Contact mechanism	Interval B, h	Operations (first, final)	Interval C, days	Result	Duration of hospitalization, days	Systolic blood pressure ≤90 mm Hg in the ER	Intensive care unit stay	Body temperature >38.5°C in the ER
1	78	M	HCC, LC	left leg	2	abrasion	18	Fas	0	death	16	Y	Y	Y
2	68	F	HB, steroid use	both legs	2	bamboo	2	Fas	0	death	2	Y	Y	N
3	55	M	LC, gout	left thigh	1	unclear	2	Fas	0	death	2	Y	Y	N
4	47	M	LC, HCC, DM	right leg	1	unclear	5	Fas	4	death	5	N	Y	N
5	58	M	Alcoholism	right leg	2	unclear	10	Fas, AK	4	death	6	Y	Y	N
6	64	M	Gout	left leg	1	cutting wound	10	Fas, STSG	20	discharge	63	N	N	N
7	77	M	Hypertension	right foot	2	drain	5	Fas	0	discharge	12	N	N	N
8	85	M	DM, CRI, steroid use	right leg	1	unclear	2	Fas, AK	11	discharge	90	Y	Y	N
9	73	M	DM, HB	left forearm	2	cutting wound	2	Fas, STSG	28	discharge	37	N	Y	Y
10	62	F	DM	left forearm	1	fish	2	Fas, Flap	20	discharge	14	N	Y	N
11	58	M	ESRD	right leg	2	fell into ditch	7	Fas, AK	10	discharge	24	N	Y	N
Mean	65.9				1.55		5.91		8.81		24.6			

M = Male; F = female; HCC = hepatic cell carcinoma; LC = liver cirrhosis; HB = hepatitis B; CRI = chronic renal insufficiency; DM = diabetes mellitus; ESRD = end-stage renal disease; Interval A = time from contact to presentation in the emergency room; Interval B = time from the first consultation to the first operation; Interval C = time from the first operation to the final operation; Fas = fasciotomy; AK = above-the-knee amputation; STSG = split-thickness skin graft; Y = yes; N = no; ER = emergency room.

Table 2. Laboratory data of patients with monomicrobial necrotizing fasciitis caused by *A. hydrophila*

Patient No.	Result	White blood cell count, n/mm^3	Banded forms, %	Segmented forms, %	Lymphocyte forms, %	Platelet count, n/mm^3	Albumin, g/dl	Creatinine, μmol/l	Alanine aminotransferase, U/l	C-reactive protein, mg/l	Positive culture
1	death	16,500	16	78	2	151,000	2.2	1.61	30	43.5	B and W
2	death	5,600	15	67	6	150,000	1.7	2.08	45	93.4	W
3	death	3,100	27	57	8	57,000	2.9	2.12	23	65.77	B and W
4	death	5,100	34	45	8	64,000	1.6	1.4	121	30	W
5	death	2,600	9	61	6	90,000	1.7	2.8	189	100	W
6	discharge	11,200	4	88	4	158,000	3	1.7	27	26.2	B and W
7	discharge	18,800	2	81.5	7.5	131,000	2.5	1.14	25	115	W
8	discharge	7,200	4	71	18	140,000	2.1	2.33	35	27.5	W
9	discharge	12,100	9	85	3	170,000	2.4	1.49	20	140	W
10	discharge	13,500	1	80	13	79,000	2.5	0.88	72	49.5	W
11	discharge	17,000	12.5	71	9.5	150,000	1.5	5.7	19	89	W
Mean		10,245	12.1	71.3	7.73	121,818	2.19	2.11	55.1	70.9	

W = Wound; B = blood.

tous, and hemorrhagic bullous skin lesions at the time of admission to the emergency room or at the time of consultation in the hospital ward.

Culture findings confirmed that the cause of monomicrobial infection was *A. hydrophila* in 11 patients and *K. pneumoniae* in 8 patients. Eight patients died (5 in the *A. hydrophila* group and 3 in the *K. pneumoniae* group), resulting in an all-cause in-hospital mortality rate of 44.4%. *A. hydrophila* specimens were isolated from wounds in 8 cases, and from blood and wounds in 3 cases. *K. pneumoniae* was isolated from wounds in 5 cases and from blood and wounds in 2 cases. Broad-spectrum antibiotics were initially administered to these patients with necrotizing fasciitis in the emergency room. These antibiotics were continued after surgery and changed to antibiotics specifically targeting cultured bacteria a few days later.

