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Contents

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STANDARD AND CONSENSUS

- 10391** Baishideng's *Reference Citation Analysis* database announces the first *Article Influence Index* of multidisciplinary scholars

Wang JL, Ma YJ, Ma L, Ma N, Guo DM, Ma LS

REVIEW

- 10399** Cholecystectomy for asymptomatic gallstones: Markov decision tree analysis

Lee BJH, Yap QV, Low JK, Chan YH, Shelat VG

- 10413** Liver transplantation for hepatocellular carcinoma: Historical evolution of transplantation criteria

Ince V, Sahin TT, Akbulut S, Yilmaz S

MINIREVIEWS

- 10428** Prostate only radiotherapy using external beam radiotherapy: A clinician's perspective

Lee JW, Chung MJ

ORIGINAL ARTICLE

Retrospective Study

- 10435** Age-adjusted NT-proBNP could help in the early identification and follow-up of children at risk for severe multisystem inflammatory syndrome associated with COVID-19 (MIS-C)

Rodriguez-Gonzalez M, Castellano-Martinez A

- 10451** Clinicopathological characteristics and prognosis of gastric signet ring cell carcinoma

Tian HK, Zhang Z, Ning ZK, Liu J, Liu ZT, Huang HY, Zong Z, Li H

- 10467** Development and validation of a prognostic nomogram for decompensated liver cirrhosis

Zhang W, Zhang Y, Liu Q, Nie Y, Zhu X

Observational Study

- 10478** Effect of medical care linkage-continuous management mode in patients with posterior circulation cerebral infarction undergoing endovascular interventional therapy

Zhu FX, Ye Q

- 10487** Effect of the COVID-19 pandemic on patients with presumed diagnosis of acute appendicitis

Akbulut S, Tuncer A, Ogut Z, Sahin TT, Koc C, Guldogan E, Karabulut E, Tanriverdi ES, Ozer A

EVIDENCE-BASED MEDICINE

- 10501** Delineation of a SMARCA4-specific competing endogenous RNA network and its function in hepatocellular carcinoma

Zhang L, Sun T, Wu XY, Fei FM, Gao ZZ

SYSTEMATIC REVIEWS

- 10516** Comparison of laboratory parameters, clinical symptoms and clinical outcomes of COVID-19 and influenza in pediatric patients: A systematic review and meta-analysis

Yu B, Chen HH, Hu XF, Mai RZ, He HY

CASE REPORT

- 10529** Surgical treatment of bipolar segmental clavicle fracture: A case report

Liang L, Chen XL, Chen Y, Zhang NN

- 10535** Multiple disciplinary team management of rare primary splenic malignancy: Two case reports

Luo H, Wang T, Xiao L, Wang C, Yi H

- 10543** Klippel-Trenaunay-Weber syndrome with ischemic stroke: A case report

Lee G, Choi T

- 10550** Vedolizumab in the treatment of immune checkpoint inhibitor-induced colitis: Two case reports

Zhang Z, Zheng CQ

- 10559** Novel way of patent foramen ovale detection and percutaneous closure by intracardiac echocardiography: A case report

Han KN, Yang SW, Zhou YJ

- 10565** Treatment failure in a patient infected with *Listeria* sepsis combined with latent meningitis: A case report

Wu GX, Zhou JY, Hong WJ, Huang J, Yan SQ

- 10575** Three-in-one incidence of hepatocellular carcinoma, cholangiocellular carcinoma, and neuroendocrine carcinoma: A case report

Wu Y, Xie CB, He YH, Ke D, Huang Q, Zhao KF, Shi RS

- 10583** Intestinal microbiome changes in an infant with right atrial isomerism and recurrent necrotizing enterocolitis: A case report and review of literature

Kaplina A, Zaikova E, Ivanov A, Volkova Y, Alkhova T, Nikiforov V, Latypov A, Khavkina M, Fedoseeva T, Pervunina T, Skorobogatova Y, Volkova S, Ulyantsev V, Kalinina O, Sitkin S, Petrova N

