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CASE REPORT



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# Shewanella soft tissue infection: case report and literature review

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KEYWORDS Shewanella; Shewanella algae; Soft tissue infection; Necrotizing fasciitis	SummaryObjective:To better understand the clinical characteristics of soft tissue infections caused by Shewanella in humans.Methods:We report a case of Shewanella soft tissue infection and review the English literature from a search of PubMed.Results:A total of 27 adults (mean age $61.1 \pm 16.0$ years) with soft tissue infections caused by Shewanella were included for analysis. Limb involvement was found in 22 (81.5%) patients, while scalp, face, perineum, lacrimal sac, and abdominal wall involvement were each found in one patient. Chronic ulcer over the leg (14 cases (51.9%)), steroid use (four cases (14.8%)), and liver cirrhosis (three cases (11.1%)) were the major underlying conditions. Shewanella bacteremia was found in 14 out of 22 patients with soft tissue infections involving the limbs. Two patients died of septicemia, giving a mortality rate of 7.4%.Conclusions:Shewanella soft tissue infections usually develop in immunocompromised patients with a preexisting cutaneous ulcer (particularly over the legs) after marine environment or

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## Introduction

Shewanella spp are motile Gram-negative bacilli with the major phenotypic characteristic of production of large

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amounts of hydrogen sulfide  $(H_2S)$  in the butt of triple sugar iron agar.<sup>1</sup> Shewanella algae and Shewanella putrefaciens are frequently found in non-human sources such as the marine environment and foodstuffs, yet are opportunistically pathogenic for humans.<sup>1</sup>

S. putrefaciens was once believed to be the major human pathogenic species in the genus Shewanella, and authors in most of the earlier reports on Shewanella human infections attributed the etiology to S. putrefaciens.<sup>2</sup> The taxon S. alga was previously considered one biogroup of the genetically heterogeneous S. putrefaciens species.<sup>3</sup> In 1990, S. alga was first recovered from red algae and was proposed to be a tetrodotoxin-producing microbe.<sup>4</sup> A subsequent study disclosed that the high G+C content in the previously recognized S. putrefaciens isolates were genetically related to S. alga, and most of the clinical S. putrefaciens isolates should therefore be reclassified as S. alga.<sup>5</sup> In 1997, S. alga was renamed S. algae.<sup>6</sup> It is likely that >80% of clinical Shewanella isolates in human infections are S. algae.<sup>2</sup>

Although S. *algae* was recognized as a new species in 1992,<sup>5</sup> misidentification of S. *algae* as S. *putrefaciens* has persisted ever since. These misidentifications have resulted from the failure of both conventional phenotypic characteristic testing and commercialized bacterial identification systems (e.g., ID 32 GN, and VITEK) in differentiating S. *putrefaciens* from S. *algae*. In humans, soft tissue infections are mostly encountered among infections reported to be caused by Shewanella species.<sup>2</sup> To better understand clinical characteristics of soft tissue infections caused by Shewanella in humans, we report a case of severe soft tissue infection caused by S. *algae* in an immunocompromised adult and review the literature.

## Case report

A 42-year-old man with an underlying hepatitis B-related liver cirrhosis was hospitalized because of fever and a swollen left leg. He had injured his left leg 2 days earlier when he was handling a seawater fish in preparation for his dinner. Some skin lesions developed when his leg was stuck by the spinous dorsal fin of the fish, and he tried to clean the oozing blood from the damaged skin by flushing it with the water in which the fish had been immersed before. Local heat and swelling over his left leg soon developed, followed by fever and rigors. Upon admission, he was acutely ill; his body temperature was 39.8 °C, and blood pressure was 90/60 mmHg. Physical examination revealed an extremely swollen left leg with edematous dark red to purple-colored skin, and some hemorrhagic bullae on the soft tissue over the distal end of the left leg and the left ankle joint.

