

# The first Italian case report of leg ulcer and sepsis caused by *Shewanella algae* in a immunocompetent patient

Pierluigi Brugnaro<sup>1</sup>, Erika Morelli<sup>1</sup>, Francesca Ebo<sup>1</sup>, Giorgio Rosini<sup>1</sup>, Francesca Cattelan<sup>1</sup>, Andrea Petrucci<sup>1</sup>, Enzo Raise<sup>1</sup>, Sandro Panese<sup>1</sup>, Stefano Grandesso<sup>2</sup>

<sup>1</sup>Infectious Diseases Department, Civil Hospital "SS. Giovanni e Paolo", Venice, Italy;

<sup>2</sup>Microbiology Unit, Clinical Pathology Department, Hospital dell'Angelo, Mestre (Venice), Italy

## SUMMARY

We describe the first Italian case of *Shewanella algae* septicemia in an immunocompetent patient with chronic leg ulcers. The patient had been exposed to seawater before the onset of symptoms. Despite the absence of severe underlying diseases, the primary soft tissue in-

fection of the leg was complicated by hematogenous dissemination.

*Keywords:* immunocompetent host, sepsis, *Shewanella algae*

## INTRODUCTION

Human infections sustained by member of the genus *Shewanella* are uncommon but an increasing number of reports of *Shewanella* invasive infections indicates the pathogenic potential role of this genus. The most common *S. algae* infections involve ears and soft tissues, but serious infections such as sepsis, endocarditis and central nervous system involvement have also been described. Most *Shewanella* infections occur during especially warm summers in temperate regions [1, 2]. Marine environment can often be implicated as the source of infection but to our knowledge no cases of invasive *Shewanella algae* infections associated with direct exposure to seawater have been described in Italy to date. We report on a case of a *S. algae* sepsis and cellulitis in a patient with lower legs ulcers.

## CASE REPORT

A 74-years-old man was referred to the Emergency Department because of a painful swelling of the left leg. High fever with chills also appeared, so he was admitted to our Department and blood cultures were taken. The patient had an history of a chronic phlebitis and recurrent cellulitis of the left leg. Two days before the onset of symptoms the patient took a bath on seawater near Ostia, in the Lazio region. On admission, the left leg was reddish and edematous; a purulent discharge was also noted from an ulcerated skin lesion. The patient was unable to walk due to the severe pain of the inflamed leg. A swab sample was collected from the cutaneous lesion for bacteriologic culture, using swab with Amies with charcoal. The patient was fully oriented and hemodynamically stable. Initial laboratory results were as follows: leucocytes 14,090/ $\mu$ L; hemoglobin 14 g/dL; platelets 118,000/ $\mu$ L; C-reactive protein 11.2 mg/dL; creatinine and liver enzyme within normal range of values. Venous ultrasonography of the lower limbs documented a small thrombotic finding on the left popliteal vein. Empirical antimicrobial treatment with

Corresponding author

Stefano Grandesso

E-mail: stefano.grandesso@aulss3.veneto.it

meropenem and levofloxacin i.v. was started and a fast improvement of clinical findings was observed.

Blood cultures were performed on admission using BD BACTEC Plus Aerobic/F and Plus Anaerobic/F media (Becton, Dickinson and Company, MD, USA). All six bottles (three for aerobic and three for anaerobic incubation) became positive during the second day of incubation. Cultures of both blood and tissue specimens, obtained from the patient's leg ulceration, yielded gram-negative non-fermentative bacilli. The colonies appeared circular, convex and smooth.

They were oxidase and catalase positive, indole and urease negative. They were identified as *Shewanella algae* by the automatic identification system Vitek 2 (bioMérieux, Marcy l'Étoile, France) using GN card with 99% probability. By using the manual identification system API ID 32 GN and ID 32 E (bioMérieux, Marcy l'Étoile, France) we yielded a good identification as *Shewanella putrefaciens* group. However both these manual systems were not able to differentiate *S. algae* from *S. putrefaciens*. The absence of acid production from maltose and sucrose, along with the growth in Mannitol Salt Agar (containing 6,5% NaCl) helped us to confirm the isolation of *S. algae*. Afterwards, it was confirmed by MALDI-TOF mass spectrometry with a 99.9% confidence value.

