

Egads It's Enterobacteriaceae: *Serratia rubidaea* Urinary Tract Infection & *Enterobacter aerogenes* Bacteremic Urinary Tract Infection

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Abstract

We present the 3rd known case of a *Serratia rubidaea* urinary tract infection in a 49-year-old male with past medical history of bilateral lower extremity paraplegia who presented to the emergency room with fever, lethargy, and red tinted urine. The *Serratia* genus, of the family *Enterobacteracia*, in particular the species *Serratia marcescens*, are important causes of infection in humans, animals, and insects, however, until the mid-1950s, this was not the case, and the organism was considered non-pathogenic and frequently used in medical experiments. *Serratia* are facultatively anaerobic, gram-negative rods, the majority with peritrichous flagella primarily inhabiting soil, water, and plant surfaces. *Serratia marcescens* is now a known pathogen, however, less frequently isolated species, including *Serratia rubidaea*, are worthy of discussion, especially due to its characteristic red color and rarity. We aim to increase the awareness *Serratia rubidaea* including its presentation, inherent antimicrobial resistance, and treatment options.

Keywords

Urinary Tract Infection, Enterobacteracia, *Serratia rubidaea*, *Serratia marcescens*, Prodigiosin, Bacteremia

1. Introduction

The *Serratia* genus, of the family *Enterobacteracia*, in particular the species *Serratia marcescens*, are important causes of infection in humans, animals, and insects, however, until the mid-1950s, this was not the case, and the organism was thought to be non-pathogenic and frequently used in medical experiments. They

are facultative anaerobic, gram-negative rods, the majority with peritrichous flagella primarily inhabiting soil, water, and plant surfaces [1]. *Serratia species* (*Serratia spp.*) currently have been associated with a full spectrum of clinical pathology, including urinary tract infections, pneumonia, wound infections, skin and soft tissue infections, bacteremia, surgical site infections and endocarditis [2].

Serratia marcescens is now an accepted clinical pathogen, however, less frequently isolated species, including *Serratia rubidaea* (*S. rubidaea*), are worthy of discussion. The *Serratia* genus is historically intriguing from its discovery to its use in numerous medical as well as military experiments including its use by the United States military as a tracer organism to monitor biological warfare, between the 1940s and 1960s. This was brought to light by the media in the 1970s, and subsequently led to a congressional investigation on the United States government's use of microorganisms on the public [3].

Serratia was originally discovered in 1819 by the Italian pharmacist Bartolomeo Bizio while investigating red-colored polenta, and his data was subsequently published in 1823. However, it was not until 1980, after numerous publications, classifications, and reclassifications that *Serratia marcescens* was officially named and accepted [3]. Currently, as of 2021, there are 23 accepted strains of *Serratia*, of which *Serratia rubidaea* is one [4].

Serratia rubidaea was originally described in 1940 as *Bacterium rubidaeum* and then reclassified as a *Serratia* species in 1973. Finally in 1980, it was officially listed as *Serratia rubidaea* after the scientific community determined a similar organism, *Serratia marinorubra*, discovered in 1944, was without difference. Its name is a contracture of the scientific name for the raspberry plant, *Rubus idaeus*, owing to its red pigment, a function of the prodigiosin, a secondary metabolite of certain *Serratia* species which led to the red discoloration discussed above. Three other strains of *Serratia* also produce this pigment, including *Serratia marcescens*, *Serratia plymuthica*, and *Serratia nematodiphila*, as do other Gram-negative bacteria, including *Pseudomonas magnesorubra* and *Vibrio psychroerythreus* [3].

While *Serratia rubidaea*, has been isolated from the respiratory tract, blood, wound cultures, and bile of human specimens, documentation of frank infection is rare. Current literature shows rare occurrences of bacteremia, urinary tract infections as well as an episode of endophthalmitis. Our objective in this case report is to bring more attention to the *Serratia spp.*, and especially the less reported subtypes including *Serratia rubidaea*. In doing so, we hope to increase knowledge of this organism, its presentation, and its treatment [3].

2. Case Presentation

Informed consent was obtained from the patient in writing regarding research and publication of this report.

