Case Report

Combination therapy with levofloxacin and cefepime to treat severe respiratory infection due to *Aeromonas caviae* after a near-drowning accident in river water

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Background: *Aeromonas* spp. are gram-negative anaerobic rods that are mainly found in water. Respiratory infections due to *Aeromonas* sp. are rare but have a high mortality rate.

Case presentation: A 43-year-old man fell into a river following an automobile accident and almost drowned. He developed a severe respiratory infection and acute respiratory distress syndrome. Ampicillin/sulbactam was given; however, *Aeromonas caviae* was detected in his blood culture. Despite treatment with levofloxacin, to which *A. caviae* was susceptible, his condition failed to improve. However, with additional treatment with cefepime, his blood culture results were negative, and his condition improved.

Conclusion: When a patient develops a respiratory infection after aspiration of river water, empiric antimicrobial therapy should be given as soon as possible to manage the risk of *Aeromonas* sp. infection.

Key words: Aeromonas caviae, cefepime, levofloxacin, near-drowning, respiratory infection

INTRODUCTION

AEROMONAS spp. are gram-negative anaerobic rods primarily found in water. Respiratory infections with *Aeromonas* spp. are rare, but the mortality rate is high.[1–3] We encountered a patient with septic shock due to infection with *Aeromonas caviae*, which he contracted during a near-drowning accident in river water. In such cases, combination therapy should be considered when previously treatment with antimicrobial agents do not provide sufficient improvement.

CASE REPORT

A 43-year-old man fell into river water following an automobile accident. He was immediately rescued and intubated orally by a physician at Yokohama Work Station Doctor Car (http://www-user.yokohama-cu.ac.jp/~er-urahp/WS_doctor_car.html), and transported to our hospital with airway and ventilator management. He was previously in good health, with no medical history prior to the day of the accident.

On admission, he was comatose, hypothermic, and in respiratory failure. His consciousness was assessed as E1VtM1 based on the Glasgow Coma Scale. His pulse rate was 91 b.p.m., with a blood pressure of 147/83 mmHg and a body temperature of 35°C. Physical examination revealed no evidence of trauma. Coarse crackles were noted throughout the lung field. His plain chest radiographs showed decreased permeability in all the lung fields (Fig. 1). Chest computed tomography showed consolidation in both lower lobes (Fig. 1). Arterial blood gas findings on a 100% fraction of inspired oxygen (FiO_2) under volume control ventilation (positive end-expiratory pressure, 0.49 kPa; tidal volume, 480 ml; respiratory rate, 15/min) were as follows: pH, 6.678; partial pressure of oxygen (PaO_2), 253.1 mmHg; partial pressure of carbon dioxide, 139.3 mmHg; calculated bicarbonate concentration, 16.0 mmol/L; base excess/deficit, −24.4 mmol/L; and lactate dehydrogenase, 13.71 mmol/L. The PaO_2 / FiO_2 ratio was 253. The patient's laboratory findings are shown in Table 1. The Sequential Organ Failure Assessment score was 18 points. Using diagnostic criteria for disseminated intravascular coagulation established by

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Received 18 May, 2021; accepted 21 Oct, 2021

Funding information

No funding information provided.

the Japanese Association for Acute Medicine, he had a score of 4 points.

The patient was initially treated with ampicillin/sulbactam (ABPC/SBT), volume expansion, vasopressors (noradrenaline and dobutamine), and glucocorticoids. However, he immediately developed septic shock, disseminated intravascular coagulation, and acute kidney injury. He became anuric and was diagnosed with stage 3 acute kidney injury, according to the Kidney Disease Improving Global Outcomes criteria. Continuous renal replacement therapy was then initiated.

Acute respiratory distress syndrome (ARDS) was diagnosed based on the Berlin criteria (PaO_2 / FiO_2, <100) on day 2 of hospitalization. Prone position therapy was initiated (>12 h), and the patient was ventilated using the airway pressure release ventilation method. On day 7, *Aeromonas caviae* was detected in his blood and sputum cultures. The antimicrobial regimen was switched from ABPC/SBT to tazobactam/piperacillin (TAZ/PIPC), as susceptibility tests indicated resistance to the former and susceptibility to the latter (minimum inhibitory concentration [MIC] ≤ 8 μg/ml). On day 9, levofloxacin (LVFX; MIC ≤ 1 μg/ml) was given based on previous recommendations.[4] However, on day 13, *A. caviae* was again detected in his blood culture. On day 20, the antimicrobial regimen was switched from TAZ/PIPC to meropenem (MEPM; MIC ≤ 1 μg/ml), and his condition improved. On day 26, however, MEPM was discontinued due to the appearance of a drug rash. By day 36, LVFX alone had failed to control the infection, with *A. caviae* growing in blood cultures. On

