Invasive infection and extraintestinal complications are rarely caused by *Plesiomonas shigelloides*, a water-borne bacterium belonging to the Vibrionaceae family. We report a case of a 16-year-old female patient with sickle beta-zero thalassemia who survived septic shock caused by *P. shigelloides* associated with secondary acute respiratory distress syndrome and disseminated intravascular coagulation. Treatment with a carbapenem was successful, and the patient recovered without any sequelae. The previous reports of *P. shigelloides* sepsis are cited, and possible pathogenic mechanisms are discussed. (Heart Lung 2010;39:335–339.)

**P**lesiomonas *shigelloides*, previously known as *Aeromonas shigelloides*, belongs to the Vibrionaceae family, which includes the genera *Vibrio* and *Aeromonas*. *P. shigelloides* is a Gram-negative facultative anaerobic bacillus with lateral or terminal flagellum, found in soil, water, and animals, that rarely causes gastroenteritis and invasive disease in immunocompetent persons. The infection with *P. shigelloides* is believed to be initially caused by contamination of the gastrointestinal tract after the ingestion of raw fish or water-contaminated foods. Warm- and cold-blooded animals, such as cats, dogs, cows, and snakes, can also be hosts, in addition to fish, mussels, oysters, and shrimp. The most usual presentation of *P. shigelloides* infection is an acute gastroenteritis, which is self-limited in immunocompetent hosts, with a predominance of secretory-type diarrhea. Several outbreaks of *P. shigelloides* gastroenteritis have been reported.

Although bacteremia caused by *P. shigelloides* has also been reported in several clinical situations, to our knowledge, *P. shigelloides* sepsis has not been previously documented in a patient with sickle beta-zero (Sβ0) thalassemia who has successfully recovered after carbapenem therapy without any sequelae. The details of this clinical case are reported.

**CASE REPORT**

We report the case of a 16-year-old female patient who was born in Orlandia, Saú Paulo, Brazil, and resides in Ribeirão Preto, São Paulo, Brazil. The patient was identified as an Sβ0 thalassemia carrier at 1 year of age, and since then she has been under medical follow-up, taking benzathine penicillin every 21 days and folic acid supplementation. She presented up-to-date immunization schedule, including vaccines against pneumococcus, meningococcus, and influenza.

The patient arrived at the emergency department reporting fever of 1-day duration, lumbar and lower limbs pain, and vomiting. She reported having a similar crisis 6 years previously, which had been treated as a sickling crisis. The patient reported 2 episodes of diarrhea without mucus, pus, or blood, which had...
started 2 days before. She denied abdominal pain or urinary symptoms. She also denied having eaten seafood. Physical examination revealed a pale, dehydrated, slightly icteric individual with a respiratory rate of 16 beats/min, arterial blood pressure of 86/40 mm Hg, and heart rate of 120 beats/min. Lung and heart auscultation were normal. The abdomen was flat, the liver was palpable 2 cm below the right costal margin and with pain on palpation, the spleen percussion revealed a solid sound, and there were no signs of peritoneal irritation. The lower limbs were painful on palpation, without edema.

Analgesia with morphine and ketoprofen was started, as well as hydration for the treatment of a supposed sickling crisis. Chest x-ray was normal. Routine urine examination provided a pH of 5.0, positive nitrite, and leukocytes 10 to 15/field, with rare clusters and the presence of bacteriuria. Laboratory records revealed the following: creatinine levels = 0.8 mg/dL, urea = 24 mg/dL, total bilirubin = 12.7 mg/dL, indirect bilirubin = 6.5 mg/dL, sodium = 137 mEq/L, potassium = 3.3 mEq/L, calcium = 1.09 mEq/L, alanine aminotransferase = 64, aspartate aminotransferase = 65, alkaline phosphatase = 550, albumin = 3.8, ferritin = 481 ng/mL, hemoglobin = 5.9 g/dL, hematocrit = 17.7%, white blood cells = 17,000/mm³ (12% bands, 67% segmented, and 21% lymphocytes), platelets = 167,000/mm³.

One unit of red blood cell concentrate was transfused. Treatment with ceftriaxone (1 g intravenously [IV] every 12 hours) and clarithromycin (500 mg IV every 12 hours) was started because there was leukocytosis with a leftward shift and hemodynamic instability. Blood sample and urine obtained by catheterization were submitted to in vitro cultures still on the day of hospitalization.

