Polymicrobial Emphysematous Pyelonephritis Secondary to *Klebsiella pneumoniae* and *Bifidobacterium Breve* in a Diabetic Patient on Peritoneal Dialysis

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Received: 10 June 2023

Accepted: 6 August 2023

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DOI 10.5001/omj.2025.18

Abstract

Emphysematous pyelonephritis (EPN) is a rare, necrotizing infection of the renal parenchyma and pelvicalyceal system caused by gas-forming organisms. We herein described a novel case of a 71-year-old Chinese female patient with poorly controlled diabetes mellitus and end-stage renal failure on peritoneal dialysis who developed polymicrobial EPN involving Klebsiella pneumoniae and Bifidobacterium breve. She was successfully treated with culture-directed parenteral antibiotics and percutaneous drainage of renal collections. To the best of our knowledge, Bifidobacterium breve is a hitherto unreported cause of emphysematous pyelonephritis. While Bifidobacterium spp. is typically a non-pathogenic gut commensal, we highlight its potential in causing opportunistic infections in immunocompromised hosts in the appropriate clinical context and describe possible mechanisms through which this occurs.

Keywords: Emphysematous Pyelonephritis; Bifidobacterium breve; Diabetes Mellitus; Peritoneal dialysis.

Introduction

Emphysematous pyelonephritis (EPN) is a rare, necrotizing infection of the renal parenchyma and pelvicalyceal system involving gas-forming pathogens such as *Escherichia coli* and *Klebsiella pneumoniae*, with typical risk factors including poorly controlled diabetes mellitus (DM), immunosuppressed states and urinary tract obstruction.[1-3] As patients with EPN may develop acute renal failure and life-threatening sepsis,[2] prompt diagnosis and timely treatment with appropriate antimicrobials and interventions for infective source control are crucial.

In diabetic patients, urinary tract infections (UTIs) are reportedly the most common form of infection, which can range from asymptomatic bacteriuria or simple cystitis to severe urosepsis, emphysematous pyelonephritis/cystitis and renal abscess formation.[4] Interestingly, more severe forms of UTI were found to be associated with type 2 DM.[4] Diabetic patients with poor glycemic control tend to have impaired humoral and cell-mediated immunity, and are therefore considered immunocompromised hosts who are susceptible to opportunistic bacterial and fungal infections.[5] Nonetheless, certain commensal bacteria such as *Bifidobacterium* sp. are still considered safe and in fact, beneficial in diabetic patients.[5]

In this article, we herein describe a novel case of an immunocompromised host with poorly controlled DM and end-stage renal failure on peritoneal dialysis who developed polymicrobial EPN involving *Klebsiella pneumoniae* and *Bifidobacterium breve*, and highlight learning points pertaining to the clinical pathophysiology, workup and management of such cases.

Case Report

A 71-year-old Chinese female, with history of poorly controlled diabetes mellitus (DM) on insulin therapy and end-stage renal failure (ESRF) on peritoneal dialysis (PD), presented with a 2-day history of gross hematuria, dysuria and fever, without abdominal/flank pain. On examination, she was haemodynamically stable and afebrile, with a soft and non-tender abdomen and negative renal angle tenderness bilaterally. Initial laboratory tests revealed leukocytosis and elevated C-reactive protein. Her urinalysis demonstrated significant pyuria and hematuria, with urine cultures growing *Klebsiella* sp. Blood cultures and PD fluid cultures were, however, negative (Table 1). Computed tomography scan of the abdomen and pelvis (CTAP) revealed bilateral renal abscesses, with the presence of gas locules located within the right renal parenchyma and pelvicalyceal system (Figure 1), consistent with Huang & Tseng class II emphysematous pyelonephritis.[6] Our patient was initially treated with empirical intravenous (IV) aztreonam (as she was allergic to ceftriaxone) and percutaneous drainage of the right-sided gas-forming infected renal collections was performed for source control. Subsequently, gram stain of the drained sample showed gram-positive bacilli, with tissue cultures revealing significant growth of both *Klebsiella* sp. and *Bifidobacterium breve*. Given that patient continued to spike fevers despite treatment with IV aztreonam, decision was made to add on IV vancomycin to cover for *Bifidobacterium* sp. Thereafter, the patient's condition rapidly improved, with resolution of fever and downtrending inflammatory markers. In total, she completed 5 weeks of antibiotics from the time of percutaneous drainage of infected renal collections, comprising 1 week of IV aztreonam followed by 4 weeks of PO ciprofloxacin, as well as 5 weeks of IV vancomycin for treatment of polymicrobial EPN. Interval CTAP performed nearing the completion of antibiotic course also demonstrated resolution of the infective renal collections.

