Septic Shock Caused By Aeromonas Daca: A Bacterium That We Have Neglected In The Past.

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Case report

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Abstract

Introduction: For decades, *Aeromonas daca* has often been mistaken for *Aeromonas hydrophila* by phenotypic identification systems and shows obvious characteristics of virulence. To our knowledge, a total of two English-language studies with relatively complete data were retrieved.

Case presentation: The patient, a 26-year-old male with no underlying disease, was admitted to our hospital for 3 days because of cough, expectoration and shortness of breath. According to blood and lavage fluid cultures and next-generation sequencing (NGS), the patient was diagnosed with an *A. daca* infection. He soon deteriorated to a critical condition complicated with septic shock and died after active rescue treatment.

Conclusions: *A. daca* infection is lethal, and an accurate taxonomy can improve our understanding of the epidemiological distribution and virulence potential of this human pathogen. Third-generation cephalosporins and carbapenems should be used cautiously in the treatment of severe *A. daca* infection, and the best regimen is cefepime or fluoroquinolones.

Introduction

Aeromonas was originally isolated from children with diarrhea in Dhaka, Bangladesh, and described in 2002. Over the past decade, increasing evidence has shown that *Aeromonas* species are widely distributed in the environment and can cause a variety of infections in humans and animals, especially in coastal areas; *Aeromonas dauricus* in particular has a special status[1]. For decades, *Aeromonas daca* has often been mistaken for *Aeromonas hydrophila* by phenotypic identification systems and shows obvious characteristics of virulence. This paper reports the diagnosis and treatment of a patient who died from an infection of *A. daca* complicated with septic shock. The clinical data of patients with *A. daca* reported in China and elsewhere in the past 5 years were retrospectively analyzed to improve clinicians' understanding of the disease.

Case Presentation

A male, born 1993-10-02, was admitted to the hospital on 2020-08-09 complaining of "cough with fatigue for 3 + days and fever for 1 + days". Three days before admission, the patient caught a cold after swimming, accompanied by cough and fatigue, and did not show significant improvement after treatment with drugs purchased from the local clinic (cephalosporins). One day prior to admission, the patient developed a fever (maximum body temperature unknown) and showed symptoms including sputum expectoration, chest pain, wheezing, shortness of breath and blood in the sputum. Therefore, the patient was treated at the local People's Hospital. A CT scan of the chest showed edema and bleeding in the right upper lobe of the lung. The hospital recommended he be seen by a doctor in a higher-tier hospital. Therefore, the patient was admitted to our hospital and was treated to improve liver and kidney function given the following findings: alanine aminotransferase 150 IU/L, aspartate transferase 84 IU/L,

creatinine 197 IU/L, and uric acid 607 ml. No obvious electrolyte abnormalities were found. There were no obvious abnormalities in blood coagulation. In the routine blood test, the total number of leukocytes was 7.06 * 10 ^ 9/L, and the percentage of neutrophils. Blood gas analysis (no oxygen inhalation) indicated pH 7.32, P_{CO2} 43 mmHg, P_{O2} 37 mmHg, HCO_3 22.21 mmol/L, Lac 4.8 mmol/L, SO_2 65%, and PCT 99.57 ng/ml. A chest CT plain scan revealed 1. bilateral lung infection and 2. fatty liver (Fig. 1). The patient was admitted to our emergency department with "severe pneumonia". A physical examination on admission revealed a temperature of 37.5°C, pulse 82 beats/min, respiratory rate 18 breaths/min, BP 129/81 mmHg, and SO_2 65%. The patient was awake, alert, and oriented but presented with cyanotic lips, clear breath sounds in both lungs, wet rales in the right lung, arrhythmia, and no pathological murmur in any of the valve auscultation areas. The patient also presented with abdominal weakness, no tenderness and rebound pain. There was no edema in either lower limb. After admission, the patient was treated with noninvasive mechanical ventilation, imipenem-cilastatin sodium 1 g Q8h combined with 600 mg Q12h as an anti-infective, reduced glutathione and polyene phosphatidylcholine to treat the liver, acetylcysteine and ambroxol to treat the expectoration symptoms, and maintenance of water and electrolyte balance and other symptomatic treatments. Despite the above treatment measures, the patient’s wheezing symptoms were not obviously relieved, and the oxygen saturation progressively decreased. At approximately 03:30 in the morning, the finger oxygen saturation decreased to 70–80% (on noninvasive mechanical ventilation), and the blood pressure dropped to 75/45 mmHg. Considering the patient's severe pneumonia complicated with septic shock, endotracheal intubation was performed immediately after communicating with the patient's family members. Diffuse bleeding in the airway could be seen under electronic bronchoscopy, mainly in the right lung, and invasive mechanical ventilation was given. After bronchoscopic balloon occlusion and drug hemostasis, the patient still had obvious bleeding in the airway, and the oxygen saturation could not be maintained normal, so he was scheduled to be treated with artificial extracorporeal pulmonary circulation (ECMO). However, while the doctors were preparing to log onto the computer, the patient had a progressive decrease in blood pressure, and his oxygen saturation could not be measured. The patient finally died after emergency treatment.

