

## Spondylodiscitis Associated with Recurrent *Serratia* Bacteremia Due to a Transjugular Intrahepatic Portosystemic Shunt (TIPS): A Case Report

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**We report a case of spondylodiscitis caused by multiresistant *Serratia marcescens* in a cirrhotic patient who had several *Serratia* bacteremias after the placement of a transjugular intrahepatic portosystemic shunt (TIPS) device. We concluded that an endovascular stent that can not be removed makes management of recurrent bacteremia difficult. Furthermore, back pain due to bacteremia is indicative of spondylodiscitis. *Serratia marcescens* can be an aggressive pathogen, causing spinal infection.**

**Key-Words:** *Serratia marcescens*, recurrent bacteremia, spondylodiscitis, TIPS.

### Case Report

A 59-year-old Caucasian man had liver cirrhosis due to alcohol abuse, which was complicated by portal hypertension and esophageal varices. Because of acute upper gastrointestinal bleeding and transesophageal sclerosis of varices, he underwent a transjugular intrahepatic portosystemic shunt (TIPS) procedure performed at our hospital. As he also had aspiration pneumonia, intravenous antibiotic therapy with cefoxitin was done for four days. There was gradual clinical improvement, and he was transferred to his local hospital. However, blood cultures collected seven days after TIPS revealed *Serratia marcescens*, which was only susceptible to cefotaxime, ceftazidime and imipenem. Imipenem was administered during seven days.

Three weeks after TIPS, the patient developed low-back pain and fever (38.5°C), without neurological involvement. Lumbar radiography and computed tomography were compatible with degenerative processes. The blood cultures showed *S. marcescens*, which was susceptible to the previously-mentioned antibiotics. Imipenem was reinitiated for another seven days. Ten weeks after TIPS, he was transferred to our department to determine the source of the bacteremia. On admission, he complained of worsening low-back pain, and he was febrile (38.3°C). Laboratory blood examination showed C-reactive protein to be 5.7 mg/dL (normal values: 0.0-0.5 mg/dL), erythrocyte sedimentation rate 48 mm/hr and white blood cell counts  $8.8 \times 10^9/L$ , with 75% segmented neutrophils. The blood cultures revealed *S. marcescens*, which was only susceptible to imipenem.

A gallium-67 citrate scan revealed an increased uptake at D9-D11, probably due to spondylodiscitis, which was confirmed by bone scanning with technetium-99m and magnetic resonance imaging. He had no central line devices, and the urine cultures were negative. The abdominal Doppler ultrasound showed a TIPS stent with a normal-direction blood

flow. Abdominal ultrasound and chest X-rays, as well as transthoracic echocardiography, were normal.

The patient could only walk with the aid of a thoracolumbar brace, and imipenem was administered from the 10<sup>th</sup> until the 45<sup>th</sup> week after TIPS, with substantial clinical improvement and discrete imaging symptom stabilization. His next presentation was 48 weeks after TIPS, with a recrudescence of fever, despite 36 weeks of antibiotic therapy. He had a satisfactory clinical condition, no longer wore a lumbar support, and the lab data (ESR, CRP, WBC) showed a good response. However, *S. marcescens* was again isolated from the blood cultures, and it had the same antibiotic-resistance pattern. Although Doppler ultrasound showed the TIPS device to have no thrombus or vegetations, we considered the hypothesis of TIPS infection or colonization by *Serratia* sp., and we established a plan to continue anti-*Serratia* treatment, possibly *ab aeterno* with imipenem or ertapenem. The patient received antibiotic therapy with imipenem for a further 50 weeks. At that time (98 weeks after TIPS) we decided to suspend antibiotic treatment, as he maintained radiological stabilization of the infectious process. Twenty-six weeks after being discharged without antibiotic therapy, he had no fever or other evidence of bacteremia, and he had no back-pain complaints. The patient was able to go about his daily activities without any disability. Radiography and clinical appearance was suggestive of vertebral bone fusion between D9-D10 and D10-D11. He had no further variceal bleeding.