Antimicrobial susceptibility testing (AST) was performed using Sensititre system with MIC plates ITNF1F (Trek Diagnostics Systems, Cleveland, Ohio, USA). We interpreted the AST according to EUCAST breakpoints for *Pseudomonas* spp. that showed no resistances to tested antimicrobials. The tested MICs were as follows: amikacin  $\leq 8$  mg/L; aztreonam 0.25 mg/L; ciprofloxacin 0.12 mg/L; levofloxacin 0.12 mg/L; colistin 2 mg/L; imipenem 4 mg/L; meropenem 0.12 mg/L; piperacillin 0.5 mg/L; piperacillin-tazobactam  $\leq 0.25$  mg/L; ticarcillin plus clavulanic acid  $\leq 8$  mg/L.

We therefore confirmed the appropriateness of the previous antimicrobial regimen, which was continued for two weeks from the beginning of the therapy. Fever and local signs of inflammation on the left leg disappeared, the laboratory results returned to normal thereafter, and the patient was discharged nineteen days after the hospital admission.

## ■ DISCUSSION

*Shewanella* spp. are widely distributed in nature, and their natural habitats are water and soil. These organisms are detected in countries with a warm climate or during summer months in temperate countries. *Shewanella* spp. are Gram-negative, motile, non-fermentative bacilli, belonging to the family *Alteromonadaceae*. They are important in the turnover of organic material. Recent results of 16S rRNA gene sequence analyses of genera from this group suggested to propose a distinct family, *Shewanellaceae*, containing about 30 *Shewanella* spp., most of which are of limited interest to clinical microbiologists. Among the seawater-acquired infections the epidemiology and clinical features of *Shewanella* infections are similar to infections involving marine bacteria, such as *Vibrio* and *Aeromonas*. *S. putrefaciens* and *S. algae* are the most frequent *Shewanella* spp. found in clinical specimens. *S. algae* can be isolated from seawater with warmer temperatures ( $>13^{\circ}\text{C}$ ) during the summer season. A large number of clinical isolates formerly identified as *S. putrefaciens* were shown to be *S. algae* by using phenotypic characteristics proposed by Nozue et al. [3]. This problem was due to the inability or difficulty of automated and manual identification systems (Vitek, API ID 32 E and ID 32 GN) to distinguish between *S. putrefaciens* and *S. algae*. Actually the two manual systems do not include *S. algae* in their database. Important differential characteristics between the two species include the ability of *S. algae* to produce mucoid colonies with  $\beta$ -hemolysis on sheep blood agar, to grow at  $42^{\circ}\text{C}$  and in 6% NaCl and reduction of nitrite. *S. algae* was also demonstrated unable to produce acid from maltose, sucrose and glucose; at the opposite it was shown to be able to produce acid from ribose. All of these biochemical characteristics are in contrast to those of *S. putrefaciens*. Moreover significant genomic differences between the two species are now evidenced by ribotyping, 16S rRNA analysis, gyrB gene sequencing, and DNA-DNA hybridization. As *S. algae* is known to be more virulent than *S. putrefaciens* and these two species seem to exhibit different pathogenicities in humans, correct identification is mandatory [1]. *S. algae* is found to be more pathogenic due to its ability for adhesion and bacterial haemolysin production [1,

