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Case Report

Urinary tract infection due to anaerobic bacteria in a two-month-old infant

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ABSTRACT

The significance of anaerobic bacteria as a pathogen in urinary tract infection (UTI) in children is unclear. A two-month-old infant presenting with poor feeding received a diagnosis of polymicrobial anaerobic UTI by next-generation sequencing and was found to have obstructive uropathy. Anaerobic bacteria may be a cause of UTI in children with urinary tract obstruction.

1. Introduction

Urinary tract infection (UTI) is a common bacterial infection in children. Although the majority of pathogens are enterobacteriaceae [1], anaerobic bacteria have been reported as a rare cause of UTI. The incidence of UTI due to anaerobic bacteria is approximately one percent of the adult population [2,3]. The significance of anaerobic bacteria as a pathogen in UTI in children is still unknown. Herein, we report a case of a 2-month-old infant with UTI associated with obstructive uropathy, which was due to polymicrobial pathogens including anaerobic bacteria.

2. Case report

A two-month-old female infant was brought to the emergency department for vomiting and poor feeding for 5 days. She was born by normal vaginal delivery with a birth weight of 3160 g. She had no apparent perinatal history except for insufficient weight gain at one-month checkup (3894 g, 20 g/day). On physical examination, she was irritable and cyanosis was observed. Her weight was 3790 g (third percentile), body temperature was 35.8 °C, pulse rate was 140/min, and blood pressure was unmeasurable. Intravenous bolus normal saline was given and blood pressure rose to 94/71 mmHg. Other physical findings were unremarkable. Peripheral blood examination showed an elevated white blood cell count of 24,000/μL. Blood urea nitrogen and creatinine levels were elevated to 51.1 mg/dL and 1.7 mg/dL, respectively. Her lymphocyte counts were within the age-related reference ranges.

A urine sample taken by catheterization showed remarkable pyuria with 100 cells per high power field. Gram staining revealed multiple polymorphic, polychromatic, Gram-positive cocci and Gram-negative rods, suggestive of polymicrobial infection. Abdominal ultrasonography demonstrated Society of Fetal Urology (SFU) grade 4 hydronephrosis and hydroureter of the left kidney with a large amount of debris, suggesting the existence of urinary obstruction and pyonephrosis (Fig. 1A,B).

Abbreviations: NGS, next-generation sequencing.

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After admission, ampicillin and cefepime were administered for coverage against polymicrobial UTI. Standard urine culture procedures were performed using 10 μL of urine, spread quantitatively onto 5% sheep blood and CPS medium and incubated aerobically at 35 °C. This revealed growth of pan-sensitive *Escherichia coli* at 10^8 CFU/mL and *Streptococcus anginosus* at 10^7 CFU/mL. Since the morphology of the Gram stain products suggested presence of anaerobic bacteria, we performed anaerobic culture procedures using 10 μL of urine, spread quantitatively onto ABHK medium and incubated anaerobically at 35 °C. This revealed growth of *Prevotella* spp. at 10^7 CFU/mL. Antibiotics were switched to ampicillin/sulbactam for coverage against *E. coli* and anaerobic bacteria according to susceptibility testing. A urinary catheter was placed for depressurization of the bladder to reduce hydronephrosis and hydroureter, and hydration procedures were performed to wash out the debris. The patient's condition gradually improved, creatinine level normalized after 3 days, and pyuria and debris accumulation resolved on day 8 (Fig. 1C,D).

A voiding cystourethrogram was performed on day 9 and grade I vesicoureteral reflux was observed in the right ureter. She attained fiftieth percentile on body weight and was discharged after completion of three weeks of antibiotic therapy. Surgical correction of the ureterovesical junction obstruction was subsequently performed and she remained healthy, without signs of immunodeficiency, for two years of follow-up.

To identify other micro-organisms in this polymicrobial infection, we performed metagenomic shotgun sequencing of the urine sample. The genomic fragments of *Prevotella melaninogenica* were detected in the greatest quantity, indicating this species was the most abundant micro-organism. In addition, *S. anginosus* and *Gardnerella vaginalis* were also detected as dominant micro-organisms (Table 1).

Table 1
List of dominant micro-organisms accounting for over 10% of total microbial reads.

Rank	Detected micro-organisms	# of reads	% of total
1	*Prevotella melaninogenica*	97,478	50.58
2	*Streptococcus anginosus*	38,020	19.73
3	*Gardnerella vaginalis*	23,569	12.23
	Total microbial reads	192,734	

3. Discussion

We encountered a two-month-old female patient with UTI due to multiple pathogens, including anaerobic bacteria, and associated with obstructive uropathy. In addition to conventional urine culture, anaerobic culture and next-generation sequencing (NGS) were helpful in identifying the pathogens.

