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Open fracture wound infections caused by *Aeromonas* species

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ABSTRACT

Background: The knowledge about *Aeromonas* infections following open fracture is limited, so the aim of this study was to the clinical characteristics of patients with open fracture wound infections caused by *Aeromonas* species. **Materials and Methods:** From 2009 to 2012, patients with open fracture wound infections caused by *Aeromonas* species were identified from a computerized database of a regional hospital and a medical center in southern Taiwan. The medical records of these patients were retrospectively reviewed. **Results:** A total of 27 patients with an open wound infections due to *Aeromonas* species were identified. The patients ranged in age from 18 to 77 years (mean, 49.6 years). Active cancer ($n = 3$, 11.1%) was the most common underlying disease. About 26% ($n = 7$) of the patients had a history of exposure to aqueous environments prior to infection. Eight patients presented with shock, but only one patient presented with hemorrhagic bullae. The majority ($n = 22$, 82%) of patients had polymicrobial infections. Among six patients who required amputation, three did not receive appropriate antibiotic initially, and three cases had initial presentations of septic shocks. The overall in-hospital mortality was 3.7%. **Conclusions:** *Aeromonas* species should be considered important causative pathogens of the open wound infections and most infections are polymicrobial. The outcome was poor, especially for patients receiving inappropriate initial antibiotic or presenting with shock.

KEY WORDS: *Aeromonas*, open fracture, trauma

INTRODUCTION

Posttraumatic infections usually develop as a result of contaminated open fractures and can occur in up to 25% of open fractures. Several risk factors included elderly, diabetes mellitus, active cancer, and immunocompromised states [1-5], were reported to be associated with posttraumatic infections. The portal of entry of the organism should be that microorganisms intrude bone directly in the setting of trauma or contiguous spread from injury to overlying soft tissue. Therefore, the possible source of organisms includes skin flora, soil organisms, or nosocomial pathogens acquired through surgical intervention.

Previous studies had shown *Staphylococcus aureus*, coagulase-negative *Staphylococci*, and aerobic Gram-negative bacilli are the most common organisms [6-8]. Rarely, *Aeromonas hydrophila* was reported to cause posttraumatic skin and soft tissue infections [9-15]. *Aeromonas* species are Gram-negative, rod-shaped bacteria that are ubiquitous in aquatic environments. These organisms are frequently isolated from fresh or brackish

water, sewage, soil, and tap water in temperate or subtropical countries, such as Taiwan [16-20]. The gastrointestinal tract is the most common site of *Aeromonas* spp. infection, and extra-intestinal infections include bacteremia, pneumonia, empyema, necrotizing fasciitis, septic arthritis, endocarditis, meningitis, urinary tract infection, skin and soft tissue infections are also reported [15-20]. Recently, we observed that the *Aeromonas* infections following open fracture is emerging. To better understand the clinical characteristics of open fracture wound *Aeromonas* infections, we perform this study to investigate this clinical entity in southern Taiwan.

MATERIALS AND METHODS

Hospital Setting and Patient Selection

This study was conducted at two hospitals located in southern Taiwan. Patients with positive cultures for *Aeromonas* species following traumatic open fracture were identified from the hospital's computerized database. The medical records of all patients were retrospectively reviewed. The following patient characteristics and laboratory findings were collected from the records: age, gender, underlying conditions (history of immunosuppressant drug use, diabetes mellitus, liver cirrhosis, end-stage renal disease, and active cancer), laboratory data (complete blood count, liver and renal function, electrolyte and biochemical test), microbiological findings, antimicrobial sensitivity test results, and patient outcome. The records and information of patients were anonymized and de-identified prior to analysis. Ethics approval was obtained from Institution Review Board of Chi Mei Medical Center in accordance with the Ethical standards of the 1964 and Declaration of Helsinki as revised in 2000.

Bacterial Isolates and Antimicrobial Susceptibilities

All isolates were identified by conventional biochemical methods and were further verified by the API-20E System (bioMérieux Vitek Inc, Hazelwood, MO, USA), the ID 32 GN System (bioMérieux Vitek Inc), or the Vitek 2 ID-GNB identification card (bioMérieux Inc, Durham, NC, USA). Antibiotic sensitivity was determined using the disk diffusion method as described by the Clinical and Laboratory Standards Institute [21].

