Something Odd and Something New: A Case of *Shewanella putrefaciens* Peritonitis and Bacteremia Treated with Intraperitoneal Cefepime

Abigail C. Santos [1,*], Christy A. Varughese [2] and Shivanjali Shankaran [1]

[1] Division of Infectious Diseases, Department of Internal Medicine, Rush University Medical Center, Chicago, IL 60612, USA; shivanjali_shankaran@rush.edu
[2] Department of Pharmacy, Rush University Medical Center, Chicago, IL 60612, USA; christy_a_varughese@rush.edu
* Corresponding author: abigailsantosmd@gmail.com

Submitted: 18 June 2021, accepted: 14 September 2021, published: 31 December 2021

Abstract: *Shewanella* spp. is a Gram-negative rod that is normally found in the marine environment and rarely causes illness in humans. Since the late 1970s, cases of *Shewanella* spp. infection have been described in the literature with a wide array of clinical syndromes and was found to be commonly seen in patients with predisposing conditions. We report a case of a 73 year old woman with end-stage renal disease on peritoneal dialysis who presented with a 3 day history of abdominal pain and was found to have *Shewanella putrefaciens* peritonitis complicated by bacteremia. She was treated in a novel and successful way by administration of intraperitoneal cefepime. This was further validated by adequate cefepime blood concentrations after drawing a cefepime serum level on day 8 of treatment. To the best of our knowledge, intraperitoneal antibiotic administration to treat both bacterial peritonitis and bacteremia has not been reported in the literature. This treatment approach could potentially be a good precedent for peritoneal dialysis patients needing antibiotics as a less invasive option for antibiotic administration.

Keywords: *Shewanella*; peritonitis; bacteremia; intraperitoneal antibiotic

How to cite: Santos, A.C.; Varughese, C.A.; Shankaran, S. Something Odd and Something New: A Case of *Shewanella putrefaciens* Peritonitis and Bacteremia Treated with Intraperitoneal Cefepime. *Priv. Pract. Infect. Dis.*, 2021, 1(2): 6; doi:10.35995/ppid1020006.

Introduction

Shewanella spp. is a saprophytic Gram-negative rod found throughout the world and mainly in marine environments [1,2]. Human infection with members of the genus *Shewanella* is rare. Infections reported in the literature include bacteremia, skin and soft tissue infection, osteomyelitis, wound infection, ear infection, cerebellar abscess, osteomyelitis, empyema, endocarditis and peritonitis [3]. The majority of these infections are from species *Shewanella algae* and *Shewanalla putrefaciens* [2]. We report a case of *Shewanella putrefaciens* peritonitis complicated by bacteremia in a patient with end-stage renal disease on peritoneal dialysis who was treated in a novel and successful way via intraperitoneal administration of cefepime.

Case Presentation

A 73 year old woman with end-stage renal disease (ESRD) on peritoneal dialysis presented with a 3 day history of abdominal pain. Abdominal pain was described as diffuse and accompanied by nausea, poor appetite and malaise. Since the abdominal pain started, her peritoneal fluid during exchanges was cloudier than usual. Persistence of the pain prompted her to come to the hospital. Review of systems was notable for constipation; she denied fevers, chills or vomiting. She had a past medical history of ESRD and was on continuous ambulatory peritoneal dialysis, type 2 diabetes mellitus, hypothyroidism and atrial fibrillation. She also recently took a short course of oral methylprednisolone. She had an allergy to ciprofloxacin and her allergic reaction was rash. Epidemiological history was notable for living in the Midwest and she denied any recent travel. She ate oysters frequently, last intake was 2 weeks prior to admission. She endorsed complying with all the necessary precautions and aseptic techniques during her peritoneal dialysis sessions.