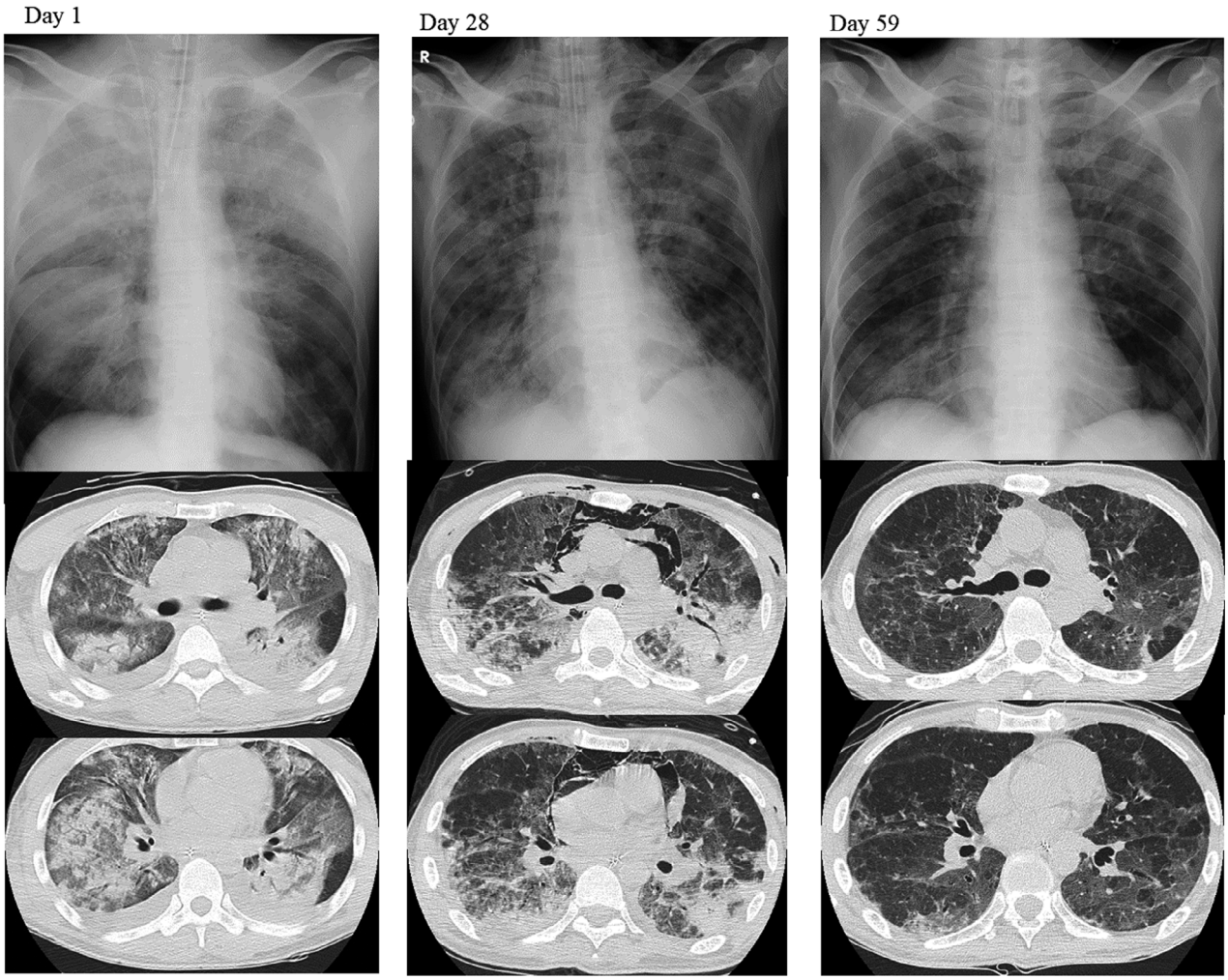

Fig. 1. Plain chest radiography and chest computed tomography on days 1, 28, and 59 of admission of a 43-year-old man with severe respiratory infection due to *Aeromonas caviae*.

