Short Report: Empyema Caused by *Aeromonas* Species in Taiwan

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Abstract. Strains of *Aeromonas* species are prevalent bacteria in coastal areas of southern Taiwan. *Aeromonas* is known as a cause of epidemic diarrheal disease, and the most common clinical manifestation is acute gastroenteritis. Extra-intestinal infections by *Aeromonas* species, such as pleural cavity, are rare. Herein, we described the six patients who developed *Aeromonas* spp.-related empyema, and was successfully treated with antimicrobial agent and drainage.

Aeromonas species, a curved Gram-negative rod, causes human infection through exposure to contaminated sea water or ingestion of contaminated seafood.¹ Acute gastroenteritis is the most common clinical manifestation of *Aeromonas* infection, however the extra-intestinal involvement, including bacteremia, necrotizing fasciitis, arthritis, endocarditis, cholangitis, meningitis, pneumonia, skin and soft tissue infection, has rarely been reported.^{1–7} Herein, we perform this study to find the cases of unusual presentation of *Aeromonas* infections—empyema and further investigate its associated clinical manifestations and microbiology characteristics.

This study was conducted at Chi Mei Medical Center, Liouying branch, a 900-bed tertiary care center in southern Taiwan. From the computerized database of the bacteriology laboratory from July 2004 to December 2011, patients whose cultures yielded *Aeromonas* species were identified. The clinical charts of all patients with empyema caused by *Aeromonas* species included in this study were retrospectively reviewed. Information regarding age, gender, underlying immunocompromising conditions including history of immunosuppressant drug use, diabetes mellitus, liver cirrhosis, end-stage renal disease, and malignancy were collected.

Each *Aeromonas* isolate identified as a halophilic Gram-negative rod was tested for cytochrome oxidase, glucose fermentation, citrate use, indole production, and ornithine decarboxylase. All isolates were identified by conventional methods and were further verified by one of the following automated detection systems: API-20E System (bioMérieux Vitek Inc., Hazelwood, MO), ID 32 GN System (bioMérieux Vitek Inc.), and Vitek 2 ID-GNB identification card (bioMérieux Inc., Durham, NC). Susceptibilities of these isolates were determined using the disk diffusion method as described by the Clinical and Laboratory Standards Institute.⁸

During the study period, a total of six patients had their pleural effusion with positive cultures of *Aeromonas* species. *Aeromonas* empyema with *Aeromonas hydrophila* was the most common species isolates ($N = 4$), followed by *Aeromonas veronii* ($N = 2$). The antibiotic susceptibilities for all *Aeromonas* spp. isolates were various according to different *Aeromonas* species. Overall, all of the clinical isolates were resistant to ampicillin and cefazolin, however, in contrast, amikacin, and gentamicin had good *in vitro* activity against all of clinical isolates. Additionally, third- or fourth-generation

cephalosporin and ciprofloxacin showed *in vitro* activity against five (83.3%) of six isolates.

The clinical characteristics of six patients with *Aeromonas* empyema are summarized in Table 1. Men comprised five of six patients (83.3%), and the age ranged from 44 to 74 years. Liver cirrhosis was the most common underlying disease, and hepatitis C virus infection was the most common etiology of cirrhosis. Add each one patient had diabetes mellitus and hepatoma, respectively. Most of them had the presentations of fever ($N = 5$, 83.3%) and dyspnea ($N = 5$, 83.3%). All of patients had jaundice with bilirubin > 2 mg/dL, but only two (33.3%) patients had leukocytosis. All of the patients had elevated C-reactive protein and hypoalbuminemia. There is no concurrent spontaneous bacterial peritonitis. All of them were classified as community-acquired infections. Although stool specimen were not obtained for culture in these patients, a review of the medical chart did not reveal any clear evidence for gastroenteritis preceding any of the episodes of *Aeromonas* infections. Furthermore, there was also no documentation of obvious environmental exposure for the patients, such as contact with bodies of water. Five (83.3%) of six episodes of *Aeromonas* infections were classified as spontaneous bacterial empyema (SBEM). All of the patients received drainage of pleural effusion and the clinical conditions response to antibiotic well.