4]. In 1992 *S. haliotis* was isolated in severe soft tissue infection: it is distinguishable by *S. algae* only with 16S rRNA analysis [5]. In 1991 the first case of infection associated with *Shewanella xiamenensis* (a nosocomial peripancreatic infection) was described [6]. *S. algae* infections are usually linked to direct contact with seawater, but even consumption of raw seafood was associated with *S. algae* septicemia [7]. Soft tissue infection of the limbs was the most common clinical finding in patients with *Shewanella* spp. infections and chronic ulcer over the legs was the major underlying condition, being reported in 51.9% among 27 adult patients [8]. It is common comorbidities in patients infected by *S. algae* [9]. *S. algae* and *S. haliotis* infections were strongly associated with diseases of the hepatobiliary tract and pancreas and the mortality rate of *Shewanella* bacteremia was higher in these patients (4, 10). Similarly to this report, our patient presented with a soft tissue infection of a leg that was previously affected by recurrent cellulitis. Several cases of cutaneous infections sustained by *S. algae* progressed to extensive myonecrosis requiring surgical intervention such as extensive debridement, fasciotomy and skin allograft [7, 11]. Bacteremia by *S. algae* was rarely reported, and the majority of these cases were seen in patients with severe comorbidities such as liver cirrhosis, or chronic renal disease requiring hemodialysis [12]. Epidural spinal abscess, purulent pericarditis, acute gastroenteritis with bloody diarrhoea and meningoencephalitis were also reported among unusual invasive infections sustained by *S. algae* [13-16]. More interestingly some clinical reports of *S. algae* isolated from clinical samples resistant to carbapenems have been described before the global spread of carbapenemase enzymes between Gram negative bacteria. Since the first description by Iwata et al. of an imipenem-resistant strain of *Shewanella algae* recovered from blood of a patient on haemodialysis, Héritier et al. analyzed the beta-lactamase content of *S. algae* isolated from clinical samples [17]. They found a chromosome-located gene that encode the beta-lactamase OXA-55 which share some identity with several Ambler class D enzymes, including those found in *Acinetobacter baumannii*. The overall catalytic activity of OXA-55 is less robust than that of other carbapenem-hydrolyzing oxacillinases, nevertheless the very likely chromosomal location of bla<sub>OXA-55</sub> and

the presence of almost identical genes in other *S. algae* isolates argue for OXA-55-type enzymes being naturally produced by *S. algae*. The propensity of *S. algae* toward resistance to imipenem was clearly described by Kim D-M et al. who reported on a case of bacteremia and spinal epidural abscess sustained by an imipenem-susceptible *S. algae* strain that subsequently became resistant to imipenem during treatment [13]. In the current case antimicrobial susceptibility testing did not reveal resistances and response to antibiotic treatment was dramatic, with a quick disappearance of systemic and local signs of inflammation. We described, to the best of our knowledge, the first report of bacteremia and skin and soft tissue infection caused by *S. algae* in Italy in a patient neither diabetic, cirrhotic nor immunocompromised. Previously Pagani et al. described a case of bacteremia and soft tissue infection in an immunocompromised patient sustained by *Shewanella*, but the isolate was eventually identified as *S. putrefaciens*. In this case the patient reported a recent holiday on the Adriatic shore, then supporting a seawater contact as a risk factor [18].

There are no standard guidelines for the treatment of *Shewanella* infection. Some reports have shown that *Shewanella* infections should be managed aggressively with a combination of surgical debridement and appropriate antimicrobials.

This case highlights the need to consider *S. algae* as a potential emerging pathogen which can cause septic complications even in patients without severe underlying comorbidities.

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**Conflicts of interest:** none

#### REFERENCES

- [1] Holt H.M., Gahrn-Hansen B., Bruun B. *Shewanella algae* and *Shewanella putrefaciens*: clinical and microbiological characteristics. *Clin. Microbiol. Infect.* 11, 347-352, 2005.
- [2] Esposito S., Noviello S., De Caro F., Boccia G. New insights into classification, epidemiology and microbiology of SSTIs, including diabetic foot infections. *Infez. Med.* 1, 3-14, 2018.
- [3] Nozue H., Hayashi T., Hashimoto Y., et al. Isolation and characterization of *Shewanella* *algae* from human

clinical specimens and emendation of the description of *S. alga* *Int. J. Syst. Bacteriol.* 42, 628-634, 1992.