In general, anaerobic bacteria are rare causes of UTI. Segura et al. [2] and Hudac et al. [3] reported that anaerobic bacteria were detected in only 0.8%–1.3% of UTI in adults. However, the incidence of UTI due to anaerobic bacteria in children is still unknown. To our knowledge, only six cases of UTI due to anaerobic bacteria in children have been reported and are summarized in Table 2. Similar to our case, the majority of the pediatric UTI cases with anaerobic bacteria had urinary tract obstruction [4,5]. This is consistent with observations in adults that documented obstructive uropathy in patients with UTI due to anaerobic bacteria [2]. Kumazawa et al. investigated the pathogenesis of anaerobic bacteria for urinary tract infection using an animal model [6]. The study showed that *Bacteroides* spp. only caused UTI in rabbits when ureters were obstructed. They suggested that ureteral obstruction may provide an anaerobic environment and lead to development of infection by anaerobic bacteria.

In the past reports of anaerobic UTI in children, anaerobic bacteria from the gastrointestinal flora were found accountable [4,5]. We detected organisms of the vaginal and oral flora, such as *Gardnerella* spp., *Prevotella* spp., and *Streptococcus* spp. in our case. No anatomical abnormality, such as vesico-vaginal fistula, was detected. Failure to thrive observed at one month of age and involvement of the maternal vaginal flora may suggest an onset during the neonatal period.

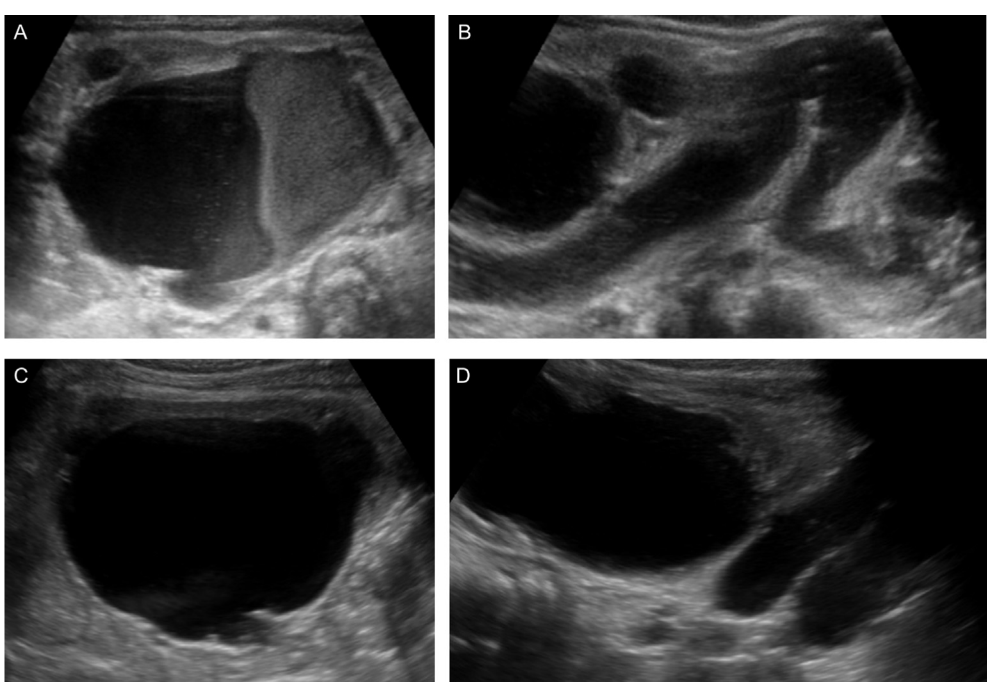

Fig. 1. Urinary ultrasonograms showing SFU grade 4 hydronephrosis with large amount of debris forming a liquid surface (A), and hydroureter in the left kidney (B), which suggested pyonephrosis on admission. Follow-up ultrasonogram demonstrating absence of debris, persistence of hydronephrosis (C), and hydroureter in the left kidney (D) on day 8.

Table 2
Summary of urinary tract infections due to anaerobic bacteria in children.