Table 1: Key Laboratory and Microbiological Investigations on Admission.

Investigation	Results	Reference Range
Laboratory Tests		
White blood cells	18.2 x 10^9/L	4-10 x 10^9/L
Hemoglobin	13.4 g/dL	12-16 g/dL
Platelets	162 x 10^9/L	140-440 x 10^9/L
Sodium	129 mmol/L	136-146 mmol/L
Potassium	3.5 mmol/L	3.6-5 mmol/L
Creatinine	646 umol/L	37-75 umol/L
Urea	9.9 mmol/L	2.7-6.9 mmol/L
Bicarbonate	25.2 mmol/L	19-29 mmol/L
Glucose	18.3 mmol/L	3.9-11 mmol/L
Calcium (**corrected**)	2.25 mmol/L	2.09-2.46 mmol/L
Magnesium	0.52 mmol/L	0.74-0.97 mmol/L
Phosphate	1.62 mmol/L	0.94-1.5 mmol/L
C-reactive protein	293 mg/dL	0.2-9.1 mg/dL
Lactate	3.5 mmol/L	0.5-2.2 mmol/L
HbA1c	9.3%	< 7%
Microbiology Tests		
Blood culture (**aerobic**)	No bacterial growth	
Blood culture (**anaerobic**)	No bacterial growth	
Urine, **full examination and microscopic examination**	> 2000 WBCs > 2000 RBCs 0 epithelial cells	
Urine culture	*Klebsiella* sp.	
Peritoneal fluid cell count	0	
Peritoneal fluid culture	No bacterial growth	
Tissue gram stain smear	Gram-positive bacilli 2+ Polymorphs 3+	
Tissue culture	*Bifidobacterium breve* *Klebsiella* sp. < resistant > ampicillin, < sensitive > Augmentin, tazocin, ceftriaxone, cefepime, aztreonam, ertapenem, gentamicin and ciprofloxacin	
Tissue culture for *Nocardia*	Negative	
Tissue acid fast bacilli smear and culture	Negative	

Tissue mycobacterium tuberculosis PCR	Negative
Tissue fungal microscopy and culture	Negative
Tissue cytology	Necroinflammatory yield – consistent with abscess Negative for malignant cells

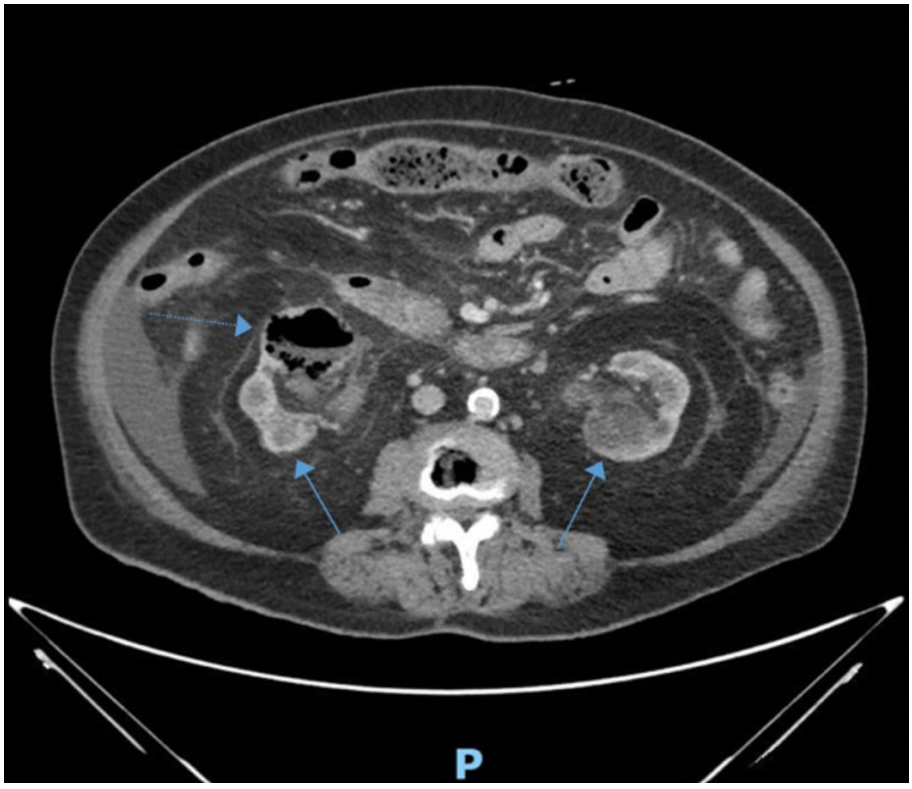

Figure 1: Contrast-Enhanced Computed Tomography of the Abdomen and Pelvis showing Bilateral Renal Abscesses and Right-Sided Emphysematous Pyelonephritis. Gas within right renal pelvicalyceal system (dash arrow). Bilateral renal abscesses Solid arrow).