[4] Khashe S., Janda J.M. Biochemical and pathogenic properties of *Shewanella algae* and *Shewanella putrefaciens*. *J. Clin. Microbiol.* 36 (3), 783-787, 1998.

[5] Byun J.H., Park H., Kim S. The phantom menace for patients with hepatobiliary diseases: *Shewanella haliotis*, often misidentified as *Shewanella algae* in biochemical tests and MALDI-TOF Analysis. *Jpn. J. Infect. Dis.* 70, 177-180, 2017.

[6] Zong Z. Nosocomial peripancreatic infection associated with *Shewanella xiamenensis*. *J. Med. Microbiol.* 60, 1387-1390, 2011.

[7] Myung D.S., Jung Y-S., Kang S.J., et al. Primary *Shewanella algae* bacteremia mimicking *Vibrio* septicemia. *J. Korean. Med. Sci.* 24, 1192-1194, 2009.

[8] Tsai M.S., You H.L., Tang Y.F., Liu J.W. *Shewanella* soft tissue infection: case report and literature review. *Int. J. Infect. Dis.* 12, 119-124, 2008.

[9] Jampala S., Meera P., Vivek V., Kavitha D.R. Skin and soft tissue infections due to *Shewanella algae* - an emerging pathogen. *J. Clin. Diagn. Res.* 9, DC16-DC20, 2015.

[10] Kim B.K., Cho S.Y., Kang B., Kim I.K., Byun J.H., Park C., Choi S.M. A case of spontaneous bacterial peritonitis with bacteremia caused by *Shewanella algae*. *Infect. Chemother.* 46, 264-268, 2014.

[11] Dominguez H., Vogel B.F., Gram L., Hoffmann S., Schaebel S. *Shewanella algae* bacteremia in two patients with lower leg ulcers. *Clin. Infect. Dis.* 22, 1036-1039, 1996.

[12] Iwata M., Tateda K., Matsumoto T., Furuya N., Mizuiri S., Yamaguchi K. Primary *Shewanella algae* septicemia in a patient on hemodialysis. *J. Clin. Microbiol.* 37, 2104-2105, 1999.

[13] Kim D.M., Kang C.I., Lee C.S., et al. Treatment failure due to emergence of resistance to carbapenem during therapy for *Shewanella algae* bacteremia. *J. Clin. Microbiol.* 44, 1172-1174, 2006.

[14] Tan C.K., Lai C.C., Kuar W.K., Hsueh P.R. Purulent pericarditis with greenish pericardial effusion caused by *Shewanella algae*. *J. Clin. Microbiol.* 46, 2817-2819, 2008.

[15] Dey S., Bhattacharya D., Roy S., Nadgir S.D., Patil A., Kholkute S.D. *Shewanella algae* in acute gastroenteritis. *Indian J. Med. Microbiol.* 33, 172-175, 2015.

[16] Brulliard C., Traversier N., Allyn J., Schaeffer C., Bouchet B., Allou N. Case Report: disseminated *Shewanella algae* infection with meningoencephalitis in a traveler secondary to marine injury in Madagascar. *Am. J. Trop. Med. Hyg.* 97 (4), 1043-1044, 2017.

[17] Héritier C., Poirel L., Nordmann P. Genetic and biochemical characterization of a chromosome-encoded carbapenem-hydrolyzing Ambler Class D beta-lactamase from *Shewanella algae*. *Antimicrob. Agents Chemother.* 48, 1670-1675, 2004.

[18] Pagani L., Lang A., Vedovelli C., et al. Soft tissue infection and bacteremia caused by *Shewanella putrefaciens*. *J. Clin. Microbiol.* 41, 2240-2241, 2003.