We sought to further confirm the diagnosis after death, but autopsy was refused after communicating with the patient's family. After active discussion in the department, a percutaneous lung biopsy was performed to obtain lung tissue samples for pathological examination and next-generation sequencing (NGS). After obtaining ethical informed consent, a percutaneous lung biopsy was performed at the bedside, and 4 grayish brown sections of soft tissue with a diameter of approximately 2 cm were obtained. Postoperative histopathology showed acute and chronic inflammatory cell infiltration (Fig. 2), bronchoalveolar lavage culture indicated hydrophilic *Aeromonas caviae*, blood culture indicated hydrophilic *A. caviae*, and lung puncture followed by tissue NGS showed *A. daca* (Table 1).

Table 1 Next-Generation Sequencing

Type	Genus and species			
	Latin name	Sequence number	Latin name	Sequence number
G^-	Aeromonas	318461	*Aeromonas dhakensis*	100226
			Aeromonas hydrophila	6782

Literature review

There are few clinical reports on *A. daca*. A total of two English-language studies with relatively complete data were retrieved. This limited search result may be related to the fact that *A. daca* has often been mistaken for *A. hydrophila* in recent decades. The patients extracted from the literature search were aged 75, 65, and 26 years. The sole female patient was complicated with essential hypertension, while the remaining two patients were healthy males. All 3 patients were diagnosed with *A. hydrophila* according to blood culture, corrected to a diagnosis of *A. daca* by gene sequencing, and died of septic shock.

Discussion And Conclusions

Aeromonas is a gram-negative bacillus that is widely distributed in freshwater, estuarine and marine environments and can cause a variety of conditions in humans, such as diarrhea, hepatobiliary infections, skin and soft tissue infections and bacteremia, especially in patients with malignant tumors or cirrhosis[2]. A previous report showed that most human infections caused by *Aeromonas* were associated with three species: *A. hydrophila*, *Aeromonas veronii* and *A. caviae*[2]. A reclassification of the genus *Aeromonas* was proposed in 2013; *A. darkii* is a newly discovered species[3]. However, in commercial phenotypic tests in clinical laboratories, *A. daca* is often mistaken for *A. hydrophila/caviae/aeruginosa*. Recent in vitro studies have shown that the pathogenicity of *A. daca* is multifactorial, and increasing evidence shows that *A. daca* is more virulent than other *Aeromonas* species[4, 5]. However, the importance of the clinical administration of treatments for *A. hydrophila* is misleading due to inaccurate species identification. With the introduction of molecular identification methods, the order of the three previously dominant species has changed dramatically. According to recent research data, *A. daca* is the second most common species, accounting for 25.7% of the identified strains[1]. In clinical studies, *A. daca* is an independent risk factor for 14-day sepsis-related death in patients with bacteremia caused by *A. aeruginosa*[6]. The 14-day infection-related mortality rate of patients with *A. daca* infection is 25%, and the 14-day infection-related mortality rate and the crude hospital mortality rate of all *A. aeruginosa* are 10.5% and 26.3%, respectively[7]. Possible pathogenic factors of some species of *Aeromonas* include toxins (cytotoxic toxins that cause cell morphological changes), proteases, hemolysins, lipases, adhesins, lectins, fimbriae, enterotoxins, various enzymes and adventitia structures (such as the S layer and capsule). Other factors that may promote toxicity include VacB[8], enolase[9] and the presence of the type VI secretory system[10–15]. Therefore, theoretically, infection with *Aeromonas* may lead to complications such as septic shock, while the toxic reaction to infection with *A. daca* is more fatal. As reported by our

unit, the patient was complicated with diffuse alveolar hemorrhage and septic shock. The disease developed rapidly, and the patient died after emergency treatment.