Characteristics of the Patients in the A. hydrophila Group

Of the 11 patients in the *A. hydrophila* group, 9 were men and 2 were women, with a mean age of 65.9 ± 11.4 years (range 47–85). One patient reported having handled fish, 1 had acquired abrasion wounds while working, 1 had had contact with dirty water in a drain, and 1 had fallen into a ditch during a motor vehicle accident. Two patients had cutting wounds and 1 had been injured while working with bamboo on a farm. Four patients were farmers and did not recall any injuries. Five patients died (a mean of 6.20 ± 5.76 days after admission), resulting in an all-cause in-hospital mortality rate of 45.5% (tables 1, 2).

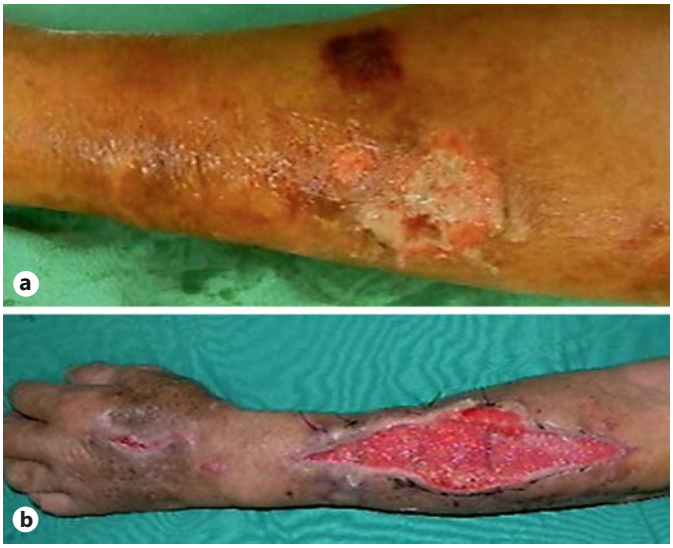
The estimated period from exposure or injury to presentation at the emergency room was 1–2 days prior to admission. The mean interval from treatment in the emergency room to the first operation was 5.91 ± 5.1 h.

Two patients had upper-limb skin lesions and 9 had lower-limb skin lesions. All of the patients initially underwent fasciotomy and debridement. Three patients underwent above-the-knee amputation after a few days due to progressive skin involvement following fasciotomy. Two patients received skin grafts, 1 patient underwent flap reconstruction, 1 patient underwent debridement, and 1 received only wound care after the initial fasciotomy (fig. 1). Three patients did not undergo any surgery following fasciotomy; these patients died. Five (53.3%) patients were hypotensive with a systolic blood pressure ≤90 mm Hg. The mean hospital stay of the patients was 24.6 ± 28.3 days (range 2–90).

All of the *A. hydrophila* isolates were susceptible to ampicillin, amikacin, ceftazidime, ceftriaxone, cefuroxime, ciprofloxacin, gentamicin, imipenem, piperacillin, and tetracycline. Broad-spectrum antibiotic therapy with third-generation cephalosporin plus vancomycin or teicoplanin was initially administered to 9 patients, and antibiotic therapy with oxacillin plus gentamicin was administered to 2 patients (cases 7 and 9).

Characteristics of the Patients in the K. pneumoniae Group

Of the 7 patients in the *K. pneumoniae* group, 6 were men and 1 was a woman, with a mean age of 59.9 ± 19.6 years (range 40–90). Three patients had acquired abrasion wounds while working, and 1 had previous chronic ulcers. One patient had had contact with seawater, and 2 did not recall any injuries. Three patients died a mean of 27.7 ± 27.4 days after admission, and the all-cause in-hospital mortality rate was 42.8% (tables 3, 4).



Color version available online

Fig. 1. A 73-year-old male with a history of hepatitis B and diabetes mellitus had left forearm and hand pain on the second day after a cutting injury. **a** Preoperative photographs of the left hand revealed skin erosion, vesicles, and subcutaneous bleeding. **b** After an emergency fasciotomy, a wound culture confirmed the presence of *A. hydrophila.* He received a skin graft on the thirtieth day after fasciotomy.