- 10600** *Serratia fonticola* and its role as a single pathogen causing emphysematous pyelonephritis in a non-diabetic patient: A case report

Villasuso-Alcocer V, Flores-Tapia JP, Perez-Garfias F, Rochel-Perez A, Mendez-Dominguez N

- 10606** Cardiac myxoma shedding leads to lower extremity arterial embolism: A case report

Meng XH, Xie LS, Xie XP, Liu YC, Huang CP, Wang LJ, Zhang GH, Xu D, Cai XC, Fang X

- 10614** Extracorporeal membrane oxygenation in curing a young man after modified Fontan operation: A case report
Guo HB, Tan JB, Cui YC, Xiong HF, Li CS, Liu YF, Sun Y, Pu L, Xiang P, Zhang M, Hao JJ, Yin NN, Hou XT, Liu JY
- 10622** Wandering small intestinal stromal tumor: A case report
Su JZ, Fan SF, Song X, Cao LJ, Su DY
- 10629** Acute mesenteric ischemia secondary to oral contraceptive-induced portomesenteric and splenic vein thrombosis: A case report
Zhao JW, Cui XH, Zhao WY, Wang L, Xing L, Jiang XY, Gong X, Yu L
- 10638** Perioperative anesthesia management in pediatric liver transplant recipient with atrial septal defect: A case report
Liu L, Chen P, Fang LL, Yu LN
- 10647** Multiple tophi deposits in the spine: A case report
Chen HJ, Chen DY, Zhou SZ, Chi KD, Wu JZ, Huang FL
- 10655** Myeloproliferative neoplasms complicated with β -thalassemia: Two case report
Xu NW, Li LJ
- 10663** Synchronous renal pelvis carcinoma associated with small lymphocytic lymphoma: A case report
Yang HJ, Huang X
- 10670** *Leclercia adecarboxylata* infective endocarditis in a man with mitral stenosis: A case report and review of the literature
Tan R, Yu JQ, Wang J, Zheng RQ
- 10681** Progressive ataxia of cerebrotendinous xanthomatosis with a rare c.255+1G>T splice site mutation: A case report
Chang YY, Yu CQ, Zhu L
- 10689** Intravesical explosion during transurethral resection of bladder tumor: A case report
Xu CB, Jia DS, Pan ZS
- 10695** Submucosal esophageal abscess evolving into intramural submucosal dissection: A case report
Jiao Y, Sikong YH, Zhang AJ, Zuo XL, Gao PY, Ren QG, Li RY
- 10701** Immune checkpoint inhibitor-associated arthritis in advanced pulmonary adenocarcinoma: A case report
Yang Y, Huang XJ
- 10708** Chondroid syringoma of the lower back simulating lipoma: A case report
Huang QF, Shao Y, Yu B, Hu XP
- 10713** Tension-reduced closure of large abdominal wall defect caused by shotgun wound: A case report
Li Y, Xing JH, Yang Z, Xu YJ, Yin XY, Chi Y, Xu YC, Han YD, Chen YB, Han Y

