

Serratia Liver Abscess Infection and Cardiomyopathy in a Patient with Diabetes Mellitus: A Case Report and Review of the Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

EF 1 **Anna Sarah Erem**
E 2 **Anna Krapivina**
DE 3 **Timothy S. Braverman**
ADE 2 **Shyam S. Allamaneni**

1 Saba University School of Medicine, The Bottom, Saba, Dutch Caribbean
2 Department of Surgery, The Jewish Hospital – Mercy Health, Cincinnati, OH, U.S.A.
3 Department of Pathology, The Jewish Hospital – Mercy Health, Cincinnati, OH, U.S.A.

Corresponding Author: Anna Sarah Erem, e-mail: a.erem@saba.edu
Conflict of interest: None declared

Patient: Female, 45
Final Diagnosis: Serrata liver abscess with diabetes mellitus and cardiomyopathy
Symptoms: Anxiety • generalized weakness
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine

Objective: Rare co-existence of disease or pathology
Background: Liver abscesses remain difficult to diagnose and treat. Risk factors include diabetes mellitus, liver cirrhosis, and immunodeficiency. The majority are pyogenic, resulting from bacterial infection. Research identifies species in the *Serratia* genus as the cause of pyogenic liver abscesses in only 0.25% of cases and only 1 *Serratia* species in each case appears to have been identified. To the best of our knowledge, the present case report is the first to involve overlapping *Serratia* species in a single liver abscess infection that induced cardiomyopathy.





Case Report: A 45-year-old woman presented to our Emergency Department (ED) for severe generalized weakness. Initial test results indicated a diagnosis of microcytic anemia, hypomagnesemia, hypokalemia, hypocalcemia, hyperglycemia, type 2 diabetes mellitus, and severe heart failure. A computed tomography scan showed a 10-cm rim-enhancing fluid collection in the right hepatic lobe. Fluid drained from the suspected abscess tested positive for *Serratia marcescens* and *Streptococcus viridans*. The patient was treated with ceftriaxone and metronidazole, which she tolerated well. The abscess decreased to less than 9.8 mm. Twenty-one weeks after discharge, the patient received a cholecystectomy. Fluid drained from the residual abscess cultured positive for a different *Serratia* species, *S. odorifera*.

Conclusions: Diabetes mellitus and acute cholecystitis were key factors in the initial infections and abscess. We also suspect this is a rare case of cardiomyopathy induced by a *Serratia* infection. The source of the *Serratia odorifera* is less certain, as it postdates placement of a percutaneous drain, raising the potential for a nosocomial infection but not precluding the possibility that both *Serratia* species were previously present.

MeSH Keywords: Cholecystitis • Diabetes Mellitus, Type 2 • Heart Failure • Liver Abscess, Pyogenic • Serratia Infections

Abbreviations: LA – liver abscesses; PLA – pyogenic liver abscess; CGD – chronic granulomatous disease; PD – percutaneous drainage; ED – Emergency Department; Dm – diabetes mellitus; CT – computed tomography; IR – interventional radiology; EGD – esophagogastroduodenoscopy; GI – gastrointestinal

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Background

Liver abscesses (LA) remain a difficult problem to diagnose and treat. The majority are a result of bacterial infection [1]. In North America, the frequency of pyogenic LA (PLA) is low, with an overall incidence of 3.6 recorded cases per 100,000 population between 1994 and 2005 [2,3]. However, the incidence of PLA is increasing and has become associated with significant in-hospital mortality [3]. PLA presents with a classic triad of fever, upper right quadrant pain, and jaundice, and is fatal if left untreated [4]. Factors associated with the risk of developing LAs include diabetes mellitus (DM), liver cirrhosis, and immunodeficiency [1]. The risk of mortality increases with age and bacteremia [3], but it remains unclear whether surgical indications are associated with increased mortality [3,5]. The major causative organisms of PLA are *Streptococcus* (29.5%), *Escherichia* (18.1%), *Staphylococcus* (10.5%), *Klebsiella* (9.2%), *Anaerobes* (8.6%), and *Pseudomonas* (3.1%) [2]. Over a 10-year study period, *Serratia* was identified as the cause of PLA in just 0.25% of cases (about 20 of 8286 cases) [2].