Blood tests revealed that his peripheral leukocyte count was  $2.7 \times 10^9/l$  (normal  $3.9-10.6 \times 10^9/l$ ) with the presence of band-form cells and metamyelocytes, and his platelet count was  $37 \times 10^9/l$  (normal  $150-400 \times 10^9/l$ ). C-reactive protein was 70.1 mg/l (normal <5 mg/l), aspartate aminotransferase was 146 (normal <37 U/l), alanine aminotransferase was 55 U/l (normal <40 U/l), and serum creatinine was 1.8 mg/dl (normal 0.4-1.4 mg/dl). A computed tomography revealed severe edematous changes of the subcutaneous tissue and muscles in the left leg. Under the impression of necrotizing fasciitis and septic shock, parenteral ceftriaxone (2 g/day) and oral doxycycline (200 mg/day) were

empirically administered after sampling blood for culture, and an emergency operation was performed. The surgical procedure included fasciotomy and extensive debridement of the devitalized soft tissue along the lateral side of the tibialis anterior of the affected leg, from the level below the knee joint to the ankle joint. The excised devitalized soft tissue disclosed suppurative necrosis on histopathology. The administered antibiotics were switched to ciprofloxacin (1200 mg/day parenterally).

Although it was hemodynamically stable after surgery, his left leg did not make a favorable clinical response. The nonexcised skin and muscles around the surgical site of his left leg were poorly perfused. On day 4 of hospitalization, cultures of blood and excised necrotic tissue sampled during the operation both yielded Gram-negative rods, which were identified as S. putrefaciens by ID 32 GN (bioMérieux Vitek, Inc., Hazelwood, MO, USA). Susceptibility testing using VITEK I automated system (bioMérieux Vitek, Inc.) indicated that the isolated microbe was susceptible to aztreonam, ampicillin/sulbactam, piperacillin/tazobactam. ceftazidime. ceftriaxone. ciprofloxacin, levofloxacin, imipenem, gentamicin, and amikacin. To definitively identify the isolated pathogen, the partial 165 rRNA gene was sequenced by PCR amplification using a universal forward primer 27F (5'-AGAGTTTGATCCTGGCTCAG-3')<sup>7</sup> and a universal reverse primer 907R (5'-CCGTCAATTCCTTT-GAGTTT-3'),<sup>8</sup> as previously described.<sup>7,8</sup> Two harvested DNA each with 881 and 895 nucleotides were sequenced by 310 Genetic Analyzer (Applied Biosystems) and were compared to those available in the GenBank database (http:// www.ncbi.nlm.nih.gov/BLAST/BLAST.cgi); they were found to be a 100% match with those of S. algae.

With regards to susceptibility, Etest on this S. *algae* isolate was performed in accordance with the instructions of the manufacturer (AB Biodisk, Solna, Sweden). The selected antimicrobials (minimum inhibitory concentrations (MICs) in  $\mu$ g/ml) were as follows: cephalothin (>256), cefotaxime (0.19), ceftriaxone (0.25), ceftazidime (0.25), ceftepime (0.047), ciprofloxacin (0.19), levofloxacin (0.25), ampicillin/sulbactam (0.75), piperacillin/tazobactam (0.125), ertapenem (0.38), imipenem (6), and meropenem (0.38). Ciprofloxacin was continued because of its favorable MIC.

In spite of antimicrobial use, progressive clinical deterioration was observed. The patient received two further debridement procedures in the affected leg, and as a result, a considerable portion of skin and muscles in his left leg was excised. All the excised tissues were suppuratively necrotic by histopathology. Because of persistent deterioration, his left leg was amputated from the level of above-knee joint on hospitalization day 16. Thereafter his course was uneventful, and the patient was discharged on day 31.