RESULTS

Clinical Characteristics

The clinical characteristics of the 27 patients with an open wound infections caused by *Aeromonas* species are summarized in Table 1. There were six episodes in 2009, 12 episodes in 2010, seven episodes in 2011, and two episodes in 2012, respectively. The patients ranged in age from 18 to 77 years (mean, 49.6 years). Most of the patients were men (n = 18, 67%). Active cancer (n = 3, 11.1%), including each one of gastric cancer, tongue cancer, and ureter cancer, was the most common underlying disease, followed by diabetes mellitus and chronic hepatitis B. No patient had liver cirrhosis or end-stage renal disease. About 26% (n = 7) of the patients had a history of exposure to aqueous environments prior to infection. Only one patient presented with hemorrhagic bullae and eight patients presented with shock. Six patients had leukocytosis with white blood cell count > 11,000/mm^3, but 20 patients had abnormal liver function results with aspartate transaminase > 50 IU/L. C-reactive protein (CRP) levels were available in eight patients, and seven (87.5%) had elevated CRP levels. The majority (n = 22, 82%) of patients had polymicrobial infections. The most common isolates obtained from patients with polymicrobial infections were *Enterococcus* species (n = 9), followed by *Pseudomonas aeruginoa* (n = 6), *Klebsiella* species (n = 3, including *K. pneumoniae* (n = 2) and *Klebsiella oxytoca* (n = 1), *Morganella morganii* (n = 3), and *Enterobacter cloacae* (n = 6) *Citrobacter freundii* (n = 2). *Shewanella algae* (n = 2), *Escherichia coli* (n = 1) *Serratia marscences* (n = 1), *Acinetobacter baumannii* (n = 1) and *Proteus vulgaris* (n = 1). One (3.7%) patient had concurrent A. *hydrophila* bacteremia.

Table 1: Clinical characteristics of 27 patients with open fracture wound infections caused by *Aeromonas* species

???	No (%) or mean±SD of patients (n=27)
Age, years, mean±SD	49.6±19.8
Age≥65 years, *n* (%)	8 (29.6)
Female, *n* (%)	9 (33.3)
Underlying condition	
Active cancer	3 (11.1)
Diabetes mellitus	2 (7.4)
Chronic hepatitis B	1 (3.7)
Alcoholism	2 (7.4)
Immunocompromised status	4 (14.8)
Water exposure	7 (25.9)
Initial presentations	
Hemorrhagic bullae	1 (3.7)
Shock	8 (29.6)
Laboratory findings	
White blood cell (cell/uL), mean±SD	13196.3±9136.0
Hemoglobin (g/dL), mean±SD	12.7±2
Platelet (cell/uL), mean±SD	219600±6200
Aspartate transaminase (IU/L), mean±SD	73.6±70.6
Total bilirubin (mg/dL), mean±SD	0.6±0.2
Albumin (g/dL), mean±SD	2.8±0.7
Urea nitrogen (mg/dL), mean±SD	18.5±8.4
Serum creatinine (mg/dL), mean±SD	1.1±0.5
CRP (mg/L), mean±SD	93.2±140.1
Polymicrobial infections	22 (81.5)
Bacteremia	1 (3.7)
Surgery treatment<48 h	21 (77.8)
Outcome	
Intensive care unit admission	9 (33.3)
Mechanical ventilation	4 (14.8)
Amputation	6 (22.2)
In-hospital mortality	1 (3.7)

CRP: C-reactive protein, SD: Standard deviation

Outcome Analysis

Six patients required amputation. Five had polymicrobial infections, and none had underlying immunocompromised condition. The only poor prognostic factor for amputation was acute respiratory failure needing the support of mechanical

ventilator [Table 2]. Overall, nine patients were admitted to the intensive care unit, and four patients had acute respiratory failure. The overall in-hospital mortality was 3.7%.

Microbiological Investigations

The results of *in vitro* susceptibility testing to various antimicrobial agents against *Aeromonas* species are shown in Table 3. All of the clinical isolates were susceptible to amikacin and imipenem, and more than 90% of clinical isolates were susceptible to third- or fourth-generation cephalosporins and ciprofloxacin.

DISCUSSION

This study on the open wound *Aeromonas* infection and had several significant findings. In this study, we documented the 27 patients who developed *Aeromonas* infection following open fractures. In fact, human infections caused by *Aeromonas* species are commonly associated with wound exposure to environmental sources or ingestion of food contaminated with *Aeromonads* [22,23]. Despite previous studies that have demonstrated that the majority of traumatic wound infections due to *Aeromonads* are water-related, only 25% of the patients in our study had a history of exposure to water prior to infection. The discrepancy, however, might be partly explained by the nature of the retrospective design of the study. We cannot obtain the detailed history from the retrospective chart review. Overall, this study suggests that physicians should keep in mind *Aeromonad* as one of the differential diagnosis of traumatic wound infections complicating open fracture.

