Shewanella spp. infections in Gran Canaria, Spain: retrospective analysis of 31 cases and a literature review

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Abstract

Introduction. Shewanella spp. can cause severe skin and soft-tissue infections, gastrointestinal infections, otitis and bacteremia, generally upon contact with seawater or consumption of raw seafood. Recently, a new condition termed 'patera foot' characterized by acute skin and soft-tissue infection has been described in irregular immigrants arriving to the Canary Islands, Spain, in rudimentary boats. Most infections are caused by a single species, Shewanella algae. The improvement of the diagnostic capabilities in clinical microbiology laboratories has resulted in a growing number of cases being reported worldwide, most of them coming from warm regions.

Case presentation. In this work, we reviewed the medical records of all the patients with Shewanella infections in the two university hospitals of Gran Canaria (the Canary Islands, Spain) during the period 2000–2016, resulting in the identification of 31 cases. We also conducted a literature review of Shewanella infections reported worldwide in recent years.

Conclusion. This case series suggests that Shewanella infections are nosocomially acquired more frequently than previously thought. In addition, the unexpectedly high proportion of multidrug-resistant isolates raises concerns.

INTRODUCTION

Shewanella spp. are Gram-negative rods abundant in marine and freshwater environments [1]. While the broad respiratory versatility of this genus has been intensively researched for biotechnological and environmental applications [2], only a few Shewanella species have been described as causative agents of human infections. Previously, Shewanella spp. had often been misidentified in the clinical microbiology laboratory, as API test strips were not sufficiently discriminatory for clinically relevant Shewanella spp. [3], leading to Shewanella algae being misidentified as Shewanella putrefaciens. Refined identification procedures have diagnosed a growing number of cases that required re-evaluation of the pathogenic potential of certain Shewanella spp., in particular S. algae. Current state-of-the-art knowledge indicates that one species, S. algae, is responsible for around 80% of all cases [3]. The molecular mechanisms enabling S. algae to cause infections are unknown. S. algae is often isolated in the context of polymicrobial infections; thus, its clinical impact has not been fully defined. However, Shewanella infections are still largely considered exceptional.

Herein, we report the experience from Gran Canaria, the Canary Islands, Spain. We retrospectively reviewed all cases of Shewanella infections diagnosed during the period 2000–2016 at the two university hospitals, Hospital Insular and the Hospital Doctor Negrín, that serve the island of Gran Canaria, with a population of approximately 850 000. We have covered the epidemiology, microbiology and outcome of the infectious episodes, and discuss our findings from a microbial ecology perspective. In addition, we conducted a literature update on recently reported cases of Shewanella infections worldwide.

METHODS

Patients

We conducted a retrospective analysis of the medical records from 2000 to 2016 at the Hospital Insular and Hospital Doctor Negrín, Las Palmas de Gran Canaria, Spain.
Demographic and epidemiological data from the patients were retrieved. Microbiological data included species identification, co-isolates and antimicrobial susceptibility, as well as clinical data and the outcome of the infection episode.

Microbiology

Bacterial identification and antibiotic-susceptibility testing differed between the two hospitals and over time, and was conducted as stated below.

Hospital Universitario Insular de Gran Canaria

Since March 2014, Shewanella spp. have been identified by matrix-associated laser desorption ionization-time of flight (MALDI-TOF) MS. Before this time, all Shewanella isolates were initially identified as S. putrefaciens by using the API20E/API20NE system (bioMérieux). At all times, phenotypic characteristics such as growth at 42 °C, growth in 6.5 % NaCl and β-haemolysis were identification criteria for S. algae. MALDI-TOF MS identification results were further validated using the Vitek-2 automatic system, as described below.

In vitro susceptibility testing was performed using the disc-diffusion method on Mueller–Hinton agar with an inoculum corresponding to a McFarland 0.5 turbidity standard. Readouts were taken after 18 h of incubation at 35 °C. Isolates were considered resistant (R), intermediate resistant (I) or susceptible (S) to the tested antibiotics following the interpretative standards of the Clinical and Laboratory Standards Institute (CLSI) for 'other non-Enterobacteriaceae' [4].