On arrival, the patients blood pressure was 119/72, heart rate 144/min, respiratory rate 22/min and temperature of 97.5 degrees Fahrenheit. Notable physical exam findings were her increased heart rate and irregular heart rhythm, abdomen was soft but diffusely tender on examination with hypoactive bowel sounds, her peritoneal dialysis catheter was in place and was clean with no surrounding skin erythema. For her initial diagnostic work-up, point of care lactic acid was 3.1 (reference range: 0.5–1.7 mmol/L). Her hemoglobin was 12.2 (reference range: 4.0–10.0 K/uL), white blood cell count was 12.32 (reference range: 4.0–10.0 K/uL) with 87% neutrophils (reference range: 46–78%) and her platelet count was 109 (reference range: 150–399 K/uL). Her serum creatinine was 10.65 (reference range: 0.65–1.0 mg/dL), which was expected given her history of ESRD. Computerized tomography (CT) scan of her abdomen and pelvis revealed findings of small bowel obstruction with a transition point in the central lower abdomen, with no findings of pneumoperitoneum and peritoneal dialysis catheter was found to be in stable positioning. A sample of peritoneal fluid was taken for analysis and was found to be cloudy with <1000/uL red blood cell count, 12,880/uL white blood cell count with 12,040/uL absolute polymorphonuclear cells.

Blood and peritoneal fluid cultures immediately returned positive with Gram-negative rods on Gram-stain (Figure 1). She was initially started on empiric intravenous piperacillin-tazobactam. Both cultures later on speciated to *Shewanella putrefaciens* (sensitive to cefepime, amikacin, levofloxacin, meropenem, piperacillin-tazobactam and trimethoprim-sulfamethoxazole).

To adequately treat both *Shewanella putrefaciens* secondary peritonitis and bacteremia we decided to switch intravenous piperacillin-tazobactam to intraperitoneal cefepime alone on day 3 of treatment. Cefepime was dosed 250 mg (125 mg/L) intraperitoneally every 6 h coinciding with her peritoneal dialysis exchanges and dwell time. The rationale for antibiotic treatment with intraperitoneal cefepime alone to treat both peritonitis and bacteremia will be discussed below. The patients abdominal pain improved, blood and peritoneal cultures cleared and peritoneal fluid white cell count decreased to 32/uL. Due to the concomitant bacteremia, a cefepime serum level was obtained to confirm adequate blood concentrations. On day 8 of intraperitoneal cefepime therapy,

a serum level drawn immediately prior to the next exchange (after a 6 h cefepime-containing dwell) resulted as 35.14 mcg/mL (*Shewanella putrefaciens* cefepime minimum inhibitory concentration (MIC) ≤4, [4]). Furthermore, on day 8, the patient started to have behavioral changes and confusion, which were concerning for cefepime-induced neurotoxicity. Thus, cefepime was switched to oral trimethoprim-sulfamethoxazole to complete the treatment course. Two days after switching to trimethoprim-sulfamethoxazole, her mentation was back at baseline. We treated her for a total of 14 days given her rapid clinical improvement, rapid clearance of bacteremia and to prevent further antibiotic related side effects. She was able to follow-up in our outpatient clinic up to a year, she has not had any relapse of her infection.

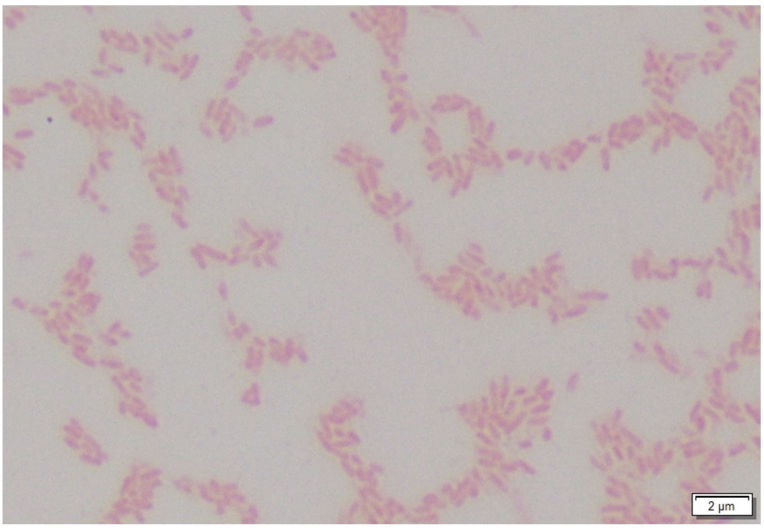

Figure 1: Culture from patients blood showing Gram-negative rods.

Discussion

Our patient was likely exposed to *Shewanella putrefaciens* when she ate oysters 2 weeks prior to her admission. Her developing small bowel obstruction and recent steroid use predisposed her to have peritonitis by causing gut translocation of the *Shewanella putrefaciens* which seeded into her peritoneum and eventually into the blood stream.