Table 2: Risk factors for amputation for open fracture wound infections caused by *Aeromonas* species

Characteristics	Limb-reserve (n=21)	Amputation (n=6)	P value
Elderly (age>65 years)	8 (38.1)	0 (0.0)	0.1951
Female	7 (33.3)	2 (33.3)	0.9374
Immunocompromised conditions	4 (19.0)	0 (0.0)	0.6140
Initial shock	5 (23.8)	3 (50.0)	0.4538
Leukocytosis	4 (19.0)	2 (33.3)	0.8521
Polymicrobial infection	17 (81.0)	5 (83.3)	0.6396
Bacteremia	1 (4.8)	0 (0.0)	0.5004
Inappropriate antibiotic treatment	2 (9.5)	3 (50.0)	0.0975
Surgical intervention<48 h	16 (76.2)	5 (83.3)	0.8510
Intensive care unit admission	5 (23.8)	4 (66.7)	0.1402
Mechanical ventilation	1 (4.8)	3 (50.0)	0.0361

Table 3: Rates of non-susceptibility of 27 isolates of *Aeromonas* species to 12 antimicrobial agents as determined by the disk diffusion method

???	All isolates (n=27)
Ampicillin	27 (100.0)
Ampicillin-sulbactam	26 (96.3)
Cefazolin	24 (88.9)
Cefuroxime	12 (44.4)
Ceftriaxone	2 (7.4)
Ceftazidime	2 (7.4)
Cefepime	1 (3.7)
Piperacillin-tazobactam	3 (11.1)
Imipenem	0 (0.0)
Ciprofloxacin	2 (7.4)
Gentamicin	1 (3.8)
Amikacin	0 (0)

Although most of the *Aeromonas* infections developed in patients with comorbidities, such as immunosuppression, diabetes mellitus, renal failure, and liver cirrhosis [22,23], only four patients were considered immunocompromised condition in this study. In contrast, most of the patients in the present work were immunocompetent. Therefore, our findings suggest that *Aeromonads* associated with traumatic wound infections can develop in immunocompromised and immunocompetent patients.

Traumatic wound infections caused by *Aeromonas* species are often associated with polymicrobial infections involving *Enterococcus* species, *Clostridium* species, and enteric bacilli [24-26]. In this study, we had similar findings that more than 80% of the cases were polymicrobial infections, and enterococcus was the most common co-pathogen. However, we noted two unusual cases had been co-infected with *S. algae*. *S. algae*, like *Aeromonas* species, mostly cause human infections after exposure to a marine environment or contaminated water [27]. Therefore, physicians treating patients with *Aeromonas* skin and soft tissue infections should be aware of co-pathogens, such as water-borne pathogens.

In this study, the outcomes were poor. Six patients required amputations for salvage management and one patient died. Among the six patients who needed amputations, three of them did not receive appropriate antibiotic initially, and three cases had initial presentations of septic shocks. Although the patients requiring amputations were more likely to develop in patients who received inappropriate antibiotic (according to the antibiotic sensitivity result of the cultured organisms) initially and had initial presentation of septic shock than the patients with limb-preserved, the difference did not reach statistical significance. The possible explanation of this finding may be due to the limited case number. However, we found that acute respiratory failure was significantly associated with amputation and suggested that the need for mechanical ventilation may be a good predictor for the poor outcome of patients with *Aeromonas* infections.

The antibiotic susceptibility patterns of the clinical isolates in this study were similar to those reported previously [23]. Although all of the isolates were not susceptible to ampicillin, the majority were susceptible to third- or fourth-generation cephalosporins, aminoglycosides, ciprofloxacin, and imipenem. Therefore, third- or fourth-generation cephalosporins as well as fluoroquinolones should be considered the antibiotic treatments of choice for patients with *Aeromonas* infections.

This study had several limitations. First, the case number is small, and some significant findings may not be found. However, our study is the largest ones in this field. Second, most of the patients had polymicrobial infections in this study and further may weaken the clinical significance of *Aeromonas* species.

In conclusion, *Aeromonas* species are important pathogens causing posttraumatic wound infections complicated open fracture. Most of the infections during the study period were polymicrobial, and enterococcus was the most common co-pathogen. The overall outcome is poor, especially for patients who did not receive initial appropriate antibiotic or presented with septic shock.