Hospital Universitario de Gran Canaria ‘Doctor Negrín’

Bacterial identification and antibiotic-susceptibility testing of the isolates was performed with the Vitek-2 (bioMérieux) automatic system. Species identification was considered positive if the type index was 0.95 or higher. The isolates were ranked resistant (R), intermediate resistant (I) or sensitive (S) to the tested antibiotics as described in the CLSI guidelines [4].

RESULTS

Case series in Gran Canaria, Spain

A total of 31 cases occurred in 31 patients with the main clinical manifestations summarized in Table 1. Twenty-three patients (74.2 %) were men and eight (25.8 %) women. The mean age of the patients was 50.7 years, ranging from 15 to 87 years. Isolates were from skin and soft-tissue infections (18), blood (8), peritoneal lesions (2), bronchial aspiration (1), bile (1) and ear swab (1). A total of 15 of the 31 isolates had been identified as S. putrefaciens; the other 16 were identified as S. algae. Fourteen of the thirty-one isolates were from polymicrobial infections with other opportunistic Gram-positive and Gram-negative pathogens. Nine infections were associated with irregular African refugees arriving in rudimentary boats after a transoceanic journey lasting several days in overcrowded conditions. During this time, they had been exposed to weather inclemencies, water splashes and prolonged immersion of their feet in seawater coming into the boats, possibly contaminated with traces of urine, faeces and dirt. Otherwise, recent exposure to seawater was only unambiguously associated with one additional case, and could not be retrieved from the history of 20 patients. One wound infection case was associated with sand contamination from a local park.

Antimicrobial-susceptibility testing revealed several multi-drug-resistant isolates (e.g. strains 5, 7, 8, 14; Fig. 1). Remarkably, uncommon for S. algae and S. putrefaciens, a number of isolates were highly resistant to aminoglycosides, cephalosporins and ciprofloxacin. In addition, sensitivity to amoxicillin/clavulanic acid, tested for in 24 strains, unravelled 18 resistant isolates. A higher number of susceptible isolates was observed for pipercillin/tazobactam. A combination of tetracyclines, β-lactams, cephalosporins and/or quinolones was required for the successful treatment of most infections in this case series.

Literature review

Here, we review 34 reports of Shewanella infection from the literature between 2013 and 2016 in the literature [5–35]. In 2013, two extensive retrospective studies from Liu et al. [36] and Vignier et al. [37], including a literature review, were reported. Therefore, the selected timeframe of our review aims to provide an update of the new cases reported since then. The reader is referred to the paper by Srinivas et al. [38] for a prospective study (2010–2014) of Shewanella spp. skin and soft-tissue infections in Kerala, India.

The mean age of patients was 52.1 years (range 0–92 years). Twenty-four patients (70.6 %) were men. Most infections occurred in countries with warm climates, which included the Mediterranean region, South-Eastern Asia and the Caribbean. In most cases, the patients presented an underlying condition, such as cardiovascular disease (12 cases), diabetes (9 cases), hepatobiliary disease (6 cases), renal disease (5 cases), cancer (5 cases) and respiratory disease (2 cases). Less than half of the patients (44.1 %) reported recent contact with seawater or consumption of seafood. Clinical presentations were mostly skin and soft-tissue infections (12 cases, 30 %), gastrointestinal infections (10 cases, 25 %), bacteraemia (6 cases, 15 %) and respiratory infections (4 cases, 10 %). Two cases of immunocompromised individuals were reported. Only for five patients was there no basal pathology or underlying condition. Twenty-two infections (56.4 %) were attributed to S. algae, whereas 35.9 % were associated with S. putrefaciens. Of note, two cases of infection were by Shewanella xiamensis [31, 39] and one case by Shewanella xiamensis, isolated from rectal swabs of a 1-year-old child [12]. S. xiamensis was not the causative agent of the infection, but its intestinal carriage mimicked the presence of a pathogenic Klebsiella pneumoniae strain that caused a previous infection in the patient. Nine isolates (23.1 %) were associated with a polymicrobial infection. A summary of the epidemiological data of the patients, clinical manifestations and antibiotic-susceptibility profiles of the
Table 1. Characteristics of *Shewanella* spp. infections in Gran Canaria between 2000 and 2016