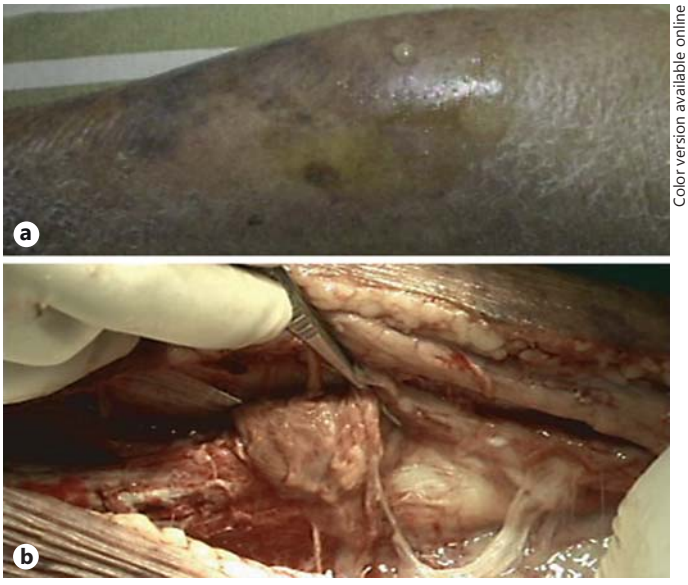


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Fig. 2. A 90-year-old female with a history of diabetes mellitus and chronic renal insufficiency had left lower leg pain for 2 days. **a** The left lower leg revealed patchy purpura and edema in the emergency room. **b** After fasciotomy, the lower leg showed yellowish pus accumulated in the fascia and muscular layer. Above-the-knee amputation was performed immediately. The cultured specimen confirmed *K. pneumoniae;* however, this patient died on the sixteenth day after admission owing to progressive septic shock and multiple organ failure.

Table 3. Characteristics of patients with monomicrobial necrotizing fasciitis caused by *K. pneumoniae*

Patient No.	Age, years	Gender	Chronic underlying diseases	Site	Interval A, days	Contact mechanism	Interval B, h	Operations (first, final)	Interval C, days	Result	Duration of hospitalization, days	Systolic blood pressure ≤90 mm Hg in the ER	Intensive care unit stay	Body temperature >38.5°C in the ER
1	84	M	DM, MI	right forearm	7	unknown	5	Fas	0	death	8	Y	Y	N
2	90	F	DM, gout, steroid use	left leg	2	abrasion	3	AK, debridement	12	death	16	Y	Y	N
3	58	M	DM, steroid use	left leg	4	abrasion	7	Fas, debridement	14	death	59	Y	Y	N
4	49	M	DM, LC, HC	right leg	7	seawater	12	Fas, STSG	30	discharge	44	N	Y	N
5	55	M	DM, HC, gout	right arm	6	abrasion	6	Fas, STSG	13	discharge	26	N	Y	N
6	43	M	DM	left leg	7	chronic ulcer	5	Fas, debridement	7	discharge	10	N	Y	N
7	40	M	DM, LC	right forearm	3	unknown	14	Fas, STSG	17	discharge	21	N	N	N
Mean	59.9				5.14		7.43		13.3		26.3			

M = Male; F = female; DM = diabetes mellitus; MI = myocardial infarction; LC = liver cirrhosis; HC = hepatitis C; Interval A = time from contact to presentation to the emergency room; Interval B = time from the first consultation to the first operation; Interval C = time from the first operation to the final operation; AK = above-the-knee amputation; STSG = split-thickness skin graft; Y = yes; N = no; Fas = fasciotomy; ER = emergency room.