REFERENCES

1. Merritt K. Factors increasing the risk of infection in patients with open fractures. J Trauma 1988;28:823-7.
2. DeLong WG Jr, Born CT, Wei SY, Petrik ME, Ponzio R, Schwab CW. Aggressive treatment of 119 open fracture wounds. J Trauma 1999;46:1049-54.
3. Gross T, Kaim AH, Regazzoni P, Widmer AF. Current concepts in posttraumatic osteomyelitis: A diagnostic challenge with new imaging options. J Trauma 2002;52:1210-9.
4. Tsukayama DT. Pathophysiology of posttraumatic osteomyelitis. Clin Orthop Relat Res 1999;22-9.
5. Patzakis MJ, Wilkins J. Factors influencing infection rate in open fracture wounds. Clin Orthop Relat Res 1989;36-40.
6. Khatod M, Botte MJ, Hoyt DB, Meyer RS, Smith JM, Akeson WH. Outcomes in open tibia fractures: Relationship between delay in treatment and infection. J Trauma 2003;55:949-54.
7. Lew DP, Waldvogel FA. Osteomyelitis. Lancet 2004;364:369-79.
8. Haas DW, McAndrew MP. Bacterial osteomyelitis in adults: evolving considerations in diagnosis and treatment. Am J Med 1996;101:550-61.
9. Karam GH, Ackley AM, Dismukes WE. Posttraumatic *Aeromonas hydrophila* osteomyelitis. Arch Intern Med 1983;143:2073-4.
10. Monaghan SF, Anjaria D, Mohr A, Livingston DH. Necrotizing fasciitis and sepsis caused by *Aeromonas hydrophila* after crush injury of the lower extremity. Surg Infect (Larchmt) 2008;9:459-67.
11. Borger van der Burg BL, Bronkhorst MW, Pahlplatz PV. *Aeromonas hydrophila* necrotizing fasciitis. A case report. J Bone Joint Surg Am 2006;88:1357-60.
12. Ebrad P, Gerry F. *Aeromonas hydrophila* infection in a case of open fracture. Presse Med 1992;21:951.
13. Charissoux JL, Dunoyer J, Pecout C, Arnaud JP, Setton D. Infection of an open fracture caused by *Aeromonas hydrophila*. A case report. Rev Chir Orthop Reparatrice Appar Mot 1990;76:141-3.
14. Simodynes EE, Cochran RM 2nd. *Aeromonas hydrophila* infection complicating an open tibial fracture. A case report. Clin Orthop Relat Res 1982;117-20.
15. Blatz DJ. Open fracture of the tibia and fibula complicated by infection with *Aeromonas hydrophila*. A case report. J Bone Joint Surg Am 1979;61:790-1.
16. Lai CC, Ding LW, Hsueh PR. Wound infection and septic shock due to *Aeromonas* trota in a patient with liver cirrhosis. Clin Infect Dis 2007;44:1523-4.
17. Lai CC, Shiao CC, Lu GD, Ding LW. *Aeromonas hydrophila* and *Aeromonas sobria* bacteremia: rare pathogens of infection in a burn patient. Burns 2007;33:255-7.
18. Chao CM, Gau SJ, Lai CC. *Aeromonas* genitourinary tract infection. J Infect 2012;65:573-5.
19. Ko WC, Lee HC, Chuang YC, Liu CC, Wu JJ. Clinical features and therapeutic implications of 104 episodes of monomicrobial *Aeromonas* bacteraemia. J Infect 2000;40:267-73.
20. Chao CM, Gau SJ, Lai CC. Empyema caused by *Aeromonas* species in Taiwan. Am J Trop Med Hyg 2012;87:933-5.
21. Clinical and Laboratory Standards Institute. Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline, M45-A2. 2nd ed. Wayne, PA: CLSI; 2010.
22. Janda JM, Abbott SL. The genus *Aeromonas*: Taxonomy, pathogenicity, and infection. Clin Microbiol Rev 2010;23:35-73.
23. Parker JL, Shaw JG. *Aeromonas* spp. clinical microbiology and disease. J Infect 2011;62:109-18.
24. Voss LM, Rhodes KH, Johnson KA. Musculoskeletal and soft tissue *Aeromonas* infection: an environmental disease. Mayo Clin Proc 1992;67:422-7.
25. Semel JD, Trenholme G. *Aeromonas hydrophila* water-associated traumatic wound infections: A review. J Trauma 1990;30:324-7.
26. Kelly KA, Koehler JM, Ashdown LR. Spectrum of extraintestinal disease due to *Aeromonas* species in tropical Queensland, Australia. Clin Infect Dis 1993;16:574-9.
27. Goyal R, Kaur N, Thakur R. Human soft tissue infection by the emerging pathogen *Shewanella algae*. J Infect Dev Ctries 2011;5:310-2.

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