Shewanella algae Bacteremia in an End-stage Renal Disease Patient: A Case Report and Review of the Literature

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Abstract

A 71-year-old man was admitted because of nausea and abdominal pain. He was receiving an erythropoiesis-stimulating agent for anemia and dysregulated iron metabolism due to stage G5 chronic kidney disease. He had a history of raw fish intake and was diagnosed with infectious enterocolitis, which worsened and led to septic shock. *Shewanella putrefaciens* grew in the blood culture, but *Shewanella algae* was identified in a 16S rRNA gene sequence analysis. We herein report a case of *S. algae* bacteremia believed to have been transmitted orally. We also reviewed previous case reports on *Shewanella* infection in end-stage renal disease patients.

Key words: anemia, chronic kidney disease, fish, iron, oral infection, sepsis

(Intern Med 56: 729-732, 2017)
(DOI: 10.2169/internalmedicine.56.7616)

Introduction

*Shewanella algae* is an unusual pathogenic bacterium in humans. Most cases were reported in patients with chronic liver disease and cancer, and cases of *S. algae* infection in end-stage renal disease (ESRD) patients are few. The problems related to clinical practice are that little is known about the etiology of *S. algae* infection in ESRD patients and that this bacterium is often confused with *Shewanella putrefaciens*, although these two species may have different pathogenicities in humans. We herein report a case of *S. algae* bacteremia in a patient with ESRD and review previous case reports on *Shewanella* infection in ESRD patients.

Case Report

A 71-year-old man was admitted to our hospital in mid-July because of a 5-day history of nausea and abdominal pain. He had been diagnosed with chronic kidney disease (CKD) due to chronic glomerulonephritis and had had an arteriovenous fistula in his left arm in preparation for renal replacement therapy since two month prior to the onset. He had been given an erythropoiesis-stimulating agent (ESA; darbepoetin alpha 180 μg/month) for renal anemia; he was not on any iron supplements. The laboratory data 1 month before the onset of symptoms showed hemoglobin of 6.9 g/dL, Fe of 141 μg/dL, transferrin saturation (TSAT) of 76.6%, and ferritin of 704 ng/mL, findings that were indicative of dysregulated iron metabolism.

He had eaten sliced raw fish or “sashimi” of mackerel and squid three days before the manifestations of nausea and abdominal pain, for which he visited the outpatient unit, where he was diagnosed with infectious enterocolitis and was given oral fosfomycin. However, his symptoms worsened, and he was admitted to our hospital five days after the onset of symptoms.

A physical examination showed that his blood pressure was 160/70 mmHg, heart rate 83 beats/min, and body temperature 39.5°C. He had abdominal tenderness without rebound tenderness. No remarkable findings were observed in the heart sounds or respiratory sounds. Leg edema was not
His condition improved; therefore, continuous hemodiafiltration was switched to hemodialysis 3 times per week. A stool culture collected on the eighth hospital day was negative. On the 13th hospital day, the antimicrobial agent was changed to levofloxacin and continued for 1 week. He was discharged on the 26th hospital day without any complications and continued maintenance hemodialysis. The bacterium recovered from the blood culture was further analyzed because the patient’s condition had deteriorated. A 16S rRNA gene sequence analysis revealed that the bacterium was *S. algae*.

**Discussion**

*S. algae* is a rare causative pathogen of bacteremia, skin and soft tissue infection, or hepatobiliary infection. We reported a case of *S. algae* bacteremia in an ESRD patient and demonstrated the probable link between raw seafood consumption and *Shewanella* infection. This patient had iron overload that was related to a dysregulated iron metabolism caused by ESRD. Raw seafood consumption by an ESRD patient may be a risk factor for *Shewanella* infection.

*Shewanella* species are Gram-negative bacteria that are mainly isolated from the marine environment. This species was once named *Pseudomonas putrefaciens*; it was originally classified in the family *Vibrionaceae* until the 1990s, when it was reclassified as genus *Shewanella* (1). Most case reports of *Shewanella* infection have described an association with exposure to seawater; such contact can cause ear infection, skin or soft tissue infection, and bacteremia (1-3). Two species, *S. putrefaciens* and *S. algae*, have been reported to be pathogenic in humans (1). It is often difficult to distinguish between these two species, because automated identification systems only include the database of *S. putrefaciens*, but not *S. algae* (2). Therefore, some authors have suggested that the previously reported *S. putrefaciens* infections may have actually been caused by *S. algae*, which is thought to be more virulent (3). The accurate distinction between these two species requires a 16S rRNA gene sequence analysis or phenotypic tests; *S. algae* can only grow at 42°C and in 6% NaCl (1). In the present case, an automated identification system (MicroScan WalkAway 96 Plus,
Siemens Healthcare Diagnostics, Tokyo, Japan) initially determined the bacterium to be *S. putrefaciens*; however, a 16S rRNA gene sequence analysis confirmed the bacterium to be *S. algae*.

*Shewanella* infection can be fulminant and fatal and is often misdiagnosed as *Vibrio vulnificus* infection, because of the similarities in their clinical manifestations (2, 4). Patients with underlying diseases, such as hepatobiliary disease or malignancy, were reported to be predisposed to *Shewanella* infection, as well as to *V. vulnificus* infection (3); the mortality rate of *Shewanella* bacteremia was increased in these patients (5). *Shewanella* species belong to the microflora of the marine environment, and exposure to seawater was reported to be one of the risk factors for *Shewanella* infection, especially in temperature regions (3). Therefore, more attention should be paid to the pathogenicity of this bacterium, especially in patients with underlying diseases who are exposed to these environments.