Serratia was not recognized as a pathogenic bacteria species until the mid-to-late 20th century. It was infamously used as a tracer microorganism by the United States military between the 1940s and 1960s because of its reddish-orange hue [6]. In a European survey performed between 2008 and 2012, *Serratia* infections accounted for 2.2% of all ICU-acquired bloodstream infections [7], and in the SENTRY Antimicrobial Surveillance Program in the United States between 2009 and 2011, it accounted for 6.0% and 4.0% of ICU and non-ICU bloodstream infections, respectively [8]. At least 14 species of *Serratia* have been identified [6]. In Canada, most isolates are *Serratia marcescens* [9], but many hospitals did not even begin specifying which *Serratia* species they had isolated in their analyses until 2011 [7]. Documented health conditions associated with *S. marcescens* infections include some that are also associated with LAs, such as DM, immunodeficiency, and alcoholism (cirrhosis) [10]. Other commonly associated conditions are cancer, burns, and corticosteroid therapy [10]. There are a few case reports of different *Serratia* species involved in PLA, particularly in immunocompromised individuals [11,12] and in those with genetic immune deficiencies such as chronic granulomatous disease (CGD) [13,14]. However, there were none we could find that describe a PLA associated with *Serratia odorifera*. *Serratia* infections have also been reported in other organs, such as the lungs [15], skin [16], and the central nervous system [17]. Here, we discuss a rare case of a 45-year-old woman with type 2 DM with severe cardiomyopathy and a PLA positive for *Serratia marcescens*, *Streptococcus viridans*, and *Serratia odorifera*. She was treated by percutaneous drainage (PD), surgery, and a combination of intravenous and oral antibiotics.

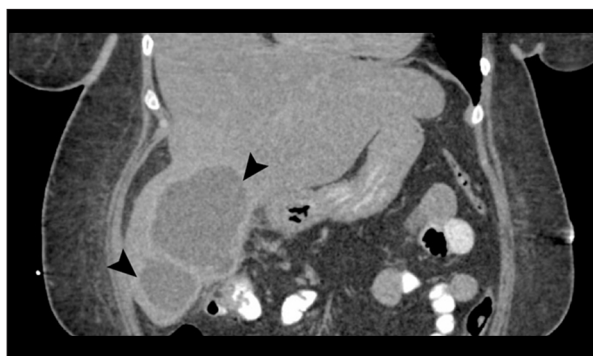


Figure 1. CT scan showing multiloculated abscess, arrows point to abscess.

Case Report

A 45-year-old woman with a history of hypertension, chronic migraines, mild anxiety, and no recent medical interventions was referred to our ED for an anemia workup. She reported increased thirst, weakness, and dyspnea for the past 7–10 days. She had dry skin on her feet and hands, and reported numbness and tingling in her lower extremities, feet, and both hands. Otherwise, her physical exam was generally unremarkable. The patient's vital signs were: blood pressure of 156/87; pulse of 91 beats per minute; body temperature of 98.2°F (36.8°C); respiration rate of 15 breaths per minute; SpO₂ 93%; and a BMI of 40.06 kg/m². She denied fever, chills, nausea, vomiting, diarrhea, melena, vaginal bleeding, dysuria, polyuria, and chest pain. The patient reported minimal alcohol use and denied smoking. There were no indications of intravenous drug use or other high-risk behaviors.