# PubMed search and literature review

We performed a PubMed search for reports on Shewanella infections that have been published since 1966 using the keywords 'Shewanella algae', 'Shewanella algae', 'Shewanella putrefaciens' (the previous name for Shewanella putrefaciens), and limited the search to the English literature and adult humans. A total of 27 adults (mean age  $61.1 \pm 16.0$  years) with soft tissue infections caused by S. algae, S. alga, S. putrefaciens or P. putrefaciens were found.<sup>9–27</sup> Demographic, clinical, and

Shewanella
soft
tissue
infection

No./sex/age (y) Reference	Underlying disease/condition	Bacteria (source) (Method of identification)	Affected site	Prescribed antibiotic(s) $\pm$ debridement	Seawate exposure
1/F/82 9, 10 <sup>b</sup>	Malnutrition, leg edema and ulcers	Pseudomonas putrefaciens, CoNS (wound) (Conventional method)	Both legs	Co-trimoxazole	Unknowr
2/F/73 11	Anemia, renal failure, bilateral leg ulcers	Pseudomonas putrefaciens (blood and wound), Pseudomonas aeruginosa, Staphylococcus aureus (wound) (Conventional method)	Both legs ulcers	Ampicillin, gentamicin	Unknown
3/F/60 12	Congestive heart failure, leprosy	Pseudomonas putrefaciens, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Moraxella spp (wound) (Unknown)	Left wrist, left leg	Co-trimoxazole	Unknown
4/M/63 13	Leg ulcers, congestive heart failure, alcoholic liver cirrhosis, gouty arthritis	Pseudomonas putrefaciens (blood/wound), CoNS, Enterobacter agglomerans, Pseudomonas fluorescens (wound) (API 20E <sup>c</sup> )	Chronic ulcers on legs	Gentamicin, chloramphenicol; co-trimoxazole, debridement	Unknown
5/F/67 14	Hypothyroidism, hypertension, stasis ulcers of both legs, right arm edema and ecchymosis	<i>Pseudomonas putrefaciens</i> , group A streptococcus (blood) (API 20E)	Both legs	Nafcillin, penicillin, gentamicin	No
6/F/34 15	Laurence–Moon–Bardet–Biedl syndrome, renal failure on dialysis, retinal pigmentation, blindness, hypogonadism, obesity	<i>Pseudomonas putrefaciens</i> (blood) (Conventional method, API Rapid NFT system <sup>c</sup> )	Both legs	Mezlocillin, gentamicin	Unknown
7/M/39 15	Prosthetic aortic valve infective endocarditis, chronic leg edema	Pseudomonas putrefaciens, group G streptococci (blood) (API 20E)	Left leg	Ceftazidime	Yes
8/M/75 16	Chronic angina, left leg edema secondary to saphenous vein harvest	Pseudomonas putrefaciens (blood) (VITEK <sup>c</sup> )	Left leg	Piperacillin, ampicillin	Yes
9/M/68 17	COPD, venous stasis, steroid use	Shewanella putrefaciens (blister aspirates) (API 20NE <sup>c</sup> )	Left ankle ulcer	Flucloxacillin, penicillin, cefotaxime, vancomycin	No
10/NA/75 18	Diabetic leg ulcer	Shewanella putrefaciens (blood) (API 20NE)	Leg ulcer	NA	Unknown
11/NA/57 18	Traumatic ulcer of lower extremity, tetanus	Shewanella putrefaciens (blood) (API 20NE)	Leg ulcer	NA	Unknown
12/NA/36 18	Traumatic ulcer of lower extremity, cellulitis	Shewanella putrefaciens, Serratia marcescens (blood) (API 20NE)	Leg ulcer	NA	Unknown
13/F/80 19	Rheumatoid arthritis, diabetes, arterial insufficiency of the legs, leg ulcers	Shewanella alga (blood) (Conventional method)	Left leg	Ampicillin and gentamicin	Unknown
14/M/69 19	Congestive heart failure, right leg ulcers	Shewanella alga (blood/wound) (Conventional method)	Right leg	Penicillin and gentamicin; ampicillin and gentamicin; cefuroxime and gentamicin;	Unknown