*Shewanella* infection in ESRD patients has rarely been reported. To our knowledge, there have been seven previously published case reports on *Shewanella* infection in ESRD patients (4, 6-11) (Table 2). All of these cases were from geographic areas with long shorelines. Two cases were reported to be caused by *S. algae* and four cases by *S. putrefaciens*; however, only two cases were further analyzed by a biochemical procedure. Five cases showed bacteremia, and one case died of necrotizing myositis. The most common route of infection was skin ulcer (3 cases), followed by catheter-related infection (2 cases); no case was related to oral intake of seafood. In the present case, the onset of symptoms was related to seafood consumption, and abdominal CT scan showed signs of infectious enterocolitis. Therefore, we concluded that the *Shewanella* infection in this patient was probably caused by dietary intake of raw fish or “sashimi”.

This was the first case of *S. algae* infection that might have been transmitted orally in an ESRD patient.

Although the reason why the ESRD patient was predisposed to *Shewanella* infection is still unclear, dysregulated iron metabolism may be a risk factor for this patient. Iron is an essential element for bacterial growth. In the mammalian host, iron is not freely available, since it binds to transferrin and is known to cause ESA-resistant anemia (19). Therefore, we speculated that the ESRD, especially the accompanying iron overload, might have been a risk factor for *Shewanella* infection and hepatobiliary diseases (4). Siderophore has a high affinity to iron and is able to displace iron from transferrin. *S. algae* was reported to produce siderophore and was capable of absorbing iron into its body (14). Patients with hepatobiliary diseases who are susceptible to *S. algae* often had the complication of iron overload. The association between *Shewanella* infection and hepatobiliary diseases may be due to iron overload (5). In the present case, the patient did not have hepatic dysfunction but did have ESRD with a dysregulated iron metabolism; his anemia was ESA-resistant, and there seemed to be excessive iron levels, although he was not taking any iron supplement. It was suspected that uremia of the patient contributed to the ESA-resistant anemia, because the patient was just starting renal replacement therapy, and the serum creatinine level on admission was extremely high. Recent studies have demonstrated that hepcidin, which reduces iron release from reticuloendothelial and hepatocyte stores, plays an important role in the disordered iron metabolism of uremia including ESA resistance (15, 16). The serum hepcidin level is related to the residual renal function and elevates in CKD and in ESRD patients (15, 17). Serum hepcidin can be removed by renal replacement therapy (18), and insufficient hemodialysis is known to cause ESA-resistant anemia (19). Therefore, we speculated that the ESRD, especially the accompanying iron overload, might have been a risk factor for *Shewanella* infection in this patient. To our knowledge, no previous report has described the status of iron metabolism in the ESRD patients with *Shewanella* infection. Therefore, further investi-

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**Table 2. Characteristics of ESRD Patients with Shewanella Infection.**

| Case | Reference | Country | Age | Sex | *Shewanella* species | Focus | Route of infection | Antibiotic therapy | Outcome |
|------|-----------|---------|-----|-----|----------------------|-------|-------------------|-------------------|---------|
| 1    | 6         | Australia | 62  | M   | *S. putrefaciens*    | Oligoarthritis, Bacteremia | Respiratory tract | FLUX, GM, PIPC, CPFX, CEZ, GM, LVFX, MINO, CFPM | Survival |
| 2    | 7         | Japan    | 64  | F   | *S. algae*           | Bacteremia | Unknown            | CFPM             | Survival |
| 3    | 8         | Australia | 69  | M   | *S. putrefaciens*    | Splenic abscess, Bacteremia | Skin ulcer | Unknown | Survival |
| 4    | 9         | USA      | 58  | M   | *S. algae*           | Myonecrosis, Bacteremia | Skin ulcer | CFPM             | Survival |
| 5    | 4         | Korea    | 67  | M   | *S. putrefaciens*    | Necrotizing fasciitis, Bacteremia | Skin ulcer | CAZ, MEMP, VCM, DOXY, GM | Death |
| 6    | 10        | USA      | 78  | M   | *S. putrefaciens*    | Bacteremia | Catheter | GM, MEMP | Survival |
| 7    | 11        | Taiwan   | 82  | F   | *S. putrefaciens*    | Bacteremia | Catheter | DRPM, AMK | Survival |
| 8    | Present case | Japan    | 71  | M   | *S. algae*           | Infectious enterocolitis, Bacteremia | Oral | MEMP, CAZ, LVFX | Survival |

**Note:**

ESRD: end-stage renal disease, FLUX: flucloxacillin, GM: gentamicin, PIPC: piperacillin, CPFX: ciprofloxacin, CEZ: cefazolin, LVFX: levofloxacine, MINO: minocycline, CFPM: cefepime, CAZ: ceftazidime, MEMP: meropenem, VCM: vancomycine, DOXY: doxycycline, DRPM: doripenem, AMK: amikacin
gation is required to validate this issue.

The limitation of this report was that the data for serum ferritin and TSAT on admission were not available. However, we measured both of these markers at one month before the onset, when the patient was in a stable condition without acute inflammation or infection. Iron status should be evaluated based on ferritin and TSAT in CKD and ESRD patients (19, 20). The ferritin level and TSAT of the patient in the present study were compatible with iron overload (21, 22). In addition, we were unable to recover *S. algae* from a stool culture on the eighth hospital day, when the patient had already received courses of an antimicrobial agent to which the bacterium was susceptible. We could not collect a stool sample at an earlier time, such as at admission, because of the patient’s critically ill condition.

In conclusion, we reported a case of *S. algae* bacteremia that was probably caused by oral intake of raw fish in an ESRD patient. In addition, a dysregulated iron metabolism in ESRD may be a risk factor for *Shewanella* infection.

The authors state that they have no Conflict of Interest (COI).

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