Discussion

EPN is a dangerous gas-forming infection of the renal parenchyma and collecting system that can potentially lead to acute renal failure, septicaemia and death. Common causative organisms usually include gram negative bacteria *Escherichia coli* and *Klebsiella pneumoniae*, with a minority of cases involving *Proteus*, *Pseudomonas*, *Streptococcus*, anaerobes, fungi and occasionally polymicrobial infections are observed.[1,2] Classical risk factors described in literature include poorly controlled diabetes mellitus, immunosuppression and urinary tract obstruction.[1,2] Major contributors implicated in the pathogenesis of EPN include poor glycemic control associated with impaired renal vascular supply and host leukocyte function, immunodeficient states, and presence of gas-forming micro-organisms and urinary stasis in structural urinary tract obstruction.[1,2,7] Management of EPN is commonly guided by the radiological staging of disease as described by Huang and Tseng,[6] and comprises systemic antimicrobial therapy, percutaneous drainage of renal abscess and/or surgical nephrectomy.[1] To the best of our knowledge, we herein described a hitherto unreported case of polymicrobial emphysematous pyelonephritis involving *Klebsiella pneumoniae* and *Bifidobacterium breve* in a diabetic patient on peritoneal dialysis, and highlight several clinical learning points.

Firstly, *Bifidobacterium breve* is a highly unusual cause of emphysematous pyelonephritis as *Bifidobacterium* spp. are typically harmless anaerobic commensal bacteria commonly found in the human gut microbiota and are in fact frequently used in probiotics with good safety profile.[8] However, there have notably been rare instances of

invasive Bifidobacterial infections reported in the context of opportunistic infections occurring in immunocompromised hosts likely due to gut bacterial translocation.[9] From literature, urinary tract infections (UTIs) involving *Bifidobacterium* sp. are extremely uncommon, with two cases described in recent years including a polymicrobial UTI involving *Candida glabrata* and *Bifidobacterium* in a patient with uncontrolled diabetes and myelodysplastic syndrome[10] and also a case of recurrent *Bifidobacterium scarovii* UTIs in an immunocompromised patient with previous history of breast cancer treated with chemotherapy and radiotherapy and on corticosteroid treatment for autoimmune hemolytic anemia.[11]

In our patient, we suspect that both her history of poorly controlled DM and ESRF on peritoneal dialysis might have predisposed her to gut bacterial translocation and subsequent opportunistic infection by *Bifidobacterium breve*. It is known that DM predisposes patients to recurrent infections as it is associated with impaired humoral and cell-mediated immunity.[12] In particular, it is reported that hyperglycemia may increase the permeability of the intestinal epithelial barrier through GLUT2-mediated mechanisms, thereby promoting gut bacterial translocation and subsequent systemic infections.[12] For ESRF patients, mechanisms of impaired immunity are often related to the accumulation of uremic toxins with the loss of kidney function.[13] In fact, ESRF is also associated with gut bacterial translocation that contributes to the phenomenon of "microinflammation"[14]. Interestingly, the recent UTI microbiome (UMB) cohort study found that a dysbiotic gut microbiome may predispose females to recurrent UTIs,[15] consistent with a recently proposed theory that the gut microbiota might actually be the main contributing source of UTIs.[16] Finally, it is known that the high dextrose content in peritoneal dialysates can worsen glycemic control in diabetic patients and even inflict damage to the peritoneal membranes.[17] As such, there have actually been isolated case reports of emphysematous pyelonephritis[18] and pyelitis[19] in patients on peritoneal dialysis, although further studies are needed to establish if there is a significant clinical association.

Finally, *Bifidobacterium* spp. isolated from sterile tissue specimens should not simply be disregarded as a contaminant.[10] In particular, in the context of an immunocompromised host with a local/systemic infection, where *Bifidobacterium* has been isolated from a potential site of infection and the patient has not adequately responded to a trial of empirical antimicrobial treatment, it may be prudent to include antibiotic cover for *Bifidobacterium* spp. with either beta-lactams, vancomycin or clindamycin.[9,20] In addition, for species like *Bifidobacterium breve*, which is associated with greater antimicrobial resistance,[20] there may even be a role for anaerobic susceptibility testing, which is not routinely performed in microbiological laboratories, should there be inadequate clinical response to standard antimicrobial treatment.