- 10721** Myocardial bridging phenomenon is not invariable: A case report
Li HH, Liu MW, Zhang YF, Song BC, Zhu ZC, Zhao FH
- 10728** Recurrent atypical leiomyoma in bladder trigone, confused with uterine fibroids: A case report
Song J, Song H, Kim YW
- 10735** Eczema herpeticum *vs* dermatitis herpetiformis as a clue of dedicator of cytokinesis 8 deficiency diagnosis: A case report
Alshengeti A
- 10742** Cutaneous allergic reaction to subcutaneous vitamin K₁: A case report and review of literature
Zhang M, Chen J, Wang CX, Lin NX, Li X
- 10755** Perithyroidal hemorrhage caused by hydrodissection during radiofrequency ablation for benign thyroid nodules: Two case reports
Zheng BW, Wu T, Yao ZC, Ma YP, Ren J
- 10763** Malignant giant cell tumors of the tendon sheath of the right hip: A case report
Huang WP, Gao G, Yang Q, Chen Z, Qiu YK, Gao JB, Kang L
- 10772** Atypical Takotsubo cardiomyopathy presenting as acute coronary syndrome: A case report
Wang ZH, Fan JR, Zhang GY, Li XL, Li L
- 10779** Secondary light chain amyloidosis with Waldenström's macroglobulinemia and internodal marginal zone lymphoma: A case report
Zhao ZY, Tang N, Fu XJ, Lin LE
- 10787** Bilateral occurrence of sperm granulomas in the left spermatic cord and on the right epididymis: A case report
Ly DY, Xie HJ, Cui F, Zhou HY, Shuang WB
- 10794** Glucocorticoids combined with tofacitinib in the treatment of Castleman's disease: A case report
Liu XR, Tian M
- 10803** Giant bilateral scrotal lipoma with abnormal somatic fat distribution: A case report
Chen Y, Li XN, Yi XL, Tang Y
- 10811** Elevated procalcitonin levels in the absence of infection in procalcitonin-secreting hepatocellular carcinoma: A case report
Zeng JT, Wang Y, Wang Y, Luo ZH, Qing Z, Zhang Y, Zhang YL, Zhang JF, Li DW, Luo XZ

LETTER TO THE EDITOR

- 10817** "Helicobacter pylori treatment guideline: An Indian perspective": Letter to the editor
Swarnakar R, Yadav SL
- 10820** Effect of gender on the reliability of COVID-19 rapid antigen test among elderly
Nori W, Akram W

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

Victor Villasuso-Alcocer, Juan P Flores-Tapia, Fernando Perez-Garfias, Andrea Rochel-Perez, Nina Mendez-Dominguez

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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 presented with 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 3 d 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 rare as a 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 this case of the female who developed emphysematous pyelonephritis.

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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*[1,2].

It has been stated that even when agent-related virulence factors, along with the underlying health condition of patients, may predispose them to EPN, diabetes mellitus with poor glycemic control has been independently associated with the odds of developing EPN[3]. Furthermore, evidence in *Escherichia 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[4].

EPN is an unusual condition originally associated with patients with diabetes mellitus[5,6] and commonly reported in single clinical case reports, although also more recently in at least one systematic review with meta-analysis[6]. The present communication was 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 2 d, accompanied by severe pain in the right flank irradiating to the ipsilateral suprapubic region and reported changes in frequency and quality of urination.

History of present illness

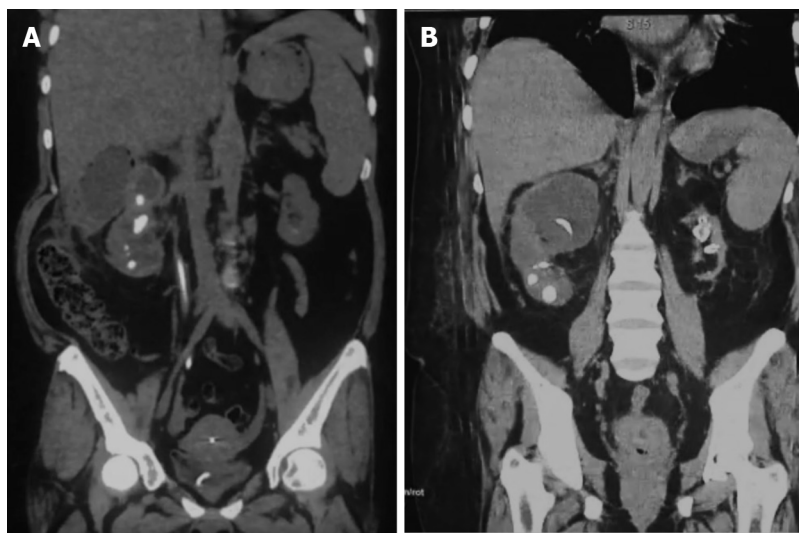
She was admitted for in-hospital care, and abdominal computerized axial tomography was performed, along with blood and urine tests, including cultures. Tomography indicated the presence of gas in the right kidney indicating EPN Huang IV and confirmed the presence of a nonfunctional left kidney (Figure 1). 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. 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.