A. daca can produce three different types of β-lactamases, namely, class C cephalosporinase, class D penicillinase and "CPHA" type B metallo-β-lactamases (MBLs)[2]; that is, it has specific enzymes for hydrolyzing carbapenem antibiotics and second- and third-generation cephalosporins. However, the production of carbapenem cannot be easily detected in traditional drug sensitivity tests unless a large number of inoculants or additional tests are used. It has been reported that when carbapenem antibiotics were used to treat *Aeromonas aeruginosa*, *A. aeruginosa* resistant to carbapenem antibiotics appeared[16]. For severe *Candida daca* infection, it is suggested that a large number of inoculations and/or additional drug sensitivity tests should be performed prior to carbapenem treatment. Therefore, third-generation cephalosporins and carbapenems should be used cautiously in the treatment of severe *A. dacarum* infection, and the best regimen is cefepime or fluoroquinolones.

A. daca infection is lethal, and accurate taxonomy can improve our understanding of the epidemiological distribution and virulence potential of this human pathogen. At present, due to the virulence and potential antimicrobial resistance of *A. daca*, accurate identification is encouraged. The authors believe that molecular biological detection should be carried out for severe infections caused by *Aeromonas* species. Therefore, the improvement of the understanding of *A. daca* can help us to further guide clinical treatment, and early accurate diagnosis and treatment are key to improving the prognosis and reducing the mortality of patients with septic shock. Third-generation cephalosporins and carbapenems should be used cautiously in the treatment of severe *A. daca* infection, and the best regimen is cefepime or fluoroquinolones.

Abbreviations

NGS: next-generation sequencing.

A: Aeromonas.

MBLs: type B metallo-β-lactamases.

Declarations

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Authors' contributions

QZ,YZ,XH and LJ participated in the research question, contributed to the data analysis,and were responsible for drafting the manuscript. QZ designed the study, gathered and analyzed data, performed

statistical analysis, wrote the manuscript, and are responsible for the integrity of the work as a whole. XH analyzed data and revised the manuscript for critical intellectual content. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author and data was publicly available on reasonable request.

