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***Serratia fonticola* and its role as a single pathogen causing emphysematous pyelonephritis in a non-diabetic patient: A case report**

Villasuso-Alcocer V *et al.* Emphysematous pyelonephritis due to *Serratia fonticola*

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## Abstract

### BACKGROUND

Diagnosis of emphysematous pyelonephritis has been described around the world for some decades, frequently associated with *Escherichia coli* and other anaerobic, gas-forming bacteria and mostly in patients living with diabetes. We present a case report of emphysematous pyelonephritis in a non-diabetic patient caused by *Serratia fonticola*, as well as a brief literature review to draw attention to this rare pathogen as a cause of pyelonephritis.

### CASE SUMMARY

A 38-year-old female presenting fever, severe pain in the right flank and changes in urinary habits. She was admitted and emphysematous pyelonephritis was confirmed by an abdominal computerized tomography and urine cultures; the latter showed *Serratia fonticola* as a single pathogen. After three days of being treated with piperacillin/tazobactam and percutaneous drainage she became afebrile, and the gas presence reduced.

### CONCLUSION

Emphysematous pyelonephritis infections in non-diabetic patients are rare but can be severe and life-threatening. This case suggests that *Serratia fonticola* infection can occur in patients undergoing invasive or instrumented procedures.

**Key Words:** *Serratia fonticola*; Emphysematous pyelonephritis; Urinary tract infections; Nephrolithiasis; Case report

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**Core Tip:** *Serratia fonticola* may still be as a rare human pathogen, either associated to asymptomatic conditions or merely a bystander among other agents, but its incidence may relate to severe cases when patients undergo invasive, instrumented procedures or underlying conditions, as presented in the case of the female who developed emphysematous pyelonephritis we here presented.

## **INTRODUCTION**

Severe necrotizing infection caused by anaerobic, gas-forming bacteria in renal parenchyma generates a condition known as emphysematous pyelonephritis (EPN), frequently linked to *Escherichia coli* (*E. coli*)<sup>[1,2]</sup>.

It has been stated that even when agent-related virulence factors, along with the underlying health condition of patients, may predispose them to emphysematous pyelonephritis, diabetes mellitus with poor glycemic control has been independently associated with the odds of developing EPN<sup>[3]</sup>. Furthermore, evidence in *E. coli* urinary tract infections suggests that insulin treatment in infected patients with diabetes may downregulate infection, which is congruent with the role of glycemic control in EPN in urinary tract infections<sup>[4]</sup>.

EPN is an unusual condition originally associated with patients with diabetes mellitus<sup>[5,6]</sup> and commonly reported in single clinical case reports although also more recently in at least one systematic review with meta-analysis<sup>[6]</sup>. The present communication is aimed at providing insights into a case where a non-diabetic patient developed EPN due to a *Serratia fonticola* (*S. fonticola*) infection, and the clinical manifestations derived from the pyelonephritis caused by this uncommon agent.

## **CASE PRESENTATION**

### ***Chief complaints***

A 38-year-old illiterate housewife from rural southeast Mexico, with bilateral urolithiasis attended a urology consultation at a highly specialized public hospital in Yucatan Mexico, as she had had a fever between 38 °C and 40 °C for the previous two days,

accompanied by severe pain in the right flank irradiated to the ipsilateral suprapubic region, and reported changes in frequency and quality of urination.

#### ***History of present illness***

She was admitted for in-hospital care and abdominal computerized axial tomography was performed, along with blood and urine tests, including cultures. Tomography indicated the presence of gas in the right kidney indicating EPN (Figure 1) Huang IV and confirmed the presence of a nonfunctional left kidney. Blood culture was unremarkable, while urine culture reported *S. fonticola* as a single pathogen, sensitive to most antibiotics but resistant to trimethoprim and nitrofurantoin.

#### ***History of past illness***

Antecedents included that she debuted with symptomatic bilateral urinary lithiasis in 2015, and she was diagnosed with chronic kidney disease Class Kidney Diseases Global Outcomes 3A that same year, while left renal exclusion was confirmed using radiotracer mercaptoacetyl triglycine gammagraphy.

#### ***Personal and family history***

In 2016 and 2017 second look percutaneous nephrolithotomy was performed, finding right ureteral stenosis due to lithiasis; JJ catheters were temporarily placed in the right kidney and removed after treatment.

#### ***Physical examination***

Fever and right flank pain irradiated to the ipsilateral suprapubic region persisted.

#### ***Laboratory examinations***

Diabetes and hypertension had been ruled out at every hospitalization, as the patient only registered normal values of fast glucose and blood pressure. The patient was treated with piperacillin/tazobactam; and a combined endoscopic intrarenal surgery was

performed to place a metallic catheter and to treat with percutaneous drainage. After three days of antibiotic, she became afebrile, gas presence due to anaerobic bacteria reduced according to imaging and a new culture was performed on day four which was reported negative. Her white blood cell count improved markedly. However, after eight days her fever relapsed and new studies were performed, finding *pseudomonas aeruginosa* as a single pathogen in her urine culture along with an increase in neutrophils and white blood cell count in general. She was therefore treated with meropenem (Figure 2).

### ***Imaging examinations***

After ten days of treatment, with tomographic and laboratory evidence for the resolution of the acute signs and symptoms, she was discharged.

### **FINAL DIAGNOSIS**

Emphysematous pyelonephritis due to urolithiasis with *S. fonticola* isolation with subsequent infection due to *pseudomonas aeruginosa*.

### **TREATMENT**

Percutaneous drainage and antibiotics

### **OUTCOME AND FOLLOW-UP**

Between her discharge in 2018 and January 2021, the patient had two more hospitalizations related to urinary tract infections, but none related to *S. fonticola*.