Table 4. Laboratory data of patients with monomicrobial necrotizing fasciitis caused by *K. pneumoniae*

Patient No.	Result	White blood cell count, n/mm^3	Banded forms, %	Segmented forms, %	Lymphocyte forms, %	Platelet count, n/mm^3	Albumin, g/dl	Creatinine, μmol/l	Alanine aminotransferase, U/l	C-reactive protein, mg/l	Positive culture
1	death	15,100	18	65.5	13.5	124,000	1.5	1.86	68	70	W
2	death	36,600	4	90	25	197,000	1.7	1.16	15	93	W
3	death	3,000	9	27.5	8	54,000	2	1.3	33	156	B and W
4	discharge	31,300	10.5	80	5	44,000	2.6	1.73	64	128	B and W
5	discharge	15,400	0	87	9	144,000	3	1.25	92	10	W
6	discharge	18,200	0	86	11	235,000	1.8	0.88	24	139	W
7	discharge	13,500	2	95	1	125,000	2	0.8	28	178	W
Mean		19,014	6.2	75.86	10.36	131,857.14	2.08	1.28	46.3	110.6	

W = Wound; B = blood.

The interval from injury to presentation at the emergency room ranged from 2 to 7 days (mean 5.14 ± 2.12). The mean interval between treatment in the emergency room and the first operation was 7.43 ± 4.04 h.

Three patients had upper-limb skin lesions and 4 had lower-limb skin lesions. Six patients initially underwent fasciotomy with debridement and 1 patient underwent an immediate above-the-knee amputation due to progressive uncontrolled initial sepsis (fig. 2). Three patients received skin grafts, and 3 underwent debridement with direct closure. No *Klebsiella* patient was febrile. Three (14.5%) patients had a systolic blood pressure ≤90 mm Hg at presentation to the emergency room; these patients died. The mean duration of hospital stay was 26.3 ± 18.8 days (range 8–59).

All *K. pneumoniae* isolates were susceptible to amikacin, ceftazidime, ceftriaxone, cefuroxime, ciprofloxacin, aztreonam, gentamicin, and imipenem. Broad-spectrum antibiotics were administered initially in the emergency room to patients with *K. pneumoniae* infection; ceftriaxone alone was given to 3, cefazolin plus gentamicin to 2, and ceftriaxone plus vancomycin to 2 patients.

Comparison of the A. hydrophila and K. pneumoniae Groups

Age, sex, wound location, degree of hypotension, fever, nature of the first surgery, laboratory data and hospital course, and interval between diagnosis and the first surgery did not differ significantly ($p > 0.05$) between the

two groups. However, the patients with *Aeromonas* infection had a significantly shorter interval between contact and admission (1.55 ± 0.52 vs. 5.14 ± 2.12 days, $p < 0.001$) and significantly lower total white blood cell counts (10,245 ± 5,828 vs. 19,014 ± 11,370 cells/mm^3, $p < 0.045$) than patients with *K. pneumoniae* infection in the emergency room (tables 5, 6).

Hepatic dysfunction with or without other conditions (diabetes, gout, or steroid use) was associated with mortality in patients with *A. hydrophila* infection ($p = 0.048$), while diabetes mellitus was associated with patients with mortality in *K. pneumoniae* infection ($p = 0.01$).

Discussion

In the present study, the interval between exposure and admission to the emergency room for patients with *A. hydrophila* infection was significantly shorter than that for patients with *K. pneumoniae* infection. The initial clinical course of *A. hydrophila* infection was characterized by more rapidly progressive disease than that of the *K. pneumoniae* infection. *A. hydrophila* infection often occurred in patients with liver cirrhosis, hepatitis, and hepatic malignancies, while *K. pneumoniae* was often associated with diabetes mellitus.

The more rapid progression of *A. hydrophila* compared to *K. pneumoniae* could be due to the fact that *A. hydrophila* can produce many virulence factors, including hemolysin, cytotoxin, aerolysin, enterotoxin, endotoxin, protease, adhesion, and lipases [12, 14, 25, 26]. These factors are associated with extensive muscular necrosis and cause damage to the liver, kidneys, and pulmonary system, resulting in septic shock and multiple organ failure [25, 26]. However, the virulence and pathogenicity of *K. pneumoniae* have been linked to its polysaccharide capsule envelope, and K1 and K2 are the most virulent serotypes [17–20]. These capsular serotypes and hypermucoviscosity phenotypes are highly resistant to serum killing and phagocytosis and have been implicated in the development of disseminated infection [18, 27]. Necrotizing fasciitis caused by *K. pneumoniae* may be a consequence of transient bacteremia, or of gut bacterial translocation, followed by bacterial seeding at the extremities [17, 18, 27]. Equally important, Ko et al. [28] reported that *A. hydrophila* caused more rapid and intense local accumulation of inflammatory cells than *K. pneumoniae* and induced a more robust proinflammatory cytokine response when inoculated intramuscularly in mice [28].