The patient’s condition progressed with worsening of jaundice and increased serum bilirubin levels. Abdominal ultrasound revealed a small amount of fluid in the Morrison space, a small volume of bilateral pleural effusion, a gallbladder of normal dimensions with slight wall thickening and containing a 2.3-cm calculus with no evidence of intra-abdominal collection, and a reduced spleen volume. The liver presented a heterogeneous appearance with a slight increase in the overall volume. Metronidazole (500 mg IV every 8 hours) was administered in combination for treatment against a probable abdominal focus of anaerobic bacteria.

The patient developed worsening of the ventilatory pattern with dyspnea and tachypnea, and was transferred to an intensive care unit (ICU). On admission to the ICU, she was dehydrated, tachypneic (respiratory rate = 34 breaths/min), icteric, pale, and afebrile. The arterial blood pressure was 80/50 mm Hg, and heart rate was 135 beats/min. Respiratory auscultation revealed sparse grunts. The abdomen was painful on superficial and deep palpation, with defense and the presence of borborygmus. At admission, the APACHE II score for the patient was 22 (a death risk of 45%) and the presence of bacteriuria. Laboratory tests at ICU admission showed arterial blood gases values: pH 7.22, PO2 88.9 torr, PCO2 28.9 torr, HCO3 11.7 mEq/L, SatO2 95%. The blood count revealed leukocytosis (white blood cells = 23,000 cells/mm³).

On the second day in the ICU, the patient presented widening of the international normalized ratio (2.21), reduced fibrinogen (107 mg/dL), increased D dimer (>10 ng/mL), and altered activated partial thromboplastin time (65.7 seconds), which characterizes disseminated intravascular coagulation. There was an increase in bilirubin (total = 23.3 mg/dL; direct = 17 mg/dL, platelets = 154,000/mm³, white blood cells = 35,000/mm³) and increased aminotransferase (80 U/L). In view of the presence of hypotension, which did not improve with volume infuse, noradrenaline was started. On the fourth day in the ICU, vasoactive amines weaning was started, and the ventilatory pattern improved, allowing a reduction in the fraction of inspired oxygen (FIo2) and positive end-expiratory pressure. On the same day, the blood culture performed on the day of hospitalization showed growth of *P. shigelloides*, detected by the Bact/Alert system (Bio Méérieux, Marcy l’Etoile, France) and identified by the NC30 Microscan panel system (Dade, West Sacramento, CA). The antibiogram demonstrated resistance to ampicillin and susceptibility to amikacin, gentamicin, sulfamethoxazole-trimethoprim, imipenem, ciprofloxacin, and ceftriaxone. Because the patient presented a peak bilirubin level on the second day of hospitalization (45 mg/dL) and maintained a febrile response (Fig 1), therapy with ceftriaxone, metronidazole, and clarithromycin (started 4 days before ICU admission) was replaced with imipenem therapy (1 g IV every 8 hours) for 14 days. Multiple urine cultures were negative for any pathogenic organisms. Multiple stool samples were tested for blood and examined microscopically for white cells, ova, parasites,
and culture, which showed they were negative for the presence of pathogens. Because the patient had not previously used any antibiotics and had no risk factors for pseudomembranous colitis, the search for *Clostridium difficile* toxin was not performed.

The patient continued to have fever, and on the sixth day in the ICU, she presented worsening of the ventilatory pattern and purulent secretion at the site of arterial catheter insertion when it was removed, and vancomycin was started. Two of 4 blood samples and the secretion from the arterial catheter revealed the growth of methicillin-resistant, vancomycin-susceptible *Staphylococcus epidermidis*.

The patient was weaned from ventilation, extubated, and returned to the ward after an ICU stay of 18 days. Laboratory records revealed that all parameters were restored to normal reference ranges. She remained in the ward and continued to have fever (2 daily peaks of 38°C). She took vancomycin for 18 days and was discharged from the hospital 8 days after being discharged from the ICU, without any sequelae.