Empyema caused by *Aeromonas* spp. has been rarely described, although such an association has been only noted in case reports^{9–13}; this study describes six cases of the *Aeromonas* empyema and provides several significant findings. First of all, most of the patients have the risk factor of liver cirrhosis, which can be related to hepatitis B virus (HBV), hepatitis C virus (HCV), or alcoholism. Although the association between *Aeromonas* infections and liver cirrhosis remains unclear, it seems that *Aeromonas* species may be particularly virulent in cirrhotic patients as previous studies.^{14–16}

The SBEM is defined as the spontaneous infection of pleural cavity, and it could develop in 13–30% of patients with hepatic hydrothorax.¹⁷ Spontaneous bacterial empyema may occur as a result of the direct translocation of bacterial from the peritoneal cavity or transient bacteremia. The most common etiologies include *Escherichia coli*, *Streptococcus* species, enterococci, and *Klebsiella pneumoniae*.¹⁸ Although it is rare for aeromonads as the etiology of SBEM, our findings and previous reports^{9–13} suggest that *Aeromonas* spp. including *A. hydrophila* and *A. sobria*, can be responsible for this rare clinical entity.

The outcomes of the patients in this series were favorable and all of them were cured by antibiotic and drainage. This is

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TABLE 1
Clinical manifestations of six patients with *Aeromonas* empyema

Case (year)	Age (years)	Sex	Underlying disease	Initial presentations	Clinical diagnosis	Pathogen	Antibiotics	Drainage of pleural effusion	Outcome
1 (2005)	56	F	HCV-related liver cirrhosis	Fever	SBEM	<i>A. hydrophila</i>	Ceftriaxone	Yes	Cure
2 (2005)	44	M	HBV-related liver cirrhosis	Fever, dyspnea	SBEM	<i>A. hydrophila</i>	Ceftriaxone + Minocycline	Yes	Cure
3 (2008)	74	M	Diabetes mellitus	Fever, dyspnea	Empyema thoracis	<i>A. hydrophila</i> , <i>E. coli</i>	Ciprofloxacin	Yes	Cure
4 (2008)	43	M	HCV- and alcoholism-related liver cirrhosis	Fever, dyspnea	SBEM	<i>A. hydrophila</i>	Ceftriaxone	Yes	Cure
5 (2009)	46	M	Alcoholic liver cirrhosis	Fever, dyspnea	SBEM	<i>A. veronii</i>	Ceftriaxone	Yes	Cure
6 (2010)	48	M	HBV- and HCV-related liver cirrhosis	Dyspnea, chest pain	SBEM	<i>A. veronii</i>	Ciprofloxacin	Yes	Cure

* HBV = hepatitis B virus; HCV = hepatitis C virus; SBEM = spontaneous bacterial empyema.

consistent with another two reported cases with negative blood culture that had survived the episodes of SBEM caused by *Aeromonas* species.^{10,13} In contrast to previous reports,^{11,12} both of the reported cases with *Aeromonas*-related SBEM had concomitant bacteremia and had the mortalities despite appropriate treatment with thoracotomy and third-generation cephalosporin. Based on the findings of these limited cases, it seems that bacteremia may be the poor prognostic factor of *Aeromonas* SBEM.

Aeromonads frequently cause human infection by the oral ingestion of contaminated or undercooked seafood.^{14,15} In coastal areas of southern Taiwan, strains of *Aeromonas* species are prevalent bacteria, and they can even be found in 88% of seafood in the markets.¹⁹ Therefore, it is possible that aeromonads can be encountered in the environment, including seafood and drinking water, and further cause invasive human infections in Taiwan.

The antibiotic susceptibility pattern of clinical isolates were similar to previous reports.^{2,20} All of them were resistant to ampicillin and first-generation cephalosporin, however, aminoglycosides still remains good *in vitro* activity against these clinical isolates. Additionally, more than 83% of *Aeromonas* isolates were susceptible to ciprofloxacin, gentamicin, and third-generation cephalosporin. Although this series is limited, we would like to suggest that fluoroquinolones, and third-generation cephalosporin, or aminoglycosides may be the antibiotic treatment of choice in this clinical setting of *Aeromonas* empyema based on our findings. However, further *in vitro* study about antibiotic-resistance, such as ampC beta-lactamases, among aeromonads still needed to guide the treatment.

Our study had one major limitation. The species of these *Aeromonas* isolates were identified by conventional biochemistry tests, which might not be reliable in identification of *Aeromonas* species in the modern bacterial taxonomy. Therefore, molecular identification usually is required for identifying *Aeromonas* species. However, as this report is a retrospective study, we did not keep the isolates for molecular identification methods. Further molecular methods should be applied for the associated study about *Aeromonas*.

In conclusion, we reported the rare clinical entity of bacterial empyema caused by *Aeromonas* spp., which could develop in immunocompromised patients, especially in patients with liver cirrhosis. Most of the clinical isolates are susceptible to fluoroquinolones, aminoglycosides, and third-generation cep-

alosporin, and the clinical outcomes of this clinical entity are favorable while there is no concomitant bacteremia.

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