| Case | Date       | Origin | Isolate       | Co-isolate | Age (years) | Sex | Exposure to seawater | Sample                  | Underlying condition                                      | Clinical findings                                      | Treatment                                      | Outcome       |
|------|------------|--------|----------------|------------|-------------|-----|----------------------|-------------------------|----------------------------------------------------------|---------------------------------------------------------|-----------------------------------------------|---------------|
| 1    | 27/10/00   | C      | *S. putrefaciens* | N          | 57          | M   | NS                   | Ear swab                | AHT, DM                                                  | Severe external otitis                             | NS                            | Favourable   |
| 2    | 19/02/01   | C      | *S. putrefaciens* | N          | 68          | M   | NS                   | Blood                  | AHT, DM, dyslipidemia, IC (bypass)                      | Fever while hospitalized at Neurology department      | NS                            | Favourable   |
| 3    | 27/05/03   | NSC    | *S. putrefaciens* | *E. coli*  | 70          | M   | NS                   | SST (abscess)          | Colon carcinoma, AHT, DM, IC (bypass surgery)           | Rectal bleeding, diarrhoea, nausea, epigastric pain, surgical wound infection | NS                            | NS            |
| 4    | 01/12/03   | NSC    | *S. putrefaciens* | N          | 56          | F   | NS                   | Blood                  | AHT, IC, DM, vascular disease (2 stents)                | Fever while hospitalized at Cardiology department     | Gentamicin+ceftriaxone                             | Favourable   |
| 5    | 06/03/04   | C      | *S. putrefaciens* | Acinetobacter *haemolyticus* | 32          | F   | NS                   | Blood                  | Severe asthma, hastral hernia, gastrooesophageal reflux, obesity, hypercholesterolaemia | NS                            | Levofloxacin                             | Favourable   |
| 6    | 23/03/04   | C      | *S. putrefaciens* | N          | 64          | M   | NS                   | Blood                  | Lung cancer (lobectomy, 2001), DM, asthma               | Pericardial effusion and pericarditis, hospitalized at Cardiology department | NS                            | Favourable   |
| 7    | 10/02/05   | C      | *S. putrefaciens* | N          | 80          | F   | NS                   | Blood                  | Colon and cervix carcinoma, choledocctectomy, pancreatic mass of unknown origin | Nausea, vomiting, fever, abdominal pain; hospitalized at Oncology department | Antibiotics (NS)               | Favourable   |
| 8    | 28/08/06   | NSC    | *S. putrefaciens* | N          | 67          | F   | NS                   | Blood                  | DM, chronic renal failure (renal transplant), AHT, IC    | Sepsis that required intensive care                  | Antibiotics (NS)               | Death (unrelated to infection)  |
| 9    | 29/06/07   | C      | *S. putrefaciens* | *Staphylococcus aureus* | 20          | M   | Y (patera)          | SST (abscess)          | Septic shock, renal failure, rhabdomyolysis             | Hypothermia after patera sinking, septic shock, cellullis in inferior limbs, malodorous purulent ulcer in a finger | Antibiotics (NS)               | Surgical debridement of the lesions; amputation of the finger; otherwise favourable |
| 10   | 21/08/07   | C      | *S. putrefaciens* | N          | 25          | M   | Y (patera)          | SST (cutaneous wound swab) | –                                      | Necrosis of the left foot (dorsal); multiple wounds on the left thigh | Piperacillin+tazobactam +doxycycline, followed by cefazolin +cephalexin | Surgical debridement of the lesions; amputation of several fingers and skin graft; slow recovery; otherwise favourable |
