CASE REPORT

Bifidobacterium—friend or foe? A case of urinary tract infection with *Bifidobacterium* species

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SUMMARY

Bifidobacterium—a commensal of the human intestine is considered non-pathogenic and has been advocated as a probiotic due to its potential beneficial effects. However, there have been case reports implicating bifidobacteria as pathogenic agents in a variety of different infectious conditions. We discuss here one such case of a complicated urinary tract infection associated with *Bifidobacterium* spp.

BACKGROUND

Bifidobacterium—an anaerobic commensal organism is part of the intestinal microbiome in humans and is also part of the normal flora of the oral cavity and the vagina. It has long been considered non-pathogenic and has been advocated as a probiotic due to its potential beneficial effects. However, there have been case reports implicating bifidobacteria as pathogenic agents in sepsis, necrotising pancreatitis and urinary tract infection (UTI).[1 2] While probiotics containing bifidobacteria are often used as a friend in conjunction with antibiotics to reduce incidence of diarrhoea, these practices should be tempered by the potential for the same bacterium to act as a foe and itself cause clinical infection.

CASE PRESENTATION

A 66-year-old Caucasian woman presented with fever and haematuria. She had experienced multiple episodes of haematuria over the previous 2 months. She did not report of frequency, urgency or dysuria. She denied abdominal pain. In the previous few months, the patient had experienced multiple episodes of UTI associated with *candida glabrata*. Medical history was also significant for myelodysplastic syndrome, hepatitis C with cirrhosis and uncontrolled diabetes. She was a non-smoker and non-alcoholic with no significant family history. Physical examination revealed a temperature of 100.4°F and she had left costovertebral angle tenderness. A foley catheter was placed which returned bloody urine. CT of the abdomen and pelvis revealed left hydronephrosis and obstructive nephrolithiasis. A percutaneous nephrostomy tube was placed by the interventional radiologist at which time a urine sample was obtained for microscopy and culture.

INVESTIGATIONS

Blood tests revealed pancytopenia with a white cell count (WCC) of 2.3×10^{-9}/L, platelets 51 000/μL and haematocrit 21.7. Creatinine was 1.27 mg/dL. Urine Gram stain revealed many (>25/lpf) WCC, many (>25/hpf) budding yeast and many (>25/hpf) Gram positive beaded rods.

Urine was incubated in 5% blood agar and chocolate agar with CO_2 at 35°C and also in Mac Conkey agar and thioglycollate broth (Remel Inc, Lenexa, Kansas, USA) with ambient air at 35°C. After 48 h of incubation, colonies of yeast were seen on the aerobic media. The thioglycollate broth revealed two different colonies. One was yeast and smears from the other colonies revealed branching Gram positive beaded rods. This broth was subcultured aerobically and anaerobically in 5% blood agar with ambient air and chocolate agar with CO_2 at 35°C for 2 days. On day 3, after adequate growth of yeast was obtained, it was set up on an API 20 C yeast identification system (bioMerieux Inc, Durhan, North Carolina, USA) and *candida glabrata* was identified (growth 2+). On day 4, the anaerobic plates from the thioglycollate broth revealed Gram positive rods. For further identification, the culture plates were incubated anaerobically for another 48 h. On day 6, identification was performed using RapID ANA II System (Remel Inc). The organism was identified as *Bifidobacterium species*. Unfortunately we did not have facilities to subspeciate the organism or perform antibiotic susceptibility testing.

TREATMENT

On admission, the patient was initiated on intravenous micafungin 100 mg every 24 h. Unfortunately she continued experiencing fevers. After nephrostomy tube placement and finding of Gram positive rods in the urine in addition to the yeast, meropenem 1 g intravenous q12 h was added to her regimen.

The fevers subsided.

Micafungin was continued for a total duration of 14 days while meropenem was given for a total of 7 days.

OUTCOME AND FOLLOW-UP

On account of the unusual presentation with an unusual organism, repeat urine cultures were obtained after completion of the antimicrobial course. One week off antimicrobials, urine cultures remained negative. Six months after completion of therapy urine cultures were negative for *candida glabrata* and *Bifidobacteria*.