### Discussion

*Serratia marcescens* is an aerobic Gram-negative bacillus that belongs to the family *Enterobacteriaceae*; when it was discovered, in the nineteenth century it was believed to be a microorganism with low virulence [1]. However, since the 1960s, it is considered to be an opportunistic human pathogen. It tends to colonize the respiratory and urinary tracts of adults in health-care institutions and has been associated with outbreaks of nosocomial infections. Among all nosocomial bacteremias, 1.2 to 1.4% are caused by *Serratia* species [2-4]. Central nervous infection caused by *S. marcescens* can occur, particularly in neonates with prior sepsis or after a neurosurgical procedure or lumbar puncture [5]. In drug addicts, it can cause endocarditis (often left-sided) and

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osteomyelitis [6,7]. Nevertheless, *Serratia* rarely affects the bones and joints [8]. Patients with nosocomial infections, diabetes mellitus, renal failure, who have a debilitated immune status, or have traumatic open wounds, as well as the elderly and drug addicts, are the most susceptible to *Serratia* infections [8,9]. These infections are associated with high mortality (25%-52%), especially when they progress to bacteremia [9-11].

*Serratia* spp. can survive under hostile conditions, including in disinfectant solutions, which can become the source for outbreaks; in addition they can spread within or among health care institutions on the hands of staff [1]. The source of most infections of the intervertebral disc is the blood; though it can also occur postoperatively. There are relatively few cases of post-operative spinal infection due to *Serratia* (two cases after elective lumbar spine surgery, one case after anterior cervical discectomy and fusion and another case after post-lumbar vertebroplasty) [9,12,13]. We also found two cases of *Serratia* osteomyelitis in recently-fractured vertebra [14].

Our patient was profoundly debilitated on admission at our hospital, and he had a respiratory tract infection. Later, he suffered from spondylodiscitis due to hematogenous dissemination of *S. marcescens* following TIPS device placement. Besides hospitalization he had other risk factors for acquiring *Serratia* infection, including prior antibiotic therapy, chronic-liver disease and an endovascular device. The definition of a TIPS device infection or endotipsitis is controversial; alternatives include sustained bacteremia in a patient with a TIPS device, with or without thrombus, plus either no other identifiable infective focus or an identifiable infective focus that is not considered to be the source of the bacteremia after intense investigation of endotipsitis characterization [15]. Although there was an identifiable infective focus (spondylodiscitis) for the bacteremia, the clinical outcome and the recurrent *Serratia* bacteremias lead us to believe that the source of the infection was colonization of the TIPS device, even though there were no signs of infection in the Doppler ultrasound exam. If the bacteremias provoke the spondylodiscitis process, we would expect worsening back pain and image symptoms each time they reoccur, which has not always been the case. Recurrent bacteremia is characterized by isolation of the same organism from the blood cultures after at least five days of appropriate antibiotic therapy [4]. Infection of a TIPS devices is rare; the estimated overall infection rate varies from 1.7 - 5.1% of the procedures performed; infection can occur several months or years after stent placement [15,16].

Removal of the intravascular device is the best recourse for management of recurrent bacteremias, but this approach is not achievable in some circumstances; this was the case for our patient, because TIPS surgical removal was not possible without liver transplantation. *Serratia marcescens* is resistant to ampicillin, macrolides and first-generation cephalosporins; treatment usually includes an antipseudomonal beta-lactam and an aminoglycoside [1,17]. Most strains are susceptible to

quinolones as well. Monotherapy with a beta-lactam is not advised because resistant mutants can be selected. Furthermore, cross-resistance to aminoglycosides can accompany beta-lactam resistance [4]. Multiresistant strains have been emerging during the last decades; therefore treatment should be based on susceptibility tests. In our case, imipenem was the first treatment choice, and it rapidly became the only option. Cefoxitin is known to be a potent beta-lactamase inducer; previous utilization can provoke cross resistance [4]. The patient was treated with imipenem for long periods, including 36 continuous weeks, followed by another 50 continuous weeks. Since the resistance pattern of this *Serratia* infection did not allow oral treatment, our patient had to remain hospitalized during long periods or had to go the hospital daily for intravenous antibiotic therapy.

In one of the largest published series of *Serratia* bacteremia (122 episodes during a 10-year period), imipenem gave the lowest resistance rate (0.87%), followed by amikacin (19.4%) and cefepime (22.6%) [4]. Nonetheless, beta-lactamase-mediated carbapenem resistance has been reported for many Gram-negative organisms, including *S. marcescens* [18,19].

Even though there is no consensus concerning the duration of antibiotic therapy in a spondylodiscitis process, we think that antimicrobial suppression should be continued for a long period.

We do not know if the lengthy antibiotic treatment period was sufficient to resolve the spondylodiscitis process or if it resulted in sterilization of a TIPS-device colonization process. However, we conclude that early diagnosis and aggressive treatment of spondylodiscitis are essential.

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