Conclusion

In conclusion, we herein described a novel case of polymicrobial EPN involving the anaerobic gut commensal *Bifidobacterium breve* as one of the causative pathogens and highlighted several learning points from this clinical vignette for management of similar cases in future.

Disclosure

Authors declared no conflicts of interest and no funding was received. Written consent was obtain from the patients.

References

1. Pontin AR, Barnes RD. Current management of emphysematous pyelonephritis. Nat Rev Urol 2009;6(5):272-279.

2. Ubee SS, McGlynn L, Fordham M. Emphysematous pyelonephritis. BJU Int 2011;107(9):1474-1478.

3. Azfar SF, Badar F, Akhtar N, Kirman S. Diabetic Women with Fever and Right Flank Pain. Oman Med J 2011;26(2):141-142.

4. Akash MS, Rehman K, Fiayyaz F, Sabir S, Khurshid M. Diabetes-associated infections: development of antimicrobial resistance and possible treatment strategies. Arch Microbiol 2020;202(5):953-965.

5. Khanam A, Hithamani G, Naveen J, Pradeep SR, Barman S, Srinivasan K. Management of Invasive Infections in Diabetes Mellitus: A Comprehensive Review. Biologics 2023;3(1):40-71.

6. Huang J-J, Tseng C-C. Emphysematous pyelonephritis. Arch Intern Med 2000;160(6):797-805.

7. Sokhal AK, Kumar M, Purkait B, Jhanwar A, Singh K, Bansal A, et al. Emphysematous pyelonephritis: Changing trend of clinical spectrum, pathogenesis, management and outcome. Turk J Urol 2017;43(2):202-209.

8. O'Callaghan A, van Sinderen D. Bifidobacteria and their role as members of the human gut microbiota. Front Microbiol 2016;7(JUN).

9. Esaiassen E, Hjerde E, Cavanagh JP, Simonsen GS, Klingenberg C. Bifidobacterium bacteremia: Clinical characteristics and a genomic approach to assess pathogenicity. J Clin Microbiol 2017;55(7):2234-2248.

10. Pathak P, Trilligan C, Rapose A. Bifidobacterium friend or foe? A case of urinary tract infection with Bifidobacterium species. BMJ Case Rep 2014;2014:2-4.

11. Barberis CM, Cittadini RM, Almuzara MN, Feinsilberg A, Famiglietti AM, Ramírez MS, et al. Recurrent urinary infection with Bifidobacterium scardovii. J Clin Microbiol 2012;50(3):1086-1088.

12. Daryabor G, Atashzar MR, Kabelitz D, Meri S, Kalantar K. The Effects of Type 2 Diabetes Mellitus on Organ Metabolism and the Immune System. Front Immunol 2020;11(July).

13. Vaziri ND, Pahl MV, Crum A, Norris K. Effect of Uremia on Structure and Function of Immune System. J Ren Nutr 2012;22(1):149-156.

14. Wang F, Jiang H, Shi K, Ren Y, Zhang P, Cheng S. Gut bacterial translocation is associated with microinflammation in end-stage renal disease patients. Nephrology (Carlton) 2012;17(8):733-738.

15. Worby CJ, Schreiber HL, Straub TJ, van Dijk LR, Bronson RA, Olson BS, et al. Longitudinal multi-omics analyses link gut microbiome dysbiosis with recurrent urinary tract infections in women. Nat Microbiol 2022;7(5):630-639.

16. Stepanova N. How Advanced Is Our Understanding of the Role of Intestinal Barrier Dysfunction in the Pathogenesis of Recurrent Urinary Tract Infections. Front Pharmacol 2022;13(March):1-8.

17. Lee MJ, Kwon YE, Park KS, Kee YK, Yoon CY, Han IM, et al. Glycemic control modifies difference in mortality risk between hemodialysis and peritoneal dialysis in incident dialysis patients with diabetes: Results from a nationwide prospective cohort in Korea. Medicine (Baltimore) 2016;95(11):1-9.

18. Borrajo Prol MP, Pérez Melón C, Santos Nores J, Camba Caride M. Emphysematous pyelonephritis in peritoneal dialysis. Nefrología 2008;28(6):663-664.

19. Anwar N, Chawla LS, Lew SQ. Emphysematous pyelitis presenting as an acute abdomen in an end-stage renal disease patient treated with peritoneal dialysis. Am J Kidney Dis 2002;40(4):1-4.

20. Moubareck C, Gavini F, Vaugien L, Butel MJ, Doucet-Populaire F. Antimicrobial susceptibility of bifidobacteria. J Antimicrob Chemother 2005;55(1):38-44.