Initial ED laboratory test results indicated that she had anemia (HGB 7.7 g/dL) with microcytosis (microcytic anemia), hypomagnesemia (0.7 mEq/L), hypokalemia (3.3 mEq/dL), hypocalcemia (5.7 mg/dL), and hyperglycemia (255 mg/dL). Type 2 diabetes mellitus (DM) with increased blood sugars (HbA1c 12.2%) due to severe illness and infection was also diagnosed. The patient was not being treated for DM at the time she was admitted. In addition, blood test results revealed that she had elevated homocysteine levels, hypoalbuminemia, elevated alkaline phosphatase levels, and thrombocytosis. Initial laboratory results also indicated low serum concentrations of iron, folic acid, vitamin D, and vitamin B12. She also had severe heart failure with an ejection fraction of 20–25% and a mild left ventricular dilation. A coronary angiogram indicated nonischemic cardiomyopathy. She also reported a significant unintentional weight loss of 40 lbs (18.1 kg) over the last 2 years, so a computed tomography (CT) scan was performed to rule out any malignancies. An infection was not suspected until this point, as she was not showing a fever or elevated white blood cell count. A CT scan showed a 10-cm rim-enhancing fluid collection centered in the right hepatic lobe, originating from the region of the gallbladder fossa

Table 1. *Serratia* isolate sensitivities.

Antibiotic	<i>Serratia marcescens</i>	<i>Serratia odorifera</i>
Amoxicillin-clavulanate	Resistant	Resistant
Ampicillin	Resistant	Resistant
ceFAZolin	Resistant	Resistant
cefepime	Sensitive	Sensitive
cefTRIAXone	Sensitive	Sensitive
Ciprofloxacin	Sensitive	Sensitive
Gentamicin	Sensitive	Sensitive
Levofloxacin	Sensitive	Sensitive
Meropenem	Sensitive	Sensitive
Piperacillin-tazobactam	Sensitive	Sensitive
Trimethoprim-sulfamethoxazole	Not Tested	Sensitive

and extending inferiorly. This was interpreted as a multiloculated abscess, possibly a result of complicated cholecystitis (Figure 1).

At this time, she was started on a course of vancomycin, meropenem, and metronidazole (she was allergic to ciprofloxacin). A PD guided by interventional radiology (IR) was placed in the abscess, yielding 192 ml of pale green, foul-smelling purulent fluid. This fluid culture tested positive for *Serratia marcescens* and *Streptococcus viridans*. The Infectious Disease team was consulted, and they recommended continuing the patient on meropenem as a longer-term antibiotic with a plan to switch her to ceftriaxone and metronidazole. The *Serratia* isolate sensitivities are summarized in Table 1.

An abdominal ultrasound (US) indicated diffusely increased hepatic echogenicity, consistent with fatty infiltration. Intrahepatic fluid collection via percutaneous catheter was observed adjacent to the gallbladder fossa. It was difficult to distinguish the collapsed gallbladder from the collection site, but there was evidence of cholelithiasis. An esophagogastroduodenoscopy (EGD) recommended by GI on suspicion of malabsorption was performed and the results were unremarkable. Seven days after initial admission, the patient was discharged on IV ceftriaxone along with oral metronidazole. At that time her LA, hypoglycemia, hypokalemia, and anemia were all improving. For her newly diagnosed diabetes, the patient was prescribed insulin on a sliding scale and was given DM counselling by the home health nurse. The patient returned 2 weeks later for a consultation and had the PD removed. At the time of the follow-up consultation, the patient had tolerated the antibiotic medications well with no

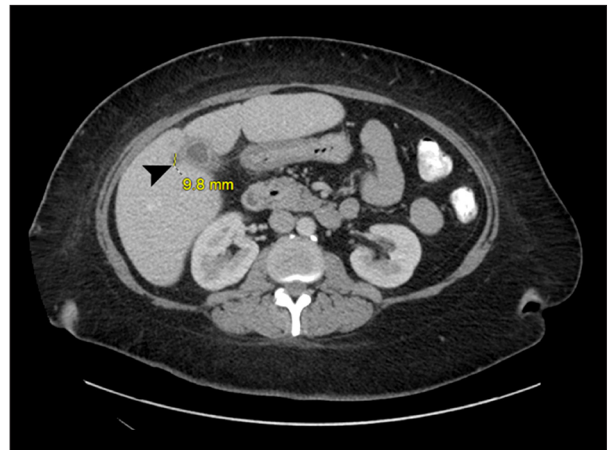


Figure 2. CT scan shows nearly resolved abscess 27 days after discharge, reduced from 10 cm to 9.8 mm in size.

major adverse effects. A follow-up CT scan performed 27 days after discharge showed near resolution of the hepatic abscess, which had reduced in size to approximately 9.8 mm (Figure 2).