The finding that patients with *Aeromonas* infection had a higher amount of banded leukocyte forms and significantly lower total white blood-cell counts than patients with *K. pneumoniae* infection in the emergency room in this study confirms the results of the animal study of Ko et al. [28]. They reported that the response of suppurative inflammation and aggregates of neutrophils might occur faster in mice with *A. hydrophila* infection than in those with *K. pneumoniae* infection [28]. We speculated that the response of suppurative inflammation might occur later with *K. pneumoniae* infection than that with *A. hydrophila* infection, and that the host can produce much more white blood cells to resist *K. pneumoniae* infection.

Finally, the finding of previous studies [10, 12, 14] that monomicrobial *A. hydrophila* infections such as necrotizing fasciitis and bacteremia have commonly been reported to be associated with liver cirrhosis and malignancy and impaired phagocytic activity of the reticuloendothelial system [10, 12, 14] confirms previous reports that cases of *K. pneumoniae* necrotizing fasciitis have shown a significant association with diabetes mellitus, present in 62.5–100% of such patients [17, 18, 27]. In this study, we also observed that hepatic dysfunction was associated with mortality in patients with *A. hydrophila* infection and that diabetes mellitus was associated with mortality in patients with *K. pneumoniae* infection. Although patients with *K. pneumoniae* necrotizing fasciitis have been reported to have a higher incidence of concomitant distant abscess, we did not find any distant abscesses in our cases [15–20].

In our previous studies, the clinical course of necrotizing fasciitis caused by Gram-negative microorganisms was more rapid and fulminant than that of Gram-positive infection, and the patients with diabetes mellitus alone had significant associations with *Staphylococcus aureus* necrotizing fasciitis [4, 29]. The mortality rate of necrotizing fasciitis caused by *S. aureus* in diabetic patients was 18.7% (6/32) [29]. The 7 cases of *K. pneumoniae* necrotizing fasciitis were associated with diabetes mellitus, resulting in a mortality rate of 42.8% in this study. The clinical signs and symptoms of necrotizing fasciitis caused by *K. pneumoniae* and *S. aureus* in diabetic patients are characteristically indistinguishable at the time of presentation, and it takes 3–4 days to obtain the results of microbiological analysis and antimicrobial sensitivity of the specimens. Due to the high mortality rate and fulminant clinical course, *K. pneumoniae* infection as well as *S. aureus* infection should be initially suspected in diabetic patients with necrotizing fasciitis.

Table 5. Comparison between the *A. hydrophila* group and the *K. pneumoniae* group for characteristics at the first consultation and treatment

Variable	*A. hydrophila* group	*K. pneumoniae* group	p value
Patients, n	11	7	
Age, years	65.9±11.4	59.9±19.6	0.42
Sex, n			0.47
Male	9	6	
Female	2	1	
Mortality rate, %	45.5	42.8	0.65
Death	5	3	
Survival	6	4	
Timing from contact to presentation to the ER, days	1.55±0.52	5.14±2.12	<0.001[a]
Death	1.6±0.55	4.33±2.52	0.049[a]
Survival	1.5±0.55	5.75±1.89	0.0007[a]
Timing from the first consultation to the first operation, h	5.91±5.1	7.43±4.04	0.52
Death	7.43±6.77	5±2	0.58
Survival	4.67±3.33	9.25±4.43	0.097
Underlying chronic disease, n			
Hepatic dysfunction and DM	2 (1)	3 (0)	
Hepatic dysfunction with or without other conditions	4 (4)	0 (0)	0.048[b]
Diabetes mellitus with or without other conditions	2 (0)	4 (3)	0.01[c]
End-stage renal disease	1 (0)	0 (0)	
Hypertension	1 (0)	0 (0)	
Gout	1 (0)	0 (0)	
Wound location, n			
Upper extremity	2 (0)	3 (1)	
Lower extremity	9 (5)	4 (2)	
Hospital stay, days	24.6±28.3	26.3±18.8	0.89
Death	6.20±5.76	27.7±27.4	0.13
Survival	40±30.8	25.2±14.2	0.4

Values are presented as means ± SD unless otherwise stated. Values in parentheses represent the number of deaths. [a] Mean $p < 0.05$ and the difference was significant. [b] Mean $p < 0.05$ and the difference was significant (association with mortality for hepatic dysfunction with or without other conditions, e.g. diabetes, gout, or steroid use). [c] Mean $p < 0.05$ and the difference was significant (association with diabetes mellitus with or without other conditions).