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Figure 1 Tomography showing bilateral renal lithiasis and left renal exclusion. A: Gas accumulation in right kidney on day 1 of hospital stay; B: At discharge.

Physical examination

Fever and right flank pain irradiating 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 fasting glucose and blood pressure. The patient was treated with piperacillin/tazobactam; a combined endoscopic intrarenal surgery was performed to place a metallic catheter and to treat with percutaneous drainage. After 3 d of antibiotic, she became afebrile. The gas presence due to anaerobic bacteria reduced according to imaging, and a new culture was performed on day 4, which was reported negative. Her white blood cell count improved markedly. However, after 8 d 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 10 d of treatment, with tomographic and laboratory evidence for the resolution of the acute signs and symptoms, she was discharged.

FINAL DIAGNOSIS

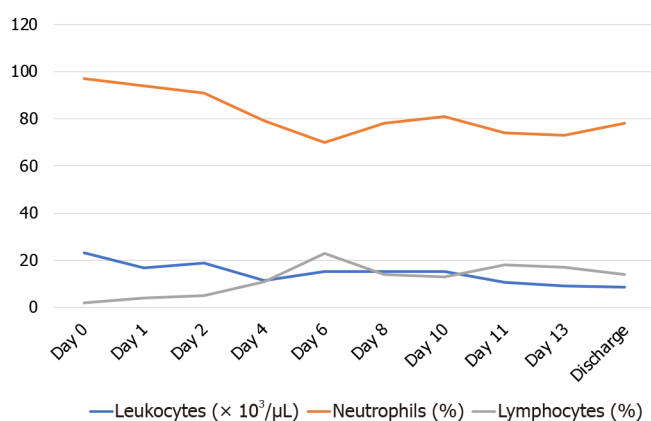
EPN due to urolithiasis with *S. fonticola* isolation with subsequent infection due to *Pseudomonas aeruginosa*.

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*.



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Figure 2 White cell count in a patient with *Serratia fonticola* related emphysematous pyelonephritis.

DISCUSSION

In previous studies, diabetes was present in 96%-98% of all patients with EPN[2,3], and renal calculi was an antecedent in approximately 7.84%[2]. 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[7]. Diagnosis is made through clinical history and computerized axial tomography, the latter being the most precise tool to confirm diagnosis.

Before the 1990s, nephrectomies were considered the most effective form of intervention, as more conservative treatment had a mortality rate of 60%-80%[8]. To date, mortality has reduced significantly and even though diabetes is still recognized as a factor increasing the propensity for proliferation of gas-forming pathogens[9], it is also recognized that diabetes is not a *sine qua non* condition. The management of patients is somewhat controversial. 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[7,10].

EPN can become a recurrent condition, as reported by Ramanathan *et al*[11] 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 suboptimal treatment is provided[7]. Katib *et al*[12] 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[13].

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[14].

Nephrectomy has been the treatment of choice when performed immediately to treat emphysematous nephritis and urosepsis[12]. 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[7,15].

S. 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*)[16].

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[17].

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[16,18,19].

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[13,18,20].

Based on clinical practice, early identification of this pathogen is important due to its structure and characteristics, which makes it 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[13,21,22].

Usually, *Serratia spp.* are nosocomial pathogens that may colonize medical devices such as urinary catheters and bronchoscopes[23]. However, in a study by Samonis *et al*[24] 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[14]. Even though *Serratia spp.* have been linked to cases of nosocomial infections[25] 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 EPN.

CONCLUSION

S. 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 this case of the female who developed EPN.

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