Table 1. Laboratory findings on admission of a 43-year-old man with severe respiratory infection due to *Aeromonas caviae*

WBC	9,640/mm^3
Hgb	16.3 mg/dl
Hct	52.3%
PLT	19.2 × 104/μl
BUN	19.1 mg/dl
Cre	1.27 mg/dl
Total bilirubin	0.5 mg/dl
AST	105 IU/L
ALT	39 IU/L
LDH	1268 IU/L
CRP	<0.04 mg/dl
APTT	89.9 s
PT-INR	1.87
Fibrinogen	182 mg/dl
D-dimer	97.1 μg/ml

Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cre, serum creatinine; CRP, C-reactive protein; Hct, hematocrit; Hgb, hemoglobin; LDH, lactate dehydrogenase; PLT, platelets; PT-INR, prothrombin time-international normalized ratio; WBC, white blood cell.

day 39, cefepime (CFPM; MIC ≤ 1 μg/ml) with LVFX improved the inflammatory response. On day 43, his blood culture tested negative, and his fever was alleviated. By day 45, the patient's C-reactive protein level had decreased to below the normal level. Cefepime was discontinued on day 51, with no observable worsening of symptoms (Fig. 2). On day 34, a tracheostomy was carried out for long-term ventilator management, from which he was weaned on day 43 and transferred to a rehabilitation hospital on day 60.

DISCUSSION

AEROMONAS spp. are gram-negative rods that are widely distributed in fresh water. Diarrheal disease is the most common manifestation of infection due to *Aeromonas* spp.,[4] which has also been associated with several extraintestinal manifestations. The organisms are implicated in osteomyelitis, meningitis, respiratory infections, pelvic abscesses, and peritonitis. Sepsis occurs in older adult patients with hematologic malignancies, severe hepatobiliary disease, certain immunocompromised conditions, or trauma.[5,6] Respiratory infections due to *Aeromonas* sp. are rare. A rapid worsening of the disease and a high mortality rate in healthy patients infected with *Aeromonas* sp. has been reported in near-drowning incidents.[2]

We initially administered ABPC/SBT, used to treat aspiration pneumonia, as we suspected that the main cause of ARDS was due to water aspiration. However, *A. caviae* was later detected in his blood and sputum cultures. Most *Aeromonas* sp. are resistant to penicillin, ampicillin, carbenicillin, and ticarcillin but susceptible to fluoroquinolones, third- and fourth-generation cephalosporins, aminoglycosides, carbapenems, chloramphenicol, and tetracyclines.[4] Furthermore, TAZ/PIPC was selected based on susceptibility testing. However, as the patient's condition failed to improve, LVFX was introduced based on a previous report[4] and the susceptibility test results. *Aeromonas caviae* is susceptible to LVFX, but there are reports of infections associated with fluoroquinolone resistance.[7,8] In our patient, LVFX was only partially effective against *A. caviae;* therefore, we included MEPM, which was later discontinued due to the appearance of a drug rash. The blood cultures finally tested negative after treatment with CFPM plus LVFX. The use of combination antimicrobial therapy for severe respiratory tract infections due to *Aeromonas* sp. has not previously been reported. Treatment with LVFX alone was ineffective in producing negative blood cultures, a temperature 37°C or less, or decreasing C-reactive protein levels, whereas the addition of CFPM led to more positive results. Therefore, combination therapy should be considered for patients who do not improve sufficiently with previously administered antimicrobials.

We note that treatment an antimicrobial regimen comprising ABPC/SBT, customarily used to treat aspiration pneumonia, for several days was ineffective in achieving any significant improvement in his septic shock status due to infection with *A. caviae*. Therefore, due to the high mortality risk of *Aeromonas* sp.-related respiratory infections,[1–3] fluoroquinolones and carbapenems should be started early if a near-drowning incident is suspected. Moreover, in severe respiratory infections due to *Aeromonas* sp., antimicrobial agents should be switched or combined if there is no improvement, even if the susceptibility testing is favorable.

CONCLUSIONS

WE ENCOUNTERED A patient with severe respiratory infection and ARDS due to *A. caviae* after a near-drowning accident in river water. We recommend that when patients develop a respiratory infection from aspiration of river water, empiric antimicrobial therapy should be immediately given to manage *Aeromonas* sp. infection.