Case No.	Age (years)	Sex	Clinical diagnosis	Isolated bacteria		Identification method	Antibiotics	Duration (days)	Outcome	Co-morbidities	Reference
				Anaerobes	Aerobes						
1	0.8	M	Bacteriuria	*Sarcina* spp.	–	Smear	Cefepime Metronidazole	14	Cured	Posterior urethral valve Bilateral VUR	5
2	4	F	Cystitis	*Bacteroides melaninogenicus*	–	Anaerobic Culture	Ampicillin (oral)	10–14	Cured	VUR (1/5) Abnormality on IVP (2/5)	4
3	7	F	Pyelonephritis	*Bacteroides adolescentis* *Peptostreptococcus asaccharolyticus*	–		Ampicillin (IV to oral)		Cured		
4	7	F	Cystitis	*Bacteroides fragilis*	–		Ticarcillin		Cured		
5	8	F	Pyelonephritis	*Bacteroides fragilis*	*Escherichia coli*		Gentamicin Carbenicillin		Relapse		
6	12	F	Pyelonephritis	*Bacteroides distasonis*	*Escherichia coli*		Gentamicin Carbenicillin		Relapse		

VUR, Vesicoureteral reflux; IVP, Intravenous pyelography.

Anaerobic culture is not recommended routinely for patients with UTI [7], and its implementation requires an index of suspicion raised by the physician and the microbiologist. In our case, anaerobic bacteria were suspected based on Gram stain findings and the presence of urinary tract obstruction. In such situations, additional anaerobic urine cultures may enhance detection of anaerobes. Metagenomic shotgun sequencing by NGS was helpful in identifying additional bacteria that were not detected by conventional culture methods [8]. In our case, addition of NGS led to the detection of *G. vaginalis,* which was not detected by anaerobic culture methods. Sabat et al. investigated the utility of NGS to detect pathogens in urine samples, which showed the potential of NGS in detecting more pathogens, including anaerobic bacteria, in urine samples from patients with UTI [9]. The shortcoming of applying NGS is the potential of detecting colonizing or non-pathogenic organisms. Thus, we complemented information with the number of genomic fragments derived from an organism and limited our list to dominant micro-organisms, which accounted for over 10% of total microbial reads. Still, criteria to determine pathogenesis remain a question for future research.

4. Conclusion

Polymicrobial infection including anaerobic bacteria may be a cause of UTI in children with urinary tract obstruction. Anaerobic culture and next-generation sequencing might be useful to identify pathogens.

Authorship statement

All authors meet the ICMJE authorship criteria. C.T., N.K., and K.S. contributed to conceptualizing the study and drafted the manuscript. R.E. and K.U. collected patient data and critically reviewed the manuscript. D.M., S.N., M.K. and A.I. critically reviewed the manuscript. I.M. contributed to the conceptualization of the study, revised the manuscript, and supervised the study.

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Conflicts of interest

The authors have no conflicts of interest relevant to this article to disclose.

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References

[1] Edlin RS, Shapiro DJ, Hersh AL, Copp HL. Antibiotic resistance patterns of outpatient pediatric urinary tract infections. J Urol 2013;190:222–7. https://doi.org/10.1016/j.juro.2013.01.069.
[2] Segura JW, Kelalis PP, Martin WJ, Smith LH. Anaerobic bacteria in the urinary tract. Mayo Clin Proc 1972;47:30–3.
[3] Hudac A, Zahradnikova I, Lamosova M, Popluharova M, Filo I. The role of anaerobic non-sporulating bacteria in urinary tract infections. Cesk Epidemiol Mikrobiol Imunol 1991;40:85–8.
[4] Brook I. Urinary tract infection caused by anaerobic bacteria in children. Urology 1980;16:596–8.
[5] Bommannan K, Gaspar BL, Sachdeva MU. Pathogenic Sarcina in urine. BMJ Case Rep 2016. https://doi.org/10.1136/bcr-2016-216991.
[6] Kumazawa J, Kiyohara H, Momose S. Significance of anaerobic bacteria isolated from the urinary tract. II. Experimental studies. Invest Urol 1976;13:309–12.
[7] Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. Clin Infect Dis 2004;38:1150–8. https://doi.org/10.1086/383029.
[8] Kashyap PC, Chia N, Nelson H, Segal E, Elinav E. Microbiome at the frontier of personalized medicine. Mayo Clin Proc 2017;92:1855–64. https://doi.org/10.1016/j.mayocp.2017.10.004.
[9] Sabat AJ, van Zanten E, Akkerboom V, et al. Targeted next-generation sequencing of the 16S-23S rRNA region for culture-independent bacterial identification - increased discrimination of closely related species. Sci Rep 2017;7:3434. https://doi.org/10.1038/s41598-017-03458-6.