cefuroxime and gentamicin; cefuroxime (oral), surgery

Table 1 (Continued)								
No./sex/age (y) Reference	Underlying disease/condition	Bacteria (source) (Method of identification)	Affected site	Prescribed antibiotic(s) $\pm$ debridement	Seawater exposure			
15/M/69 20	Chronic cholecystitis, cholelithiasis	Shewanella putrefaciens, Escherichia coli (pus) (ID 32 GN <sup>c</sup> )	Abdominal wall infections and abscess	Ceftazidime and gentamicin; cephalexin	Unknown			
16/F/53 20	Aplastic anemia, steroid use, fish puncture wound (finger)	Shewanella putrefaciens, Staphylococcus aureus, viridans streptococci (pus) (ID 32 GN)	Right middle finger	Piperacillin and vancomycin	Unknown			
17/M/71 20	Obstructed nasolacrimal duct	Shewanella putrefaciens, Pseudomonas aeruginosa (pus) (ID 32 GN)	Dacryocystitis	Cephalexin, drainage	Unknown			
18/M/53 20	Rectal cancer, intra-abdominal carcinomatosis	Shewanella putrefaciens (pus) (ID 32 GN)	Perineal abscess	Ceftazidime and gentamicin	Unknown			
19/M/73 20	Alcoholism, fatty liver	Shewanella putrefaciens (blood/wound) (ID 32 GN)	Periorbital area	Cefotaxime, clindamycin and gentamicin	Unknown			
20/M/61 21	COPD, vascular insufficiency of the lower extremities	Shewanella putrefaciens (wound) (VITEK)	Right foot abscess	Ceftriaxone and clindamycin, co-trimoxazole (oral), I/D	No			
21/M/67 22	SLE, asthma, steroid use, chronic leg ulcers	Shewanella putrefaciens (wound) (API 20NE)	Left leg	Penicillin and gentamicin, ciprofloxacin (oral)	Yes			
22/M/36 23	Healthy	Shewanella putrefaciens, Staphylococcus aureus, Enterococcus faecalis (wound) (Unknown)	Both hands	Flucloxacillin, ceftriaxone	Yes			
23/M/66 24	Multiple myeloma, renal insufficiency	Shewanella alga (blood) (API 20NE and GNI <sup>c</sup> )	Both forearms	Ceftazidime, amikacin	No			
24/M/87 25	Cushingoid appearance	Shewanella putrefaciens (blood) (VITEK II <sup>3</sup> and ID 32 GN)	Left forearm	Ampicillin/sulbactam, ampicillin (oral)	Yes			
25/M/27 26	Healthy	Shewanella putrefaciens (wound) (ID 32 GN)	Scalp	Ciprofloxacin, debridement	Yes			
26/F/67 27	Chronic renal failure on maintenance hemodialysis	Shewanella putrefaciens (wound) (VITEK, BBL Crystal <sup>c</sup> )	Left thigh	Ceftazidime, minocycline, oxacillin, fasciotomy, debridement	No			
27/M/42 Current case	Liver cirrhosis, hepatitis B	Shewanella algae (blood/wound) (Identification of 16S rDNA sequence)	Left leg	Ciprofloxacin, debridement	Yes			

M, male; F, female; CoNS, coagulase-negative staphylococci; COPD, chronic obstructive pulmonary disease; SLE, systemic lupus erythematosus; NA, not available.

All patients survived except for patient cases 5 and 19 who died of sepsis and patient case 18 who died of underlying diseases.

<sup>a</sup> Pseudomonas putrefaciens is the previous name for Shewanella putrefaciens and Shewanella alga is the previous name for Shewanella algae.

<sup>b</sup> Case No. 1 was separately reported in two different articles.