We present the 3rd known case of *Serratia rubidaea* urinary tract infection in

a 49-year-old male, with a past medical history of spinal cord injury due to gunshot wound, with associated bilateral lower-extremity paraplegia, and persistent hypotension on midodrine, who presented to the emergency room complaining of several days of insomnia, fatigue, and lethargy [5] [6]. Additionally, the patient complained of orange-red colored urine, as well as decreased urine output. At baseline, the patient has difficulty voiding and uses a condom catheter and ambulates with a motorized assistance device.

Initial vitals on admission showed an elevated temperature of 102.1 degrees Fahrenheit, tachycardia, hypotension, and oxygen saturation of 98% on 2 liters nasal canula. Laboratory values showed leukocytosis with left shift, hyponatremia, elevated creatinine, lactic acidosis and troponemia (Table 1). Urinalysis was remarkable for orange color and turbid appearance as well the presence of bacteria, white blood cells, and positive leukocyte esterase (Table 2). Computerized tomography (CT) scanning of the kidneys showed two right sided, non-obstructing,

Table 1. Initial vitals & laboratory values.

INITIAL VITALS	
Temperature (°F)	102.1
Pulse (bpm)	115
Blood Pressure (mmHg)	74/53
Oxygen saturation (SpO ₂)	98% on 2 liters nasal canula
LABORATORY VALUES	
<i>Complete Blood Count</i>	
White Blood Cells (K/mm ³)	18.5
Absolute Neutrophils (K/mm ³)	16.6
Hemoglobin (GM/dL)	14.3
Hematocrit	40.8
Platelets (10 ³ /uL)	257
<i>Basic Metabolic Panel & Additional Values</i>	
Sodium (mmol/L)	126
Potassium (mmol/L)	3.3
Chloride (mmol/L)	92
Carbon Dioxide (mmol/L)	20
Blood Urea Nitrogen (mg/dL)	22
Creatinine (mg/dL)	2.0
Lactic Acid (mmol/L)	2.8
Troponin (ng/mL)	3.01

Legend: °F—Degrees Fahrenheit; BPM—beats per minute; mmHg—millimeters of mercury; SpO₂—peripheral capillary oxygen saturation measured by pulse oximetry; K/mm³—thousand per cubic millimeter; GM/dL—grams per deciliter; 10³/uL—thousand cells per microliter; mmol/L—millimoles per liter mg/dL—Milligrams per deciliter; ng/mL—Nanograms per milliliter.

Table 2. Urinalysis, urine culture & blood culture.

MICROBIOLOGY	
<u>Urinalysis (Straight Catheterization)</u>	
Color	Orange
Appearance	Turbid
Urine pH	6.0
Urine Protein	2+
Urine Glucose	Negative
Urine Ketones	Negative
Urine Blood	3+
Urine Nitrite	Negative
Urine Bilirubin	Negative
Urine Leukocyte Esterase	3+
Urine WBC (WBC/ μ L)	7008
Urine RBC (RBC/ μ L)	53
Urine Bacteria (Bact/ μ L)	7336
<u>Urine Culture (Straight Catheterization)</u>	
	Organism 1: <i>Serratia rubidaea</i> —100,000 CFUs
	Organism 2: <i>Enterobacter aerogenes</i> —20,000 - 30,000 CFUs
<u>Blood Culture (Peripheral Venous)</u>	
	<i>Enterobacter Aerogenes</i>

Legend: WBC/ μ L—white blood cells per microliter; RBC/ μ L—red blood cells per microliter; Bact/ μ L—bacteria per microliter; CFUs—colony forming units.

renal calculi measuring 12 millimeters (mm) and 4.4 mm without evidence of hydronephrosis (**Figure 1, Figure 2**). Fluid resuscitation with normal saline was started immediately, blood and urine cultures were drawn, and empiric antibiotic coverage with piperacillin/tazobactam and vancomycin was administered.

On day two, both blood and urine samples grew gram negative, lactose fermenting bacilli, vancomycin was discontinued at this time. On day four, urine cultures returned positive for *Serratia rubidaea* 100,000 colony forming units (CFUs) as well as *Enterobacter aerogenes* 20,000 - 30,000 colony forming units. Blood cultures returned positive in both bottles for *Enterobacter aerogenes*. At this time, all previously abnormal laboratory values had normalized, and the patient was afebrile and normotensive.

