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MINI REVIEW

Anaerobic Bacteria Causing Urinary Tract Infections: A Mini Review

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Abstract

Urinary Tract Infections (UTIs) can be commonly caused by aerobic bacteria, but anaerobic bacteria can also be rarely responsible for these infections. Anaerobes are often misidentified or even overlooked as aetiological agents of UTI. They may be quite significant in many predisposing conditions. This review article explores the role of anaerobic bacteria in causing UTIs, the diagnostic challenges and treatment options as well.

Key Words: *UTI; Anaerobes; Infection*

Introduction

Urinary tract infections (UTIs) are among the most commonly encountered bacterial infections, affecting millions of people worldwide and adult females more often than adult males. Many bacteria are reported from UTI. While aerobic bacteria such as *Escherichia coli* are known to be primary culprits, anaerobic bacteria can also cause UTIs, particularly in certain patient populations or risk groups. Urinary Tract Infections (UTIs) caused by anaerobic bacteria have only rarely been reported. Since anaerobic bacteria are also commensals of the genitourinary tract, their presence in a urine sample adds ambiguity in making a definitive diagnosis of anaerobic UTI and makes diagnosis difficult. It is also well known that standard urine culture is the gold standard method for the detection, identification and antimicrobial susceptibility testing of uropathogens. Nonetheless, both the difficulties in establishing them as pathogens and the scarcity of reported anaerobic UTI cases has led to overall discontinuation of routine Urine Culture under an Anaerobic Atmosphere (UCAA) [1]. Anaerobic bacteria can cause different types of Urinary Tract Infections (UTIs), such as cystitis, pyelonephritis, perinephric abscess, pyelitis and others. Anaerobic bacteriuria is common in catheterized patients in intensive care units [2].

Materials and Method

Thorough and meticulous literature search using MeSH (Medical Subject headings) terms were used to access information regarding anaerobic bacteria causing UTI.

Epidemiology

Anaerobic UTI is definitely much less common than aerobes causing UTI and it can cause between 0.8-3% of all UTIs. Anaerobic bacteria, viruses and *Chlamydia* spp. are rare causes of UTI. Direct bowel spread, the already existing urethral microbiota and bacteremia

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are all potential sources of anaerobic UTI. UTI caused by anaerobic bacteria has also been documented in children. *Bacteroides fragilis*, *B. melaninogenicus*, *Peptococcus asaccharolyticus* and *Bifidobacterium adolescentis* are anaerobic uropathogens seen in children. However, overall, the prevalence of anaerobes in UTI is rare. In a study from the USA, a total of 810 urine cultures were investigated from 600 individuals. Pure cultures of obligate anaerobic strains of bacteria could be isolated from 5 individuals and in mixed cultures from 36 subjects [3]. Thus, anaerobes causing UTI is not very common, but they are, nonetheless potent urinary pathogens.

Anaerobic bacteria in UTIs

Anaerobic bacteria are typically found in the gastrointestinal tract and can enter the urinary tract through the urethra. These bacteria thrive in environments with low oxygen levels, thus making the urinary tract a suitable habitat. Anaerobes have been reported from the following types of UTI: para- or periurethral cellulitis or abscess, acute and chronic urethritis, cystitis, prostatic and scrotal abscesses, acute and chronic prostatitis, periprostatic phlegmon, ureteritis, pyelitis, periureteritis pyelonephritis, renal abscess, scrotal gangrene, pyonephrosis, metastatic renal infection, perinephric abscess and retro-peritoneal abscess [4].

Common anaerobic bacteria implicated in UTIs include *Bacteroides*, *Fusobacterium* and *Clostridium* species. Other rare bacteria like *Actinotignum schaali* have also been incriminated as causes of anaerobic UTI. *Actinotignum schaalii* (formerly known as *Actinobaculum schaalii*) is a small gram-positive, non-motile, facultative anaerobic coccid rod showing slow growth. It is a member of the family Actinomycetaceae, which is frequently overlooked or considered as a contaminant in urine specimens. Although it has often been underestimated as a cause of UTI since the initial description of the genus, this species is, indeed the most frequently reported in many human infections. The current protocol for urine cultures can lead to a delay in the correct diagnosis. So, the recommendation is that clinicians consider unusual pathogens such as *A. schaalii* as a cause of UTI when common bacterial agents cannot be established. Therefore, the visualization of gram-positive bacilli in microscopy of urine, with no microbiological growth in conventional aerobic culture methods should incite the search for unusual pathogens including *A. schaalii* [5].

In our experience, anaerobic gram-positive cocci (*Peptostreptococcus* spp.) are also an important cause of UTI. We have tested this by culturing urine sample in Robertson's cooked meat medium for 48 hours. *Peptostreptococcus asaccharolyticus* is also a cause of renal abscess as mentioned in the literature [6]. The gram-positive anaerobic diphtheroid rod, *Varibaculum* spp., is also a rare pathogen incriminated in UTI [7].

Surgical procedures like TUI (trans-urethral instrumentation) increases the chances of occurrence of anaerobic UTI [8]. Similar to UTIs caused by aerobes, patients with risk factors are more likely to suffer from UTIs brought on by facultative gram-positive bacteria, including those that may necessitate anaerobic incubation, like *Actinotignum shaalii* and *Gardnerella vaginalis* [9]. There is a danger of anaerobic UTIs in several settings. Additionally, anaerobes may coexist with aerobic pathogens in urine and cause UTI. Figure1 below shows urine culture on Robertson's cooked meat medium (Figure 1).