| 11   | 13/08/08   | C      | *S. putrefaciens* | N          | 74          | M   | NS                   | Blood                  | AHT, colon carcinoma, liver and lung metastases, choledocctectomy | Sepsis of abdominal origin, high fever, vomiting, diarrhoea, unconsciousness, dehydration | Piperacillin+tazobactam +levofloxacin             | Favourable   |
| 12   | 04/09/08   | C      | *S. algae*       | N          | 21          | M   | Y (patera)          | SST (ulcer)          | Septic shock, renal failure, rhabdomyolysis             | Multiple dermal erosions in the legs                  | Linezolid                             | Favourable   |
| 13   | 05/09/08   | C      | *S. algae*       | Bacteroides *thetaiotaomicron* | 24          | M   | Y (patera)          | SST (phlyctena)         | –                                      | Dehydration, rhabdomyolysis, contusions in the legs | Cefazidime+doxycycline                             | Debridement, skin graft, amputation of one phalanx and two fingers; slow recovery; favourable |
| 14   | 09/09/08   | C      | *S. algae*       | *A. salmonicida* | 20          | M   | Y (patera)          | SST (cutaneous biopsy) | –                                      | Vomiting and diarrhoea after ingestion of seawater, anorexia (6days), fever, dehydration, cutaneous excoriations, tumefaction, cellullis in left leg with phlyctena | Imipenem+ceftazidime +doxycycline +clindamycin | Debridements, amputation of several fingers; slow recovery; favourable |
| Case | Date       | Origin | Co isolate | Age (years) | Sex | Exposure to seawater | Sample | Clinical findings                                                                 | Treatment                                                                 | Outcome   |
|------|------------|--------|------------|-------------|-----|---------------------|--------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-----------|
| 15   | 09/09/08   | C      | S. putrefaciens | 20          | M   | Y (patera)          | SST (wound) | General health deterioration Right knee arthritis                                  | Cefotaxime+amoxicillin/clavulanic acid (NS)                                  | Favourable |
| 16   | 09/12/08   | C      | S. algae   | 20          | M   | Y (patera)          | SST (wound) | Compliated scale of choleystasis in the right arm Traumatic wound in the left     | Ciprofloxacin+vancocin + vancomycin + amoxicillin/clavulanic acid (NS)         | Favourable |
| 17   | 12/10/10   | C      | S. algae   | 72          | M   | NS                  | SST (exudate from catheter site) | Chronic renal disease, renal transplant (1999), peritoneal dialysis catheter (2010), multiple myeloma, osteoporosis | Metronidazole + other antibiotics (NS)                                           | NS         |
| 18   | 04/09/10   | C      | S. putrefaciens | 70          | M   | NS                  | Blood | Fever                                                                          | Cefotaxime+amoxicillin/clavulanic acid                                          | NS         |
| 19   | 14/03/11   | C      | S. algae   | 70          | M   | NS                  | SST (abscess) | AHT, dyslipidaemia, chronic liver disease, alcoholism Traumatic wound in the left parieto-occipital region with necrotic, malodorous areas; fever | Ceftriaxone (NS)                                                                | Favourable |
| 20   | 05/10/11   | NSC    | S. algae   | 87          | M   | NS                  | SST (abcess) | Abdominal pain; faecal vomiting; constipation; sepsis from peripheric insertion central catheter | Ciprofloxacin+vancomycin + amoxicillin/clavulanic acid (NS)                     | Favourable |