Sensitivities for *Enterobacter aerogenes*, in both blood and urine, came back with resistances to ampicillin, ampicillin-sulbactam, cefazolin, ceftriaxone and cefuroxime. Sensitivities to *Serratia rubidaea*, returned positive with resistances to the same, except it had intermediate susceptibility to ampicillin-sulbactam, and not full resistance (**Table 3, Table 4**).

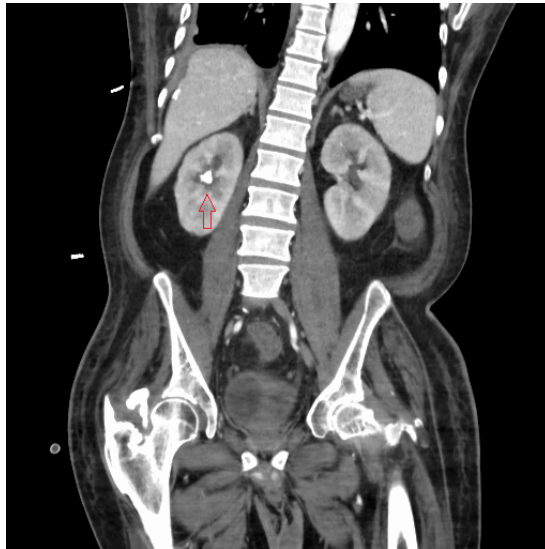


Figure 1. CT Scan Abdomen & Pelvis—Coronal View showing 12 mm non-obstructing right upper pole renal calculi (red arrow).



Figure 2. CT Scan Abdomen & Pelvis: Coronal View showing 4.4 mm non-obstructing right lower pole renal calculi (red arrow).

Table 3. Urine cultures & antibiotic sensitivities.

Urine Culture	<i>Serratia rubidaea</i>		<i>Enterobacter aerogenes</i>	
	Susceptibility	MIC	Susceptibility	MIC
Amikacin	S	<16	S	<16
Ampicillin	R	>16	R	>16
Ampicillin/Sulbactam	I	16/8	R	>16/8
Aztreonam	S	<4	S	<4
Cefazolin	R	>16	R	>16
Cefotaxime	S	8	S	8

Continued

Ceftazidime	S	4	S	4
Ceftriaxone	R	8	R	32
Cefuroxime	R	>16	R	16
Ertapenem	S	<1	S	<1
Gentamicin	S	<4	S	<4
Imipenem	S	<1	S	<1
Levofloxacin	S	<2	S	<2
Meropenem	S	<1	S	<1
Nitrofurantoin	S	<32	S	<32
Piperacillin/Tazobactam	S	<16	S	<16
Tigecycline/Tygacil	S	<2	S	<2
Tobramycin	S	<4	S	<4
Trimethoprim/Sulfamethoxazole	S	<2/38	S	<2/38

Legend: MIC—Minimum inhibitory concentration.

Table 4. Blood cultures and antibiotic sensitivities.

Blood Culture	<i>Enterobacter aerogenes</i>	
	Susceptibility	MIC
Amikacin	S	<16
Ampicillin	R	>16
Ampicillin/Sulbactam	R	16/8
Aztreonam	S	<4
Cefazolin	R	>16
Cefepime	S	<4
Cefotaxime	S	8
Ceftazidime	S	4
Ceftriaxone	R	8
Cefuroxime	R	16
Ertapenem	S	<1
Gentamicin	S	<4
Imipenem	S	<1
Levofloxacin	S	<2
Meropenem	S	<1
Piperacillin/Tazobactam	S	<16
Tigecycline/Tygacil	S	<2
Tobramycin	S	<4
Trimethoprim/Sulfamethoxazole	S	<2/38

Legend: MIC—Minimum inhibitory concentration.

The patient continued to receive piperacillin-tazobactam every 6 hours for a total of 14 days in hospital. Vancomycin was discontinued after two doses. Repeat blood cultures were negative, and the patient remained afebrile. Subsequently, he was discharged on an additional 3 days of trimethoprim-sulfamethoxazole twice a day. Unfortunately, the patient never presented to our clinic for outpatient follow-up.