Table 6. Comparison between the *A. hydrophila* group and the *K. pneumoniae* group for laboratory data at the first consultation in the emergency room or ward

	White blood cell count, n/mm^3	Banded forms, %	Segmented forms, %	Lymphocyte forms, %	Platelet count, n/mm^3	Albumin, g/dl	Creatinine, μmol/l	Alanine aminotransferase, U/l	C-reactive protein, mg/l
All patients (n = 18)									
A. hydrophila group (n = 11)	10,245±5,828	12.1±10.5	71.3±13.1	7.73±4.6	121,818±41,080	2.19±0.52	2.11±1.31	55.1±53.8	70.9±39
K. pneumoniae group (n = 7)	19,014±11,370	6.21±6.64	75.9±23.3	10.4±7.62	131,857±69,420	2.09±0.53	1.28±0.4	46.3±28.5	110.6±57.4
p value	0.045[a]	0.2	0.6	0.37	0.7	0.68	0.13	0.7	0.098

[a] Mean $p < 0.05$ and the difference was significant.

In this study, there were several limitations. First, we did not detect the capsular serotype K1/K2. Genotype K1 strains are significantly virulent and predominant in the East; however, we need to identify the roles of these genotypes in necrotizing fasciitis. The second limitation was that we could not reduce the mortality associated with monomicrobial *A. hydrophila* and *K. pneumoniae* necrotizing fasciitis, and we did not identify the causes of death even though we performed early diagnosis and surgical intervention.

Conclusion

Monomicrobial necrotizing fasciitis caused by *A. hydrophila* and *K. pneumoniae* had similar clinical courses and high mortality rates. The initial clinical course of *A. hydrophila* infection was characterized by more rapidly progressive disease than that of *K. pneumoniae* infection. Patients with hepatic dysfunction and necrotizing fasciitis should be suspected of having *A. hydrophila* infection, and diabetic patients with necrotizing fasciitis should be suspected of having *K. pneumoniae* infection initially if they have no history of contact with seawater or raw seafood.