At a 3-month follow-up appointment, an echocardiogram (ECHO) showed normal ventricular function. Twenty-one weeks after discharge, the patient underwent an interval cholecystectomy, performed robotically. An intra-operative US demonstrated an intrahepatic residual abscess (approximately 1×1×3 cm) located deep in the gallbladder fossa. The gallbladder itself was densely adherent to the cystic plate. After it was dissected away from the plate, the abscess was unroofed, and a small amount of serous fluid was evacuated. The fluid was sent for culture and, interestingly, the specimen revealed a different species of *Serratia*, *S. odorifera*. The cholangiogram revealed no filling defects, an intact biliary tree, and free flow of the contrast into the duodenum. The patient tolerated the procedure well, with no complications. At a 3-week follow-up after surgery, she reported that her energy level was much better. At her 3-month follow-up visit, she reported that she was feeling normal.

Discussion

Generally inhabiting aquatic or soil environments, *Serratia* is a gram-negative rod-shaped bacterium with at least 14 different related species. It is the 10th most common isolate in bloodstream infections found in the ICU. Case reports of pathogenicity have been reported in all but 2 species – *S. glossinae* and *S. nematodiphila* – which inhabit the tsetse fly *Glossina palpalis gambiensis* and the nematode *Heterorhabditoides chongmingensis*, respectively. *Serratia marcescens* is the most frequently observed isolate, but other species, such as *S. liquefaciens*, *S. ficaria*, and *S. odorifera*, are commonly reported in blood, urine, wound, and sputum cultures. First described as a new species by Grimont in 1978 [18], *S. odorifera* is divided into 2 biovars

(1 and 2) and has a very distinct potato-like odor. *S. odorifera* has been identified in infections of the respiratory tract as well as in blood, bile, and open wounds [19]. The species is known to cause sepsis, with significant morbidity, and is associated with high mortality rates in neonates and patients with compromised immune systems [20]. *Serratia* species are commonly associated with catheter-related bloodstream infections, in secondary bloodstream infections of the urinary and digestive tracts, infections after surgery, pneumonia, and nosocomial outbreaks attributed to non-sterilized medical supplies.

However, liver abscesses associated with *Serratia* infections are relatively rare (Table 2), and all cases documented here, excluding the one described by Balakrishna and his colleagues [21], include known risk factors for liver abscesses, *Serratia* infections, or both. This includes our patient, whom as a result of her diabetes, was immunocompromised, which made her predisposed to liver abscesses. The association between DM and infections caused by Enterobacteriaceae (of which *S. marcescens* is a member) was documented in a large series of 1317 Danish patients from 1992 to 2001 [27]. The authors found that the risk of bacteremia infection was higher in adults less than 65 years old and higher in female patients. They also concluded that 10% of enterobacterial infections might be the result of diabetes. DM has also been shown to be a predisposing factor for LAs; in fact, some studies indicate it as a concomitant condition in as many as 29.3–44.3% of LA cases [1,28,29]. Certain DM features, such as hyperglycemia, have been indicated as major factors contributing to higher risk of infection [1,30]. We could not determine whether *S. marcescens* was an opportunistic colonizer of the *Streptococcus*-induced hepatic abscess or vice-versa, but the patient responded well to PD and intravenous antibiotics followed by a prolonged course of oral antibiotics. Multiple liver abscesses were reported in the case of a 48-year-old Japanese man infected by *S. rubidaea* working in a fresh fish store [12]. His immune system was likely compromised due to a clinical history of alcoholic hepatitis and alcohol-induced chronic pancreatitis. Grieco et al. (1973) also found several small abscesses in a 32-year-old man who presented with stomach ulcers and a history of alcoholism [26]; his blood cultures were positive for *S. marcescens*, but *Pseudomonas aeruginosa* was also recovered from the PLA. In the treatment of pancreatic cancer in a 69-year-old Japanese woman, a single PLA formed as a result of an indwelling percutaneous transhepatic cholangio-drainage tube placed next to the left hepatic duct [11]. *S. marcescens* was detected in the fluid of an upper abdominal subcutaneous abscess and the PLA. The author's postulated that the drainage tube could have spread the infection from the abdominal abscess to the PLA. Treatment with ciprofloxacin slightly reduced the size of the PLA, but her systemic conditions deteriorated, and she died. The exact cause of death was unknown because the patient's family would not permit