3. Discussion

Urinary tract infections (UTIs) are the 3rd most prevalent type of infections in human medicine behind respiratory and gastrointestinal infections and are a significant source of morbidity both inpatient and outpatient. The most common causative organisms are from the *Enterobacterales* order, including the genus *Escherichia* and *Klebsiella*. Notably however, less commonly isolated organisms from the genus *Citrobacter*, *Enterobacter* and *Serratia* are seen with more complicated UTIs, including those involving catheters and functional or anatomic defects in the genitourinary tract. Furthermore, these infections are more frequently associated with pyelonephritis, recurrence, and prolonged therapy in large part due to their antibiotic resistance which is discussed below [7].

The genus *Serratia* of the family *Enterobacteriaceae*, are facultatively anaerobic, gram-negative rods, the majority with peritrichous flagella, primarily inhabiting soil, water, and plant surfaces. They have been implicated in pneumonias, intravenous catheter-associated infections, urinary tract infections, osteomyelitis, and endocarditis [1]. As of 2021, there are 23 identified *Serratia* species of which *Serratia rubidaea* is one [4]. Of the *Serratia* species, *Serratia marcescens* is by far the most clinically isolated. One large, multi-year study of *Serratia* borne infections showed that 92% of infections were caused by *Serratia marcescens*, 4% by *Serratia liquifaciens*, 1% by *Serratia odorifera*, 1% by *Serratia rubidaea*, and 2% non-speciated or speciated but of insignificant amount [8].

The *Serratia* species utilize several virulence factors including DNase, lipase, gelatinase, hemolysin, proteases, chitinase, chloroperoxidase, as well as multiple isozymes of alkaline phosphatase. Additionally, they produce a red pigment named prodigiosin as well as biosurfactants and biofilms [9]. Last, further complicating their nature and increasing their threat, *Serratia spp.* are intrinsically resistant to ampicillin and amoxicillin with or without the presence of β -lactamase inhibitors, as well as first-generation cephalosporins, macrolides, nitrofurantoin, and colistin [10]. It is noted that the *Serratia rubidaea* which grew in our patient's urine culture was sensitive to nitrofurantoin, however at high minimum inhibitory concentrations (MIC) (Table 3).

As previously discussed, *Serratia rubidaea*, is one of four *Serratia* species which produce prodigiosin, a secondary metabolite which causes a red discoloration and is closely associated with the species [11]. Among the *Serratia* species, *S. rubidaea* is infrequently clinically isolated, and as of this writing, has only been cultured twice in the setting of a urinary tract infection. The first instance was in

a 36-year-old paraplegic male in 2006, and the second, a 40-year-old diabetic female in 2016, demonstrating a seeming prevalence for anatomic or immunocompromised individuals [5] [6].

Our patient is a 49-year-old male, with a past medical history of spinal cord injury due to gunshot wound, with associated bilateral lower-extremity paraplegia who used condom-catheters to aid in micturition. He presented to the hospital with fever, lethargy and orange-red colored urine and was found to have bacteriuria with both *Serratia rubidaea* (>100,000 CFUs), as well as *Enterobacter aerogenes* (20,000 - 30,000 CFUs). Additionally, he was found to be bacteremic with *Enterobacter aerogenes*. The literature is clear that spinal cord injury is associated with UTIs due to its effect on the genitourinary system [12]. Our patient used external “condom” catheters, which have a lower infection rate than traditional urethral catheters, however, are still prone to infection, especially with frequent manipulation [13] [14]. We postulate both his functional anatomic changes, as well as his use of external catheters may have played a role in his infection with this organism. In this case, it was of utmost importance to treat the patient empirically with broad-spectrum antibiotics until cultures were speciated and sensitivities returned, due to his risk factors for infection, and *Serratia rubidaea*'s intrinsic resistance to multiple antibiotics.

4. Conclusion

Serratia marcescens is now a known cause of pathogenicity in humans, however, new *Serratia* species continue to be identified, and adding to the literature is essential to document their potential morbidity. This is the 3rd reported case of a urinary tract infection from *Serratia rubidaea*, and the 2nd in a paraplegic individual. Its unique antibiotic resistance patterns, as well as likely requirement for inpatient treatment make it a critical organism to treat empirically if clinical suspicion warrants, especially when presented with its characteristic red pigment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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