| 21   | 06/06/12   | C      | S. algae   | 50          | M   | NS                  | SST (abcess) | Chronic renal failure Acute peritonitis in patient with peritoneal dialysis | Ceftriaxone (NS)                                                                | NS         |
| 22   | 23/06/13   | NSC    | S. algige   | 71          | F   | NS                  | FNS | Polytrauma after impact with a zodiac (thorax, abdomen, pelvis and right arm) | Imipenem+linezolid (empirical); changed to ciprofloxacin after antibiogram | Favourable |
| 23   | 02/06/14   | C      | S. putrefaciens | 40          | F   | NS                  | SST (wound) | Infection and necrosis signs in the arm, foot, and thigh after car accident | Ceftriaxone                                                                         | Favourable |
| 24   | 25/09/14   | C      | S. algige   | 43          | M   | NS                  | Y  | Supracondylar fracture with a zodiac (thorax, abdomen, pelvis)                  | Ceftriaxone                                                                         | NS         |
| 25   | 12/09/14   | C      | S. algige   | 36          | M   | NS                  | SST (wound) | Infection and necrosis signs in the arm, foot, and thigh after car accident | Ceftriaxone                                                                         | Favourable |
| 26   | 17/09/15   | C      | S. algige   | 67          | M   | NS                  | SST (wound) | Infection and necrosis signs in the arm, foot, and thigh after car accident | Ceftriaxone                                                                         | NS         |
| 27   | 11/09/15   | C      | S. algige   | 32          | M   | Y (patera)          | SST (wound) | Infection and necrosis signs in the arm, foot, and thigh after car accident | Ceftriaxone                                                                         | Favourable |
| 28   | 17/09/15   | C      | S. algige   | 67          | M   | NS                  | SST (wound) | Infection and necrosis signs in the arm, foot, and thigh after car accident | Ceftriaxone                                                                         | NS         |
| 29   | 21/09/15   | C      | S. algige   | 15          | M   | Y (patera)          | SST (wound) | Infection and necrosis signs in the arm, foot, and thigh after car accident | Ceftriaxone                                                                         | Favourable |
Infections caused by *Shewanella* spp. are being continuously reported, with the causative agent being mainly *S. algae*. Of note, isolates from 2000 to 2007 in our case series were identified as *S. putrefaciens*, potentially due to experimental limitations [3]. In contrast, 81% of cases retrieved from 2008 were identified as *S. algae*. State-of-the-art methods can discriminate between *S. algae* and *S. putrefaciens* on the basis of their biochemical and phenotypic characteristics [1]. Similar tests have been reported, though, to be inconclusive for discrimination of *S. algae* from other emerging pathogenic *Shewanella*, thereby requiring molecular techniques that include 16S rRNA and/or *gyrB* DNA sequencing for accurate species identification [39, 40]. Byun et al. reported the inability to discriminate between *S. algae* and *S. haliotis* on the basis of biochemical and phenotypic assays [39]. Even 16S rRNA sequencing, not routinely conducted in the clinical microbiology laboratory, can be insufficient to determine the identity of an isolate at the species level (E. Fernández-Rodríguez et al., unpublished results). Characteristics that can contribute to the virulence of *S. algae* are the presence of haemolysin genes, the ability to adhere to human epithelial cells, biofilm formation and exotoxin production, including tetrodotoxin [11], which might be associated with food intoxications [41].