References

1 Bellapianta JM, Ljungquist K, Tobin E, et al: Necrotizing fasciitis. J Am Acad Orthop Surg 2009;17:174–182.
2 Morgan MS: Diagnosis and management of necrotizing fasciitis: a multiparametric approach. J Hosp Infect 2010;75:249–257.
3 Angoules AG, Kontakis G, Drakoulakis E, et al: Necrotizing fasciitis of upper and lower limb: a systematic review. Injury 2007; 38S:18–25.
4 Tsai YH, Huang KC, Shen SH, et al: Microbiology and surgical indicators of necrotizing fasciitis in a tertiary hospital of Southwest Taiwan. Int J Infect Dis 2012;16:e159–e165.
5 Anaya DA, Bulger EM, Kwon YS, et al: Predicting death in necrotizing soft tissue infections: a clinical score. Surg Infect 2009;10: 517–522.
6 Bair MJ, Chi H, Wang WS, et al: Necrotizing fasciitis in Southeast Taiwan: clinical features, microbiology, and prognosis. Intern J Infect Dis 2009;13:255–260.
7 Oncul O, Erenoglu C, Top C, et al: Necrotizing fasciitis: a life-threating clinical disorder in uncontrolled type 2 diabetic patients. Diabetes Res Clin Pract 2008;80:218–223.
8 Tsai YH, Hsu RW, Huang TJ, et al: Necrotizing soft tissue infections and sepsis caused by *Vibrio vulnificus* compared with those caused by *Aeromonas* species. J Bone Joint Surg Am 2007;89:631–636.
9 Tsai YH, Huang KC, Huang TJ, et al: Fatal necrotizing fasciitis caused by *Aeromonas sobria* in two diabetic patients. Clin Orthop Relat Res 2009;467:846–849.
10 Wu CJ, Chen PL, Tang HJ, et al: Incidence of *Aeromonas* bacteremia in Southern Taiwan: *Vibrio* and *Salmonella* bacteremia as comparators. J Microbiol Immunol Infect 2014;47: 145–148.
11 Ko WC, Chuang YC: *Aeromonas* bacteremia: review of 59 episodes. Clin Infect Dis 1995;20: 1298–1304.
12 Ko WC, Lee HC, Chuang YC, et al: Clinical features and therapeutic implications of 104 episodes of monomicrobial *Aeromonas* bacteraemia. J Infect 2000;40:267–273.
13 Furusu A, Yoshizuka N, Abe K, et al: *Aeromona hydrophila* necrotizing fasciitis and gas gangrene in a diabetic patient on hemodialysis. Nephrol Dial Transplant 1997;12:1730–1734.
14 Chao CM, Lai CC, Tang HJ, et al: Skin and soft-tissue infections caused by *Aeromonas* species. Eur J Clin Microbiol Infect Dis 2013; 32:543–547.
15 Dalal A, Ahluwalia M, Urban C: *Klebsiella pneumoniae* necrotizing fasciitis associated with lung abscess. Infect Dis Clin Pract 2009; 17:48–51.
16 Kohler JE, Hutchens MP, Sadow PM, et al: *Klebsiella pneumoniae* necrotizing fasciitis and septic arthritis: an appearance in the Western hemisphere. Surg Infect (Larchmt) 2007;8:227–232.
17 Cheng NC, Yu YC, Tai HC, et al: Recent trend of necrotizing fasciitis in Taiwan: focus on monomicrobial *Klebsiella pneumoniae* necrotizing fasciitis. Clin Infect Dis 2012;55:930–939.
18 Lee SS: *Klebsiella pneumoniae* is an emerging major pathogen in necrotizing fasciitis. Clin Infect Dis 2012;55:940–942.
19 Ho PL, Tang WM, Yuen KY: *Klebsiella pneumoniae* necrotizing fasciitis associated with diabetes and liver cirrhosis. Clin Infect Dis 2000;30:989–990.
20 Mita N, Narahara H, Okawa M, et al: Necrotizing fasciitis following psoas muscle abscess caused by hypermucoviscous *Klebsiella pneumoniae*. J Infect Chemother 2012;18:565–568.
21 Mazita A, Abdullah A, Primuharsa SH: Cervical necrotizing fasciitis due to *Klebsiella*. Med J Malaysia 2005;60:657–659.
22 Tsai YH, Hsu RW, Hung KC, et al: Systemic *Vibrio* infection presenting as necrotizing fasciitis and sepsis: a series of thirteen cases. J Bone Joint Surg Am 2004;86:2497–2502.
23 Tsai YH, Huang TJ, Hsu RW, et al: Necrotizing soft-tissue infections and primary sepsis caused by *Vibrio vulnificus* and *Vibrio cholerae* non-O1. J Trauma 2009;66:899–905.
24 Clinical and Laboratory Standards Institute: Performance Standards for Antimicrobial Susceptibility Testing: Nineteenth Informational Supplement – M100-S19. Wayne, CLSI, 2009.
25 Brenden RA, Huizinga HW: Pathophysiology of experimental *Aeromonas hydrophila* infection in mice. J Med Microbiol 1986;21:311–317.
26 Wu CJ, Wu JJ, Yan JJ, et al: Clinical significance and distribution of putative virulence markers of 116 consecutive clinical *Aeromonas* isolates in Southern Taiwan. J Infect 2007; 54:151–158.
27 Chang CM, Lee HC, Lee NY, et al: Community-acquired *Klebsiella pneumoniae* complicated skin and soft-tissue infections of extremities: emphasis on cirrhotic patients and gas formation. Infect 2008;36:328–334.
28 Ko WC, Chiang SR, Yan JJ, et al: Comparative pathogenicity of bacteraemic isolates of *Aeromonas hydrophila* and *Klebsiella pneumoniae*. Clin Microbiol Infect 2005;11:553–558.
29 Tsai YH, Hsu RW, Hung KC, et al: The comparison of necrotizing fasciitis and sepsis caused by *Vibrio vulnificus* and *Staphylococcus aureus*. J Bone Joint Surg Am 2011;93: 274–284.