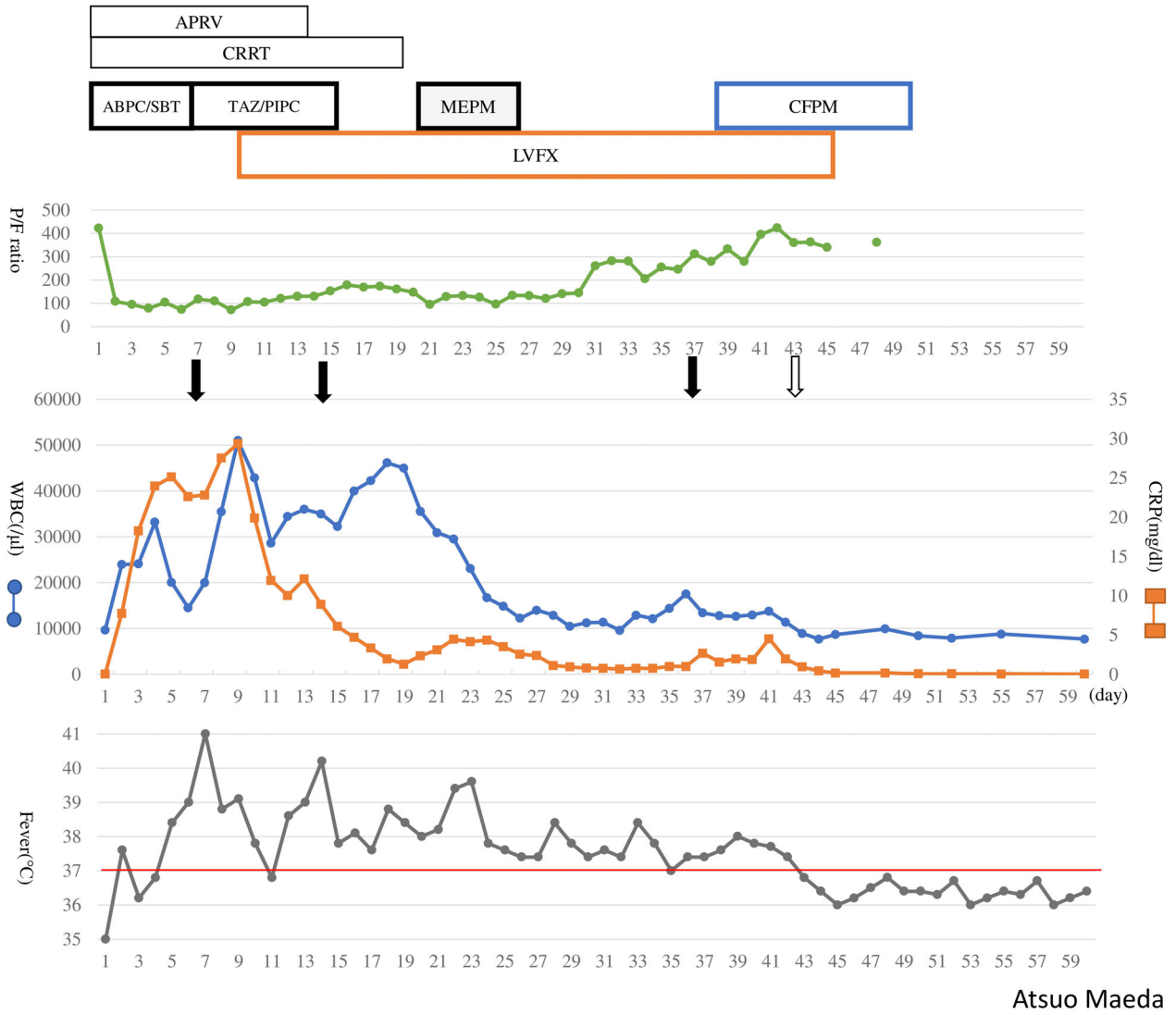

Fig. 2. Clinical course of a 43-year-old man with severe respiratory infection due to *Aeromonas caviae*. ABPC/SBT, ampicillin/sulbactam; APRV, airway pressure release ventilation; CFPM, cefepime; CRP, C-reactive protein; CRRT, continuous renal replacement therapy; LVFX, levofloxacin; MEPM, meropenem; P/F, PaO_2/FiO_2; TAZ/PIPC, tazobactam/piperacillin; WBC, white blood cell. Black arrow, positive blood culture; white arrow, negative blood culture.

ACKNOWLEDGMENTS

WE THANK EDITAGE for English language editing.

DISCLOSURE

Approval of the research protocol: N/A.
Informed consent: Informed consent was obtained from the patient to publish this case report and any accompanying images.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflicts of interest: None.

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