Ethics approval and consent to participate

This case report received approval from The First Affiliated Hospital of Chongqing Medical University Ethics and Research Committee. This document is available upon request.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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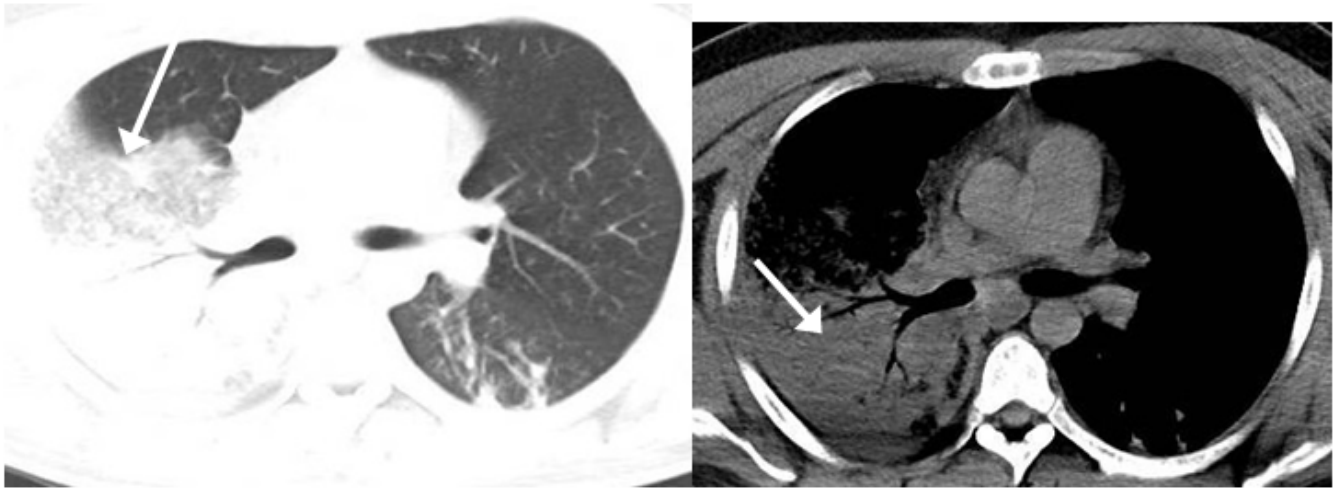
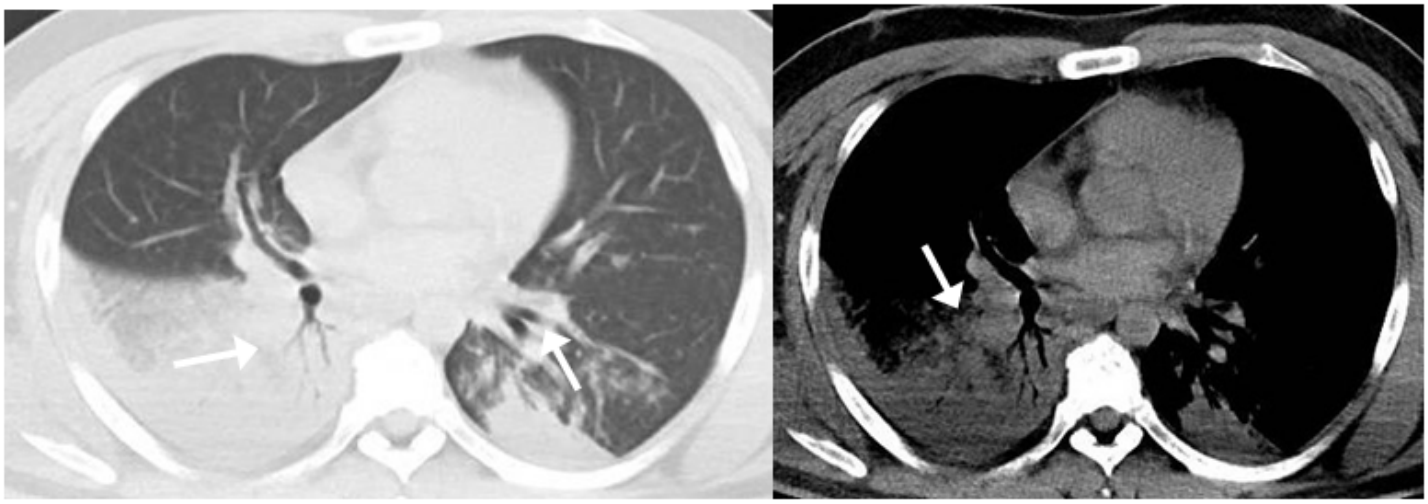
Figures



A Consolidation of the posterior segment of the upper lobe of the right lung.

B Bronchial inflation sign can be seen.



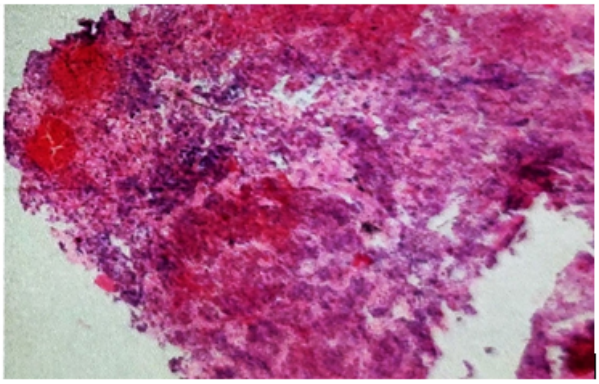
C Consolidation of the posterior segment of the lower lobe of the right lung

D Bronchial inflation sign can be seen.

Figure 1

Chest CT scan on 2020-08-09 shows consolidation of the posterior segment and lower lobe of the right lung.

General and microscopic



Pathological diagnosis: Acute and chronic inflammatory cell infiltration in the fibrinoid exudate and a piece of muscle tissue. No malignant tumor cells were found.

Figure 2

Pathological report of percutaneous pulmonary puncture