The role of molluscan shellfish as a vehicle for transmission of bacterial and viral pathogens to humans has been well documented [5]. Most common organisms linked to shellfish related illnesses are *Vibrio* spp. (*V. parahaemolyticus, V. vulnificus* and *V. cholerae*), *Salmonella*, norovirus and hepatitis A virus. A study was performed on the microbiological flora of oysters and seawater from commercial oyster harvesting sites in Delaware Bay, New Jersey and of the 1421 bacterial isolates identified, 170 (12%) of the isolates were *Shewanella putrefaciens* [6].

Shewanella spp. are ubiquitously distributed in nature; however, the majority of these bacteria appear to be originally from the marine environment [4]. Human infections with *Shewanella* spp. are rare; the majority of these infections are from species *Shewanella algae* and *Shewanalla putrefaciens* [2]. The infections reported in the literature include bacteremia, skin and soft tissue infection, osteomyelitis, wound infection, ear infection, cerebellar abscess, empyema, endocarditis, intraabdominal infection and peritonitis [3]. These infections are commonly seen among patients with predisposing conditions such as immunocompromised status, renal failure, hepatobiliary disease, diabetes or those involved in trauma [4]. Vignier et al. reported 16 cases and also analyzed 56 articles published in PubMed from 1973 to 2011 [7]. They found 239 cases of *Shewanella* spp. infection.

Exposure to the marine environment was reported in 44% of these patients. Bacteremia was the most common complication (28%), it was associated with skin and soft tissue infection, abdominal/biliary tract infection or respiratory infection. Infection was considered serious (hypotension, organ failure or death) in 21% of the cases. Members of this genus are generally susceptible to third and fourth generation cephalosporins, carbapenems, beta-lactamase inhibitor combinations, aminoglycosides, chloramphenicol, erythromycin, aztreonam and quinolones [4].

We approached our patients treatment of *Shewanella putrefaciens* peritonitis and bacteremia in a novel and successful way by consolidating therapy into just intraperitoneal cefepime. The physiologic characteristic of the peritoneal cavity not only helps remove toxic metabolites from the body, but also provides a useful portal of entry in the body for several pharmacologic agents [8]. Pharmacologic agents such as intraperitoneal antibiotics are used as a treatment for peritoneal dialysis associated peritonitis and intraperitoneal chemotherapy is used as a treatment for some intra-abdominal malignancies. To the best of our knowledge, we have not encountered a case of sole intraperitoneal antibiotic use to treat both bacterial peritonitis and bacteremia.

A pharmacokinetics study of intraperitoneal cefepime in automated peritoneal dialysis by Elwell et al. concluded that for both automated peritoneal dialysis and continuous ambulatory peritoneal dialysis patients, patients would achieve adequate serum concentrations if treated with standard doses of cefepime 1000 mg intraperitoneally once every 24 h [9]. The bioavailability using this route was reported to be 84.3% ± 6.2%. According to this study, maximum serum levels after a 1000 mg dose were reached after 6 h and averaged 38.5 ± 5.1 mcg/mL. At the end of the dosing interval at 24 h, the mean trough serum concentration were 15.8 ± 3.6 mcg/mL which is well above the MIC for susceptible organisms at 8 mcg/mL. In the International Society for Peritoneal Dialysis (ISPD) guidelines [10], there is a suggestion of 125 mg/L (range given as 100–125 mg/L) as a maintenance dose for each exchange or 1000 mg daily. Each peritoneal bag administered to our patient was 2 L (thus 250 mg total) and this was given every 6 h. On day 8 of intraperitoneal cefepime therapy, a serum level drawn immediately prior to the next exchange (after a 6 h cefepime-containing dwell) resulted as 35.14 mcg/mL. Compared to the mean trough level around 15 mcg/mL reported from Elwell and colleagues, this patients level is twice as high. Her symptoms of neurotoxicity, along with its resolution by stopping intraperitoneal cefepime, indicate that she had adequate serum levels. This also indicates that this dose could be too high in her case. ISPD guidelines only mentions serum drug monitoring for intraperitoneal vancomycin and aminoglycosides. This case proves that monitoring cephalosporin levels is also important in mitigating toxicity risk.