**DISCUSSION**

Bacteremia caused by *P. shigelloides* infection is a rare event. After the review report of Lee et al\(^{11}\) referring to 21 cases, only 6 new case reports have been documented worldwide.\(^{8,10,12,14,15}\) Most cases of *P. shigelloides* sepsis have been observed in immunocompromised hosts and neonates.\(^{11-15}\) Bacteremia due to *P. shigelloides* has been described in several clinical situations, including biliary tract diseases,\(^{8}\) polymicrobial bacteremia,\(^{9}\) human immunodeficiency virus-related immunodeficiency,\(^{10}\) immunosuppression after allogeneic bone marrow transplantation,\(^{11}\) leukemia,\(^{12}\) and multiple myeloma,\(^{13}\) as well as in patients with hemochromatosis,\(^{14}\) thalassemia intermedia hematologic disorder,\(^{15}\) and functional\(^{16}\) or anatomic\(^{18}\) splenectomy. Cases of severe infection associated with acute respiratory distress syndrome and disseminated intravascular coagulation, as well as extraintestinal diseases, such as spleen abscess,\(^{15}\) ophthalmitis,\(^{3}\) meningitis,\(^{19,20}\) cellulitis,\(^{21,22}\) and orchi-epididymitis\(^{23}\) have also been reported. The most severe events are more frequently seen in patients with impaired immunologic function or those with hepatobiliary disturbances, including biliary lithiasis, when cholestasis and cholangitis would support infection. Despite the relevance of these factors, their role in the development of severe infection is not totally elucidated. There is no evidence to support
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the relationship between the presence of gallbladder disease or calculus and the recurrence of bacteremia.

The mortality rate is usually high, ranging from 62% to 88%.11,15,24,25 Successful treatment relies on the early identification of the organism and implementation of effective antibiotics.11 To the best of our knowledge, this report represents the first case of P. shigelloides sepsis documented in Brazil.

Because P. shigelloides is usually self-limiting gastroenteritis, antibiotic therapy is reserved for cases of extraintestinal disease or for patients who present with bloody or prolonged bouts of diarrhea, which usually shorten the clinical course.24 Because of the broad variations in the strain susceptibility, the selection of therapy is usually guided by the results of appropriate antibiogram tests.24 P. shigelloides is susceptible to co-trimoxazole, quinolones, imipenem, aminoglycosides, chloramphenicol, and third-generation cephalosporins.11,21,24,25 The antibiogram usually reveals resistance to ampicillin and carbenicillin, as well as sensitivity to the cephalosporins, quinolones, and carbapenem compounds.2,4,15,26 Aminoglycosides are generally ineffective.15

Although P. shigelloides is a bacterium with a relatively low virulence, it can be fatal when patients with underlying immunocompromising diseases are infected, even when obvious clinical signs of immunodeficiency are absent.

The role of P. shigelloides and the exact mechanism underlying sepsis have not been totally elucidated. Laboratory studies with P. shigelloides have generally shown that although a few strains may be invasive,27 the lack of properties typically found in other enteric pathogens, such as enterotoxin and cytotoxin production, is generally observed in most isolates.28-30

A few studies have reported the potential virulence-associated properties of P. shigelloides strains, describing that 4 of the 5 types have been shown to be beta-lactamase positive.31 A single study has demonstrated that P. shigelloides produces a proteic/lipopolysaccharidic complex toxin that causes both cytotoxicity and enteropathogenicity.6

It has been reported that P. shigelloides is an intestinal pathogen that uses heme as an iron source. The P. shigelloides heme use system consists of 10 genes, 7 of which permit heme transport and 3 of which are associated with the use of heme as an iron source once it is inside the cell.32

It has been proposed that chronic iron overload may be marked by a tendency to infection because it leads to plasma iron occurring in a low-molecular-weight form, loosely bound to albumin iron.15 This form of iron promotes formation of highly reactive hydroxyl radicals, stimulates peroxidation of membrane lipids, and may have a central role in the pathogenesis of tissue damage in hemochromatosis. In addition, low-molecular-weight iron complexes may be readily available for invading bacteria.15 Although the role played by iron regulation in the virulence of P. shigelloides remains controversial,14,32,33 it is possible that patients with Sβo thalassemia, who are chronically dependent on transfusions, become more susceptible to P. shigelloides because of the development of iron overload. In fact, iron overload in thalassemia may be a result of not only repeated blood transfusions but also excessive intestinal iron absorption. Even though patients with transfusion-dependent anemias have had dramatic gains in terms of life expectancy in the deferoxamine era, the mortality in patients with thalassemia is still unacceptably high.34 It is possible that in addition to iron-induced heart failure, which is the major cause of death in patients with thalassemia,33 severe bacterial infections may contribute to morbidity and mortality in iron-overloaded patients with thalassemia.

CONCLUSIONS

There is a novel well-established belief that all cases of true bacteremia (ie, not contamination) should be treated promptly. A number of studies have shown that a delay in the institution of appropriate antibiotic therapy correlates with poor outcome in the setting of sepsis or bacteremia.35 Our findings add new data to this hypothesis by showing that the prompt treatment and good outcome of the present case report of a patient with P. shigelloides bacteremia in association with Sβo thalassemia is in accord with previous studies supporting the prompt institution of antimicrobials for bacteremia and sepsis.

REFERENCES