DISCUSSION

Bifidobacterium is a genus of Gram-positive, non-motile obligate anaerobic bacteria comprising of more than 30 species. They are natural inhabitants of the gut in humans and animals. They are also

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found in the oral cavity and vagina. Gut microbes play an important role in the normal function of the bowel.[3] There is a large volume of published laboratory studies indicating protective benefits of *Bifidobacterium* and *Lactobacillus* against various infections.[4 5] Owing to *Bifidobacterium*'s role in modulation of gastrointestinal immunity and health, it is widely used as a probiotic. The exact mechanism by which probiotics work has also been investigated extensively. An in-vitro study showed that *bifidobacterium* reduces the colonic lipopolysaccharide and hence decreases the proinflammatory state.[6] *Bifidobacterium* has been reported to significantly decrease the symptoms of irritable bowel syndrome and reduce the frequency of acute infectious diarrhoea.[7 8]

Unfortunately, this organism has also been implicated in different infectious conditions. There are case reports of *Bifidobacterium* as the causative agent in necrotising pancreatitis[9] sepsis[10] epidural abscess[11] fatal pulmonary infection[12] and dental caries.[1] Other cases may remain undiagnosed since *Bifidobacterium* is considered normal flora and potentially could be dismissed as a contaminant in laboratory specimens. Owing to its very slow growth and difficulty in identification, *Bifidobacterium* could also potentially be mistaken for other Gram positive rods such as *Actinomyces spp*.[2] For proper identification, 16 S rRNA gene sequencing should be employed. As seen in our case, and other reports in the literature—if isolated in large quantities from a clinically appropriate specimen, *Bifidobacterium* should be considered causative agent of infection.

UTIs with *Bifidobacteria* are rare. On review of literature we found one published case report of UTI associated with *Bifidobacterium scardovii* in an 88-year-old woman on immunosuppression who had recurrent episodes of UTI. The species were identified using PCR amplification and sequence analysis of the 16S rRNA gene.[13]

We feel that *Bifidobacteria* was one of the pathogenic agents (along with *candida glabrata*) in our patient's UTI. Clinically—she continued experiencing fevers in spite of micafungin therapy for *candida glabrata*. Hence meropenem was initiated as emperic broad antibiotic coverage for the urinary tract while awaiting definitive identification of pathogen in the urine culture—in this patient who had experienced repeated UTIs in the past. In the urine cytology, the yeast as well as the Gram-positive rods were too numerous to count. Hence it cannot be determined which of the two was more prominent. Fevers subsided after nephrostomy and initiation of meropenem. It will be impossible to differentiate the individual effects of nephrostomy procedure versus antibiotic. The authors feel it is a combination of antibiotic as well as relief of obstruction by the nephrostomy that contributed to patient's defervesce. We recovered significant growth of the *Bifidobacterium* species (3+) in pure culture from urine specimen obtained at the time of nephrostomy tube placement. We were able to elicit history of probiotic use in our patient. Interestingly she had been prescribed *Lactobacillus acidophilus* and not *Bifidobacterium* when she was treated with antibiotics for her previous UTI.

Although probiotics have been declared safe even in immune-compromised populations such as premature neonates,[14] there have been isolated cases of septicemia with *Bifidobacterium* in a neonates[15] and infants[16] while being on probiotic therapy. This raises concern regarding the wide-spread use of probiotics. Our review of literature reveals that the administration of probiotics to immune-compromised, chronically ill patients, premature infants and those with indwelling catheters may predispose them to probiotic sepsis and hence should be used with caution.[7 8]

Our case illustrates that in rare situations, *Bifidobacterium* may be an unusual cause of UTI. Health personnel especially physicians and laboratory technicians should be aware that *Bifidobacterium* is not just a commensal but also a potential pathogen.

Learning points

- Probiotics containing *Bifidobacteria* should be used with caution.
- *Bifidobacteria* spp are difficult to grown on routine culture media.
- If a specimen obtained from normally sterile tissue or fluid grows *Bifidobacteria* spp it should not be dismissed as a contaminant.

Competing interests None.

Patient consent Obtained.

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