an autopsy. In a 59-year-old Italian-American man, a sub-hepatic abscess developed after a laparoscopic cholecystectomy, and *S. ficaria* was detected in blood cultures. This species is specifically associated with figs, fig trees, and the fig pollinator wasp [22]. The man reported trimming a fig tree 2 months before his initial illness. This coincided with the time period during which fig wasps pollinate female fig trees. In this case it appears that *S. ficaria* may have been an opportunistic colonizer of the abscess that developed after a cholecystectomy. Another recent case report documented the occurrence of a PLA in an immunocompetent 42-year-old Indian man [21]. He had high-grade fever for 10 days, was treated with oral antibiotics, and sent home, but he returned a few days later with high fever, leukocytosis, and localized abdominal tenderness. Although blood and urine cultures were sterile, aspirate from the PLA revealed an *S. Grimesii* infection that was successfully treated with a combination of piperacillin and tazobactam over a 2-week period. In our case, the origin of the *Serratia* infection was less clear. Our patient did not have preceding surgical interventions or cirrhosis (commonly associated with *S. marcescens* infections). She was, however, diagnosed with DM, which is commonly associated with PLAs [1] and *S. Marcescens* infections [10]. Our patient was also diagnosed with cholecystitis. Although rare, there are cases in the literature of suspected community-acquired *Serratia* infections directly related to cholecystitis [31,32].

Lastly, we suspect that our patient's cardiomyopathy was the result of several factors, including her unmanaged diabetes, electrolyte abnormalities, and *Serratia* infection. Uncontrolled chronic diabetes is commonly associated with electrolyte abnormalities such as hypokalemia, hypomagnesemia, and hypocalcemia [33,34]. Hypomagnesemia in diabetics can be caused by low dietary Mg²⁺ intake [33,34] and can also be associated with hypoalbuminemia, which was observed in our patient [33]. Hypomagnesemia in critically ill patients can further be exacerbated by infection [35], such as our patient's PLA infection. The vitamin D deficiency, hypoalbuminemia, and hypomagnesemia observed in our patient can worsen hypocalcemia in diabetic patients [33]. A 2018 case report linked electrolyte abnormalities, including hypokalemia, hypomagnesemia, and hypocalcemia, to cardiomyopathy [36]. The cardiomyopathy was readily ameliorated by electrolyte supplementation [36]. The relationship between infection and cardiomyopathy was discussed by Patel et al in a 2015 review [37]. The infectious causes of cardiomyopathy were predominantly viral, but less common bacterial pathogens have also been implicated [37]. In another 2015 review, 14 cases of cardiomyopathy were linked to bacterial infection. Of the cases where the strains were identifiable, 57.1% were gram positive and 42.9% were gram negative [38]. We were unable to find any cases described in the literature in which cardiomyopathy was induced by a *Serratia* infection.

Table 2. *Serratia* and liver abscess literature search results.