Figure 1) *Urine culture on Robertson's cooked meat medium.*

Predisposing factors

Age more than 65 years, Diabetes mellitus, concomitant bacteremia and malignancies have been thought to be strong risk factors for UTI due to anaerobes, especially those caused by *Clostridium* spp. Transurethral instrumentation can also be a risk factor for development of UTI due to anaerobes. Researchers have also observed an increase in the number of anaerobic bacteria in urine voided following prostatic massage of infertile men [4].

Diagnostic challenges

Diagnosing UTIs caused by anaerobic bacteria can be challenging owing to their slow growth and the requirement for specialized culture techniques. Standard urine cultures often fail to detect anaerobes, leading to underdiagnosis. Several authors have said that the presence of pyuria and bacteriuria, with a negative routine urine culture result, should strongly indicate a possibility of anaerobic UTI. Advanced techniques such as molecular methods and proteomics are increasingly being used to identify these pathogens. Numerous researches have shown that UCAA (urine culture in anaerobic environments) might be helpful in clinical settings [9]. Suprapubic aspiration of urine may also help in better diagnosis of anaerobic UTI, particularly in children and adult females. In addition, UCAA and therapy based on results of antimicrobial susceptibility testing may be necessary to achieve good results. As routine diagnostic techniques may be insufficient to detect and identify anaerobic bacteria in patients with UTIs, Enhanced Quantitative Urine Culture (EQUC) can yield better results. EQUC is carried out by plating urine samples onto different media to be incubated in both aerobic and anaerobic conditions with prolonged incubation time. Other newer techniques such as 16S rRNA gene sequencing, qualitative PCR and Next Generation Sequencing (NGS) can also be contemplated [2]. A large fraction of fastidious and anaerobic bacteria (22.43%) is not detected under culture conditions but only by using PCR. This group of bacteria can bypass the standard culture conditions used in routine diagnostic laboratories for examining urine specimens [10]. Figure 2 below shows *Peptostreptococcus* spp. in gram stain (Figure 2).

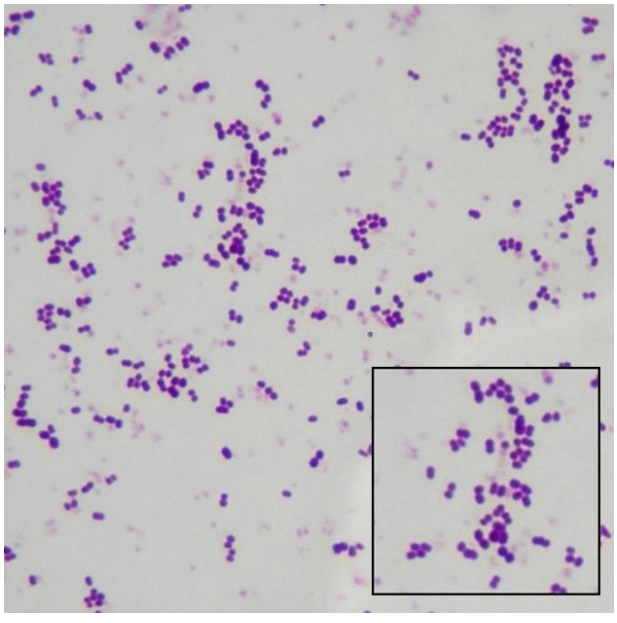

Figure 2) *Peptostreptococcus spp. in gram stain (source: www.microbiologyinpictures.com).*

Treatment options

The treatment of anaerobic UTIs requires a different approach compared to aerobic UTIs. Antibiotic susceptibility testing is crucial to determine the appropriate antimicrobial therapy. Commonly used antibiotics include metronidazole, clindamycin and beta-lactam/ beta-lactamase inhibitor combinations.

Discussion

Anaerobes are rare but important causes of UTI in man. Many studies quote that anaerobes are responsible for about 0.8% cases of UTI. In children also, polymicrobial anaerobic UTI is not very uncommon. Anaerobic bacteria may be a significant cause of UTI in children with urinary tract obstruction [11]. Direct bowel spread, the already existing urethral microbiota and bacteremia are all potent sources of anaerobic UTI [1]. Anaerobic bacteria are infrequently found as causative agents of Urinary Tract Infection (UTI). As an additional factor, the difficulty of establishing them as pathogens due to the possibility of colonization or contamination has led laboratories to discontinue routine anaerobic urine culture. MALDI-TOF MS (Matrix-Assisted Laser Desortion Ionization Time of Flight Mass Spectrometry), directly used in urine specimens, may be a viable option to quickly detect UTI caused by *P. anaerobius* or any other anaerobic bacteria [12]. Anaerobic culture of urine may also be helpful. Newer techniques like metaculturomics and metagenomics have made diagnosis of anaerobes in urine much simpler. Since the introduction of molecular and proteomic methods in modern microbiology, anaerobic bacteria have been increasingly recognized at unexpected infection sites and anaerobic UTIs do not seem to be an exception. So, the current flow chart for diagnosis of UTI should also include the techniques used for isolating anaerobic bacteria.

Conclusion

Anaerobic bacteria, although less common, can cause UTIs and present unique diagnostic and therapeutic challenges. Increased awareness and the use of conventional UCAA as well as advanced diagnostic techniques can help establish and improve the detection and management of these infections.

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