### **DISCUSSION**

In previous studies, diabetes was present in 96%-98% of all patients with EPN<sup>[2,3]</sup>, and renal calculi was an antecedent in approximately 7.84%<sup>[2]</sup>.

In general, gas-forming bacteria are the cause of emphysematous infections, but, when it comes to pyelonephritis, the infection is attributed to *Escherichia coli* in more than 50% of cases and less often to other gram-negative bacteria<sup>[7]</sup>. Diagnosis is made through

clinical history and computerized axial tomography, the latter being the most precise tool to confirm diagnosis.

Before the decade of the 1990s, nephrectomies were considered the most effective form of intervention, as more conservative treatment had a mortality rate of 60%-80%<sup>[8]</sup>. To date, mortality has reduced significantly and even although diabetes is still recognized as a factor increasing the propensity for proliferation of gas-forming pathogens<sup>[9]</sup>, it also recognized that diabetes is not a *sine qua non* condition. The management of patients is somewhat controversial, and while some authors suggest that the nephrectomy could provide a better prognosis in subjects with two or more risk factors, other authors suggest that medical management and drainage are currently sufficient for treating these patients<sup>[7,10]</sup>. EPN can become a recurrent condition, as reported by Ramanathan *et al* <sup>[11]</sup> in a three-case report communication; in the case of our patient EPN reappeared while the patient was still under clinical care, giving the opportunity to be treated promptly. Altogether, current evidence regarding EPN indicates that this condition is still potentially fatal, particularly when a timely diagnosis is not established, or sub-optimal treatment is provided<sup>[7]</sup>. Katib *et al* in 2020 reported *S. fonticola* as a community-acquired urinary tract infection, affirming that globally this represented the third clinical case in which isolation of *S. fonticola* in an asymptomatic patient was reported. Therefore, the present case review may be the first reporting of a severe symptomatic infection due to *S. fonticola* causing EPN<sup>[12]</sup>.

Community-acquired infections are susceptible to improvement with various antibiotics, but the evidence from a case in which biliary tract infection due to *S. fonticola* occurred in a hospital environment pointed to a particularly resistant variant<sup>[13]</sup>.

Nephrectomy has been the treatment of choice when performed immediately to treat emphysematous nephritis and urosepsis<sup>[14]</sup>. For the case we have presented, nephrectomy was not an option, as the patient had a single functional kidney. Percutaneous drainage has been linked to lower mortality than medical management or emergency nephrectomy, and therefore, it was the treatment of choice<sup>[7,15]</sup>.

### *Serratia fonticola*, characteristics and peculiarities of clinical importance for human health

In 1979, *Serratia spp* was identified as a member of the Enterobacteriaceae family. This study included the type, neotype and the genetic relationship of these strains by means of DNA-DNA hybridization, and the relationship between them and the *Serratia spp.* strains known so far (*S. marcescens*, *S. liquefaciens*, *S. plymuthica* and *S. rubidaea*)<sup>[16]</sup>.

*Serratia spp.* belong to the Enterobacteriaceae family, which has been widely studied over the years, and there have been multiple changes to the number of species included in this family. Strains of this pathogen produce DNAase, gelatinase and lipase extracellularly, which means they can be easily differentiated from other Enterobacteriaceae genera<sup>[17]</sup>.

*S. fonticola* is a peritrichous, motile rod-shaped gram-negative enterobacteria that was first isolated in water and soil. There are reports that show *S. fonticola* can also be isolated in plants, aquatic environments, bird feces, some mammals and reptile skin wounds. When isolated, its growth occurs within a nutrient agar medium at temperatures of 30-37 °C<sup>[16,18,19]</sup>.

In 1990, it was identified as a human pathogen in a patient wound infection abscess localized on the thigh. Since then, *S. fonticola* has mainly been identified in open wounds (mostly due to trauma); and in the respiratory, gastrointestinal, and urinary tracts. Recently, some reports have identified *S. fonticola* in the biliary tract<sup>[12,18,20]</sup>.

Based on clinical practice, early identification of this pathogen is important since, due to its structure and characteristics, it is resistant to a wide range of antibiotics. This can be linked to the fact that *S. fonticola* harbors an inducible chromosomal B-lactamase AMPC and a FOMA-type, which not only generates resistance to antibiotics (including cephalosporins up to the third generation) but can also allow factors for antimicrobial resistance to be transmitted to other bacteria, thus increasing the risk of a rapid evolution from a sectorial infection to a polymicrobial bacteremia and even septicemia<sup>[12,21,22]</sup>.

Usually, *Serratia spp.* are nosocomial pathogens that may colonize medical devices such as urinary catheters and bronchoscopes<sup>[23]</sup>. However, in a study by Samonis *et al*<sup>[24]</sup>



where *Serratia spp.* was identified as a community-acquired infection, the predominant species was *S. marcescens*. *S. fonticola* was first described as a bystander in a patient in whom it was isolated along with other agents in a urine culture; the patient was a man with neurogenic bladder paraplegia due to a combat injury and related to urinary tract catheterization<sup>[13]</sup>. Even though *Serratia spp* have been linked to cases of nosocomial infections<sup>[25]</sup> and uncomplicated urinary tract infection in more susceptible patients with underlying urinary conditions and/or chronic kidney disease, *S. fonticola* may also be linked to severe clinical manifestations, as in this case, which was exacerbated by impaired renal function and urolithiasis, leading to emphysematous pyelonephritis.

## **CONCLUSION**

*Serratia fonticola* may still be rare as a human pathogen, either linked to asymptomatic conditions or merely a bystander among other infective agents, but its incidence may lead to severe cases when patients undergo invasive, instrumented procedures or have underlying conditions, as presented here in the case of the female who developed emphysematous pyelonephritis.

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