A total of 14 of 31 *Shewanella* isolates in the case series were part of polymicrobial infections in combination with other opportunistic Gram-positive and Gram-negative pathogens (e.g., *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*). The skin has a temperature of around 30°C, which, in combination with the infection history, may have contributed to a successful colonization. In general, *Shewanella* infections are more frequent in males than females, although it is not yet known if this is a consequence of genetic or socio-cultural factors with a higher exposure rate [1] in our case study. The higher exposure rate of *Shewanella* isolates in our study compared to the patient group being tested may be due to the higher number of patients with a history of being at sea for multiple days. The skin has a temperature of around 30°C, which, in combination with the infection history, may have contributed to a successful colonization.

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**Table 1.**

| Case | Date   | Origin | Isolate | Co-isolate | Age (years) | Sex | Exposure to seawater | Sample | Underlying condition | Clinical findings | Treatment                                      | Outcome          |
|------|--------|--------|---------|------------|-------------|-----|----------------------|--------|----------------------|-----------------|-----------------------------------------------|------------------|
| 30   | 18/05/16 | NSC    | *S. algae* | N          | 60          | F   | NS                   | SST (surgical) wound | Obesity, smoking, diverticular disease, Arnold-Chiari malformation, waiting for abdominal surgery | Desloughing, malodorous wound with necrotic signs; no fever, stable | Piperacillin-tazobactam | Favourable |
| 31   | 07/07/16 | C      | *S. algae* | *Staphylococcus aureus* | 68          | M   | NS                   | SST (abscess) | DM, arrhythmia, diabetic foot; left leg amputated (infra-condylar) | Pain, cyanosis and necrosis in right foot | Amoxicillin/clavulanic acid + metronidazole | Infra-condylar amputation of right leg; otherwise favourable |

AHT, Arterial hypertension; C, community; DM, diabetes mellitus; DVT, deep venous thrombosis; F, female; IC, ischaemic cardiomyopathy; M, male; N, no; NS, not stated; NSC, nosocomial; SST, skin and soft tissue; XDR, extensively drug resistant; Y, Yes.

*The patient was not exposed to seawater directly, but to sand from a local park.*
Septic shock, dehydration, rhabdomyolysis and multiple skin lesions were common conditions among the irregular travellers after their ocean journey on small, rudimentary fishing boats, termed pateras. In fact, a condition termed ‘patera foot’ has been coined to describe *Shewanella* skin and soft-tissue infections in the lower limbs of these patients, likely from a pre-existing skin lesion that comes into contact with contaminated water. Those patients were generally young, with a good health status before travelling [45]. Infections, caused by *S. algae* in 66.7% of the patients, were very aggressive, involving cellulitis, abscesses and necrosis. Surgical debridement was carried out, but the response to broad-spectrum antimicrobial chemotherapy was generally poor. Amputation of one or several fingers was necessary in most cases. Recovery was very slow, but otherwise favourable. Among local people, 14 patients presented underlying hypertension, hypercholesterolaemia, obesity or diabetes, complicated with chronic cardiovascular conditions or cancer. These risk factors have been associated with *Shewanella* spp. and other opportunistic infections [1].

*Shewanella* infections have been frequently associated with coastal areas and warm climates. Located in the sub-tropical Penicillins Cephalosporins Carba- penem Aminoglycosides Fluoro quinolone Tetracyclines T/S

| Isolate | A/C | P/T | CTX | CEP | IMP | GEN | TOB | AMK | CIP | MIN/TET | TIG | T/S |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------|-----|-----|
| 1       |     |     |     |     |     |     |     |     |     |         |     |     |
| 2       |     |     |     |     |     |     |     |     |     |         |     |     |
| 3       |     |     |     |     |     |     |     |     |     |         |     |     |
| 4       |     |     |     |     |     |     |     |     |     |         |     |     |
| 5       |     |     |     |     |     |     |     |     |     |         |     |     |
| 6       |     |     |     |     |     |     |     |     |     |         |     |     |
| 7       |     |     |     |     |     |     |     |     |     |         |     |     |
| 8       |     |     |     |     |     |     |     |     |     |         |     |     |
| 9       |     |     |     |     |     |     |     |     |     |         |     |     |
| 10      |     |     |     |     |     |     |     |     |     |         |     |     |
| 11      |     |     |     |     |     |     |     |     |     |         |     |     |
| 12      |     |     |     |     |     |     |     |     |     |         |     |     |
| 13      |     |     |     |     |     |     |     |     |     |         |     |     |
| 14      |     |     |     |     |     |     |     |     |     |         |     |     |
| 15      |     |     |     |     |     |     |     |     |     |         |     |     |
| 16      |     |     |     |     |     |     |     |     |     |         |     |     |
| 17      |     |     |     |     |     |     |     |     |     |         |     |     |
| 18      |     |     |     |     |     |     |     |     |     |         |     |     |
| 19      |     |     |     |     |     |     |     |     |     |         |     |     |
| 20      |     |     |     |     |     |     |     |     |     |         |     |     |
| 21      |     |     |     |     |     |     |     |     |     |         |     |     |
| 22      |     |     |     |     |     |     |     |     |     |         |     |     |
| 23      |     |     |     |     |     |     |     |     |     |         |     |     |
| 24      |     |     |     |     |     |     |     |     |     |         |     |     |
| 25      |     |     |     |     |     |     |     |     |     |         |     |     |
| 26      |     |     |     |     |     |     |     |     |     |         |     |     |
| 27      |     |     |     |     |     |     |     |     |     |         |     |     |
| 28      |     |     |     |     |     |     |     |     |     |         |     |     |
| 29      |     |     |     |     |     |     |     |     |     |         |     |     |
| 30      |     |     |     |     |     |     |     |     |     |         |     |     |
| 31      |     |     |     |     |     |     |     |     |     |         |     |     |