First author	Date	Age/sex	Liver abscess	Pathogens	Underlying conditions	Treatment (duration)	Outcome	Suspected cause of infection
Balakrishna [21]	2018	42/M	Yes	<i>Serratia grimesii</i>	None described	Piperacillin, Tazobactam (11 days)	Discharged in stable condition	None speculated
Khattou [13]	2018	2/F	Yes (multiple)	<i>Serratia marcescens</i>	CGD, Hx of respiratory infections, hyperleukocytosis, immunocompromised	Ceftriaxone + Gentamicin + Metronidazole (not reported)	Good progress, being treated for CGD	CGD
Hashemi [22]	2016	59/M	Sub-hepatic abscess	<i>Serratia ficaria</i>	Cholecystitis, cholecystectomy, renal stone	Ciprofloxacin & ertapenem (4 weeks & several weeks)	Discharged, re-admitted extra drainage required, eventually made excellent recovery	Infection from trimming a fig tree, plus surgery
Watanabe [11]	2005	69/F	Yes	<i>Serratia marcescens</i>	Pancreatic head cancer, subcutaneous abscess, immune compromised	Ciprofloxacin (13 days)	Recovered, afebrile, abscess reduced from 10–8 cm, her condition later worsened, and she died	Suspect infection resulted from drainage tube placement
Lee [23]	2005	57/M	No	<i>Serratia odorifera</i> 1	Chronic alcoholic liver disease, chronic hepatitis C, paranoid schizophrenia, chronic bronchitis, history of injection drug use	ticarcillin, tobramycin (48 h), ticarcillin/clavulanate (21 days)	Patient did well and was discharged	Community, patient had <i>S. odorifera</i> 1, bacteremic pneumonia, port of entry could have been lungs
Herman [14]	2002	1 day/M	Yes (multiple)	<i>Serratia marcescens</i>	CGD, pneumonitis, immune compromised	Undefined Antibiotics	Lesions were resolved	CGD
Okada [12]	2001	48/M	Yes (multiple)	<i>Serratia rubidaea</i>	Alcoholic hepatitis, calcified pancreatitis, diabetes, immune compromised	SBT/CPZ and TOB, dopamine (115 days)	Afebrile, liver/kidney function, improved, discharged 4 months later, ambulatory	Either endogenous infection in an immune compromised host or oral ingestion, patient worked in fresh fish store

Table 2 continued. *Serratia* and liver abscess literature search results.

First author	Date	Age/sex	Liver abscess	Pathogens	Underlying conditions	Treatment (duration)	Outcome	Suspected cause of infection
Cook [24]	1998	73/F	No	<i>Serratia odorifera</i> 1	Diabetes, thrombocytopenic purpura, chronic renal failure, diabetes, cirrhosis, nephrectomy, surgery 30 years ago for benign tumor	Diabetes, thrombocytopenic purpura, chronic renal failure, diabetes, cirrhosis, nephrectomy	Patient died 9 days later due to gram negative urosepsis	Community-acquired, portal of entry suspected to be urinary tract, patient susceptible due to underlying cirrhosis
Chmel [25]	1988	67/M	No	<i>Serratia odorifera</i>	Cirrhosis, hepatorenal syndrome, hepatic encephalopathy, gastrointestinal tract bleeding	Amikacin, cefoxitin	Patient improved with 48 h	Community-acquired, source unknown, patient susceptible due to underlying cirrhosis
Grieco [26]	1973	32/M	Yes (multiple)	<i>Serratia marcescens</i> , <i>Pseudomonas aeruginosa</i>	Melena, increased alcohol consumption, urticarial reaction to penicillin, gastrectomy, gastrojejunostomy	Gentamicin & polymyxin B/185 days & 84 days	Drainage ceased after more than 185 days	Portal vein bacteremia, multiple surgeries

Conclusions

The risk factors for liver abscesses include DM and a compromised immune system, both of which were present in our patient. Our literature search identified 7 cases of PLA associated with *Serratia* infection, 3 cases of *Serratia odorifera* infections associated with chronic liver disease, and 2 cases that establish a potential link between cholecystitis and *Serratia* infections. From this data we conclude that DM and cholecystitis were key contributing factors in the original liver abscess infection. We suspect that this *Serratia* infection was a major etiological factor of the nonischemic cardiomyopathy in a patient compromised by uncontrolled DM. The source of the *Serratia*

odorifera is less certain than that of the *Serratia marcescens*. It postdates the placement of a percutaneous drain, raising the potential for a nosocomial infection. However, this does not preclude the possibility that both species of *Serratia* were present when the patient originally presented.

Acknowledgements

We would like to thank the dedicated staff at the Jewish Hospital – Mercy Health. Special thanks also to Beth Wayne, Clinical Research Educator at the Jewish Hospital, for proof reading this manuscript and Lisa McCormick, Manager of the Health Science Library, for help finding and retrieving literature.

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