Our case highlights that intraperitoneal antibiotic administration could achieve therapeutic serum levels by successfully treating both peritonitis and bacteremia caused by an organism that has the potential to become virulent. This novel treatment approach could potentially open other avenues for antibiotic administration for peritoneal dialysis patients. Intraperitoneal administration of antibiotics could potentially be less invasive especially in patients who will be needing a longer course of antibiotics. Further pharmacokinetic studies on antibiotics would need to be done to explore drugs that could potentially be used via intraperitoneal administration.

Author Contributions: Writing—Original Draft Preparation and Revision, A.C.S.; Writing—Review and Editing, C.A.V., and S.S.; Supervision—S.S.

Funding: This research received no external funding.

Informed Consent Statement: Written informed consent was obtained from the subject involved in this case report.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Chen, Y.; Liu, Y.; Yen, M.; Wang, J.; Wang, J.; Wann, S.; Cheng, D. Skin and Soft—Tissue Manifestations of *Shewanella putrefaciens* Infection. *Clin. Infect. Dis.* **1997**, *25*, 225–229. [CrossRef] [PubMed]
2. Holt, H.M.; Gahrn-Hansen, B.; Bruun, B. *Shewanella algae* and *Shewanella putrefaciens*: Clinical and microbiological characteristics. *Clin. Microbiol. Infect.* **2005**, *11*, 347–352. [CrossRef] [PubMed]
3. Oh, H.S.; Kum, K.A.; Kim, E.-C.; Lee, H.-J.; Choe, K.W.; Oh, M.D. Outbreak of *Shewanella algae* and *Shewanella putrefaciens* Infections Caused by a Shared Measuring Cup in a General Surgery Unit in Korea. *Infect. Control. Hosp. Epidemiol.* **2008**, *29*, 742–748. [CrossRef] [PubMed]
4. Yousfi, K.; Bekal, S.; Usongo, V.; Touati, A. Current trends of human infections and antibiotic resistance of the genus Shewanella. *Eur. J. Clin. Microbiol. Infect. Dis.* **2017**, *36*, 1353–1362. [CrossRef] [PubMed]
5. DePaola, A.; Jones, J.L.; Woods, J.; Burkhardt, W.; Calci, K.R.; Krantz, J.A.; Bowers, J.; Kasturi, K.; Byars, R.H.; Jacobs, E.; et al. Bacterial and Viral Pathogens in Live Oysters: 2007 United States Market Survey. *Appl. Environ. Microbiol.* **2010**, *76*, 2754–2768. [CrossRef] [PubMed]
6. Richards, G.P.; Watson, M.A.; Crane, E.; Burt, I.G.; Bushek, D. *Shewanella* and *Photobacterium* spp. in Oysters and Seawater from the Delaware Bay. *Appl. Environ. Microbiol.* **2008**, *74*, 3323–3327. [CrossRef] [PubMed]
7. Vignier, N.; Théodose, R.; Barreau, M.; Baubion, E.; Olive, C.; Cabié, A.; Hochedez, P. Human Infection with *Shewanella putrefaciens* and *S. algae*: Report of 16 Cases in Martinique and Review of the Literature. *Am. J. Trop. Med. Hyg.* **2013**, *89*, 151–156. [CrossRef] [PubMed]
8. Chaudhary, K.; Haddadin, S.; Nistala, R.; Papageorgio, C. Intraperitoneal drug therapy: An advantage. *Curr. Clin. Pharmacol.* **2010**, *5*, 82–88. [CrossRef] [PubMed]
9. Elwell, R.J.; Frye, R.; Bailie, G.R. Pharmacokinetics of Intraperitoneal Cefepime in Automated Peritoneal Dialysis. *Perit. Dial. Int.* **2005**, *25*, 380–386. [CrossRef] [PubMed]
10. Li, P.K.-T.; Szeto, C.C.; Piraino, B.; De Arteaga, J.; Fan, S.; Figueiredo, A.E.; Fish, D.N.; Goffin, E.; Kim, Y.-L.; Salzer, W.; et al. ISPD Peritonitis Recommendations: 2016 Update on Prevention and Treatment. *Perit. Dial. Int. J. Int. Soc. Perit. Dial.* **2016**, *36*, 481–508. [CrossRef] [PubMed]