Fig. 1. Heatmap showing the antibiotic-susceptibility profile of *S. algae* and *S. putrefaciens* isolates from Gran Canaria, Spain. Strain numbers refer to case numbers in Table 1. A/C, amoxicillin/clavulanic acid; P/T, piperacillin/tazobactam; CTX, cefotaxime; CEP, cephe- pime; IMP, imipenem; GEN, gentamicin; TOB, tobramycin; AMK, amikacin; CIP, ciprofloxacin; MIN/TET, minocycline/tetracycline; TIG, tigecycline; T/S, trimethoprim/sulfamethoxazole. Colour code: red, resistant; orange, intermediate; green, susceptible; grey, not tested.
Atlantic Ocean, the Canary Islands match such a profile, even though the mean water temperature of around 21 °C is lower than that of other ‘hotspots’ around the equator or the tropics. Indeed, seasonal *Shewanella* infection episodes related to unusually warm conditions have been reported in Denmark [46] and Australia [47]. Even if a seasonal correlation cannot be deduced, most infections in our study were diagnosed from June to November, matching the time when a peak in the number of pateras arriving at the Canary Islands, due to the good weather conditions at sea, is registered. Sea contact, even with materials placed at sea or consumption of seafood, which are reported risk factors for *Shewanella* infections, however, was not reported for most patients. The only case from a local person with documented contact with seawater was a 43-year-old man who impacted with the helix of an inflatable boat while diving. The patient suffered multiple traumatic injuries from which *S. algæ* was isolated in pure culture.

Remarkably, six patients were hospitalized at the time of the infection, therefore 19.4% of infections were potentially nosocomial. The source of the infection could be identified in only one case (patient 30). The *S. algæ* isolate was obtained several days after admission, without clear signs of infection. In this afebrile patient, a surgical wound abscess had been vacuum-drained. To avoid obstructions, the vacuum-assisted closure had been washed regularly, and on some occasions surgeons made replacements of the device. Washings had been performed with hypertonic saline solution, thereby contributing to the presence of the *S. algæ* isolate.

*Shewanellae* are susceptible to most antibiotics, including aminoglycosides, fluoroquinolones, extended-spectrum cephalosporins, β-lactamase inhibitors, carbapenems, macrolides, aztreonam and trimethoprim/sulfamethoxazole [48]. However, the emergence of resistant strains is a concern [49, 50], as highlighted for several isolates in our case series. The antibiotic susceptibility of the isolates in this case series was highly variable including a number of multidrug-resistant strains (Fig. 1). Seventeen isolates were resistant to amoxicillin/clavulanic acid. Given that clavulanic acid is an efficient inhibitor of class A β-lactamases [51], such resistance suggests the presence of class B, C and/or D β-lactamases, as reported to be present in several *Shewanella* spp. including *S. algæ* [52–54]. Resistance to a combination of piperacillin/tazobactam, with a broader spectrum than amoxicillin, was observed, as well as resistance towards the third-generation cephalosporin cefotaxime and the fourth-generation cephalosporin cefepime. Resistance to aminoglycosides is uncommon in *Shewanella* spp.; however, resistance to gentamicin, tobramycin and amikacin was observed. Indeed, the amikacin-resistant isolate (14) exhibited broad-spectrum resistance to all the tested penicillins and aminoglycosides. Several strains also displayed resistance towards antibiotics typically effective towards *shewanellae*, including carbapenems, tetracyclines, trimethoprim/sulfamethoxazole and fluoroquinolones (Fig. 1). Also of note is the marked differences in the antimicrobial-resistance profile observed in the isolates from patients univocally exposed to seawater during the same trip (e.g. 12–14 and 18–19), indicating that these infections involved different *S. algæ* strains.