<sup>c</sup> ID 32 GN, API 20E, API 20NE, VITEK, VITEK, II, API Rapid NFT system, GNI, and BBL Crystal are commercial devices, which were used manually, semi-automatically, or automatically for the identification of bacteria.

laboratory information for these patients are summarized in Table 1.

Of the 27 patients with soft tissue infections, limb involvement (18 lower and four upper limbs) was found in 22 (81.5%), while scalp, face, perineum, lacrimal sac, and abdominal wall involvement were each found in one patient. With regard to the leading underlying diseases/conditions, chronic ulcer over the leg (14 cases (51.9%)) resulting from a variety of causes including venous stasis, arterial insufficiency, diabetic foot, chronic leg edema, or traumatic wounds was most commonly found, followed by steroid use (four cases (14.8%)) and liver cirrhosis (three cases (11.1%)). Shewanella bacteremia was found in 14 of the 22 patients with soft tissue infections involving the limbs (11 cases of monomicrobial bacteremia and three of polymicrobial bacteremia), and in one of the five cases of soft tissue infection involving other anatomic sites. Overall, two patients died of septicemia, giving a mortality rate of 7.4%.

#### Discussion

Out of more than 30 already known *Shewanella* species, only *S. putrefaciens* and *S. algae* are considered pathogenic for humans.<sup>2</sup> The reason why *S. algae* causes more infections in humans than *S. putrefaciens* is not fully understood. Some investigators have hypothesized that the bacterial hemolysin produced by the culprit *S. algae* plays an important role in the pathogenesis of human infection.<sup>17</sup>

Remarkably, in addition to a variety of immunocompromising conditions, a preexisting chronic ulcer over the lower limb was found in more than 50% of the affected patients. Because *Shewanella* species normally exist in the marine environment, the cutaneous breaches on the legs of these immunocompromised patients served as a portal of entry for the opportunistic pathogens during their recreational activities.

Unlike the previously reported cases of *Shewanella* soft tissue infections, our case was clinically fulminant and resembled the rapidly progressive soft tissue infections caused by *Vibrio vulnificus*<sup>28</sup> and *Aeromonas* species,<sup>29</sup> which are characterized by the emergence of bullae and rapid development of progressive necrotizing fasciitis and septic shock. The clinical manifestations of this case suggest that when it comes to the etiology for a severe soft tissue infection, *S. algae*, *V. vulnificus*, and *Aeromonas spp* should all be included in the differential diagnosis. The possibility that the initial debridement was inadequate in our patient cannot be excluded in view of the fact that deterioration subsequently developed rapidly under prompt and aggressive surgery in combination with effective antibiotics.

Earlier studies have demonstrated that aminoglycosides, levofloxacin, third- and fourth-generation cephalosporins, piperacillin, and carbapenems are active *in vitro* against *S. putrefaciens*.<sup>30,31</sup> The antimicrobial susceptibilities of our clinical isolate were similar to those described previously.<sup>25,31</sup> Of note, imipenem had a higher MIC against the clinical *Shewanella* isolates than meropenem, as has been shown in other reports.<sup>30,31</sup> In terms of antimicrobial susceptibility, some *Shewanella* isolates are intrinsically resistant to imipenem,<sup>31</sup> while some that were originally susceptible to imipenem may develop resistance to this antibiotic after clinical exposure to it.<sup>32</sup> A chromosomeencoded carbapenem-hydrolyzing Amber class D  $\beta$ -lactamase harbored by the microbes has been reported to be responsible for the high MIC of imipenem against *S. algae* isolates.<sup>31</sup> Further study is warranted to clarify the role of empirical treatment with a carbapenem in soft tissue infections in patients with marine exposure.

Given the possible catastrophic consequences, education on the prevention of *Shewanella* soft tissue infections in atrisk people (e.g., the immunocompromised or elderly with a cutaneous ulcer) relating the need to avoid exposure to the marine environment or seawater may be of importance.

Conflict of interest: No conflict of interest to declare.

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