*S. algæ* is in fact the environmental reservoir of *qnrA* genes that confer resistance to quinolones [55, 56]. Four variants of this gene (*qnrA2-5*) have been found to be chromosomally encoded in *S. algæ* [57]. Since quinolones are extensively used in aquaculture and are stable in seawater, selective evolutionary pressure transfers these genes to enterobacteria [57, 58], giving rise to the widespread problem of plasmid-mediated resistance to quinolones in Enterobacteriaceae [59, 60]. Furthermore, *S. algæ* is frequently reported to be resistant to colistin [3, 61]. Resistance to colistin in *S. algæ* is mediated by the expression of ethanolamine phosphotransferase (EptA), which alters the lipopolysaccharide in the outer membrane [62].

The literature review of the last 4 years gives further support to the findings from our case series, such as the abundance of patients without recent contact with aquatic environments and/or consumption of products of marine origin. Consequently, the origin of the isolates is frequently unknown and might suggest a more widespread distribution of pathogenic *Shewanella* spp. than previously thought. Water supply systems, soil or foods can be contaminated with *Shewanella* spp. A recently reported case of intestinal colonization by *S. xiamenensis* suggests temporary colonization of the human host by *Shewanella* spp. and transfer of *blaOXA-48*-like genes to *K. pneumoniae* [12].

Even though *Shewanella* spp. infections in humans are scarce, the number of reports has significantly increased over the last decade, suggesting that species within the *Shewanella* genus, in particular *S. algæ*, have indeed a pathogenic potential. *Shewanella* spp., particularly in warm coastal areas, can be considered emerging pathogens.

Herein, we have reported a case series in Gran Canaria, Spain. In a significant number of cases, the patients were irregular immigrants with patera foot syndrome, developed after prolonged exposure to seawater, which often led to amputation, followed by a complex recovery process. The response to broad-spectrum antibiotics, generally, third or fourth generation cephalosporins or alternatively, aminoglycosides, piperacillin/tazobactam, ciprofloxacin or tigecycline, recommended as an empirical therapy [63] was poor. In general, a concerning antibiotic-resistance profile that includes resistance to these commonly used antibiotics has been observed. Indeed, the arising of antibiotic resistance in *Shewanella* spp. is a concern, even if a relatively low number of infections have been reported. The genetic markers that confer such resistance, which may be horizontally transferred to other pathogenic bacteria, are still poorly characterized.

An interesting finding is the ability of *Shewanella* to colonize the human body. *Shewanella* spp. are known for their broad respiratory versatility. In an anoxic
microenvironment such as the intestinal tract, *Shewanella* spp. may take advantage of the abundance of terminal anaerobic electron acceptors to colonize such niches. Indeed, several publications describe *Shewanella* spp. colonization in marine animals [64–66]. The presence of *shewanellae* in a variety of human tissues has been reported in the context of different microbiome studies [67–69]. It is not clear, though, whether this is the result of a transient colonization or a more permanent condition. Interestingly, a recent study in patients with and without sphincter of Oddi laxity strengthens the latter hypothesis [70]. Such colonization might also explain the high proportion of cases unrelated to recent contact with seawater. Certainly, a better understanding of the microbial ecology of the genus *Shewanella* and its pathogenic potential is required.

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Conflicts of interest
The authors declare that there are no conflicts of interest.

Ethical statement
Informed patient consent was not necessary because of the retrospective nature of the study, the anonymization/dissociation of patient data and the fact that results did not affect the clinical management of patients.

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