

## 26-Year-Old Man With Recurrent Urinary Tract Infections

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A 26-year-old male college student presented with 1 week of constant, right lower quadrant, throbbing abdominal pain that was worse after eating and accompanied by bilious emesis. He had experienced similar, albeit less severe and self-limited, episodes of abdominal pain during the preceding 6 months. He denied fevers or chills but had lost 4.5 kg (10 lbs) in the past 6 months. During the same time period, he was treated twice with antibiotics for urinary tract infections (UTIs) after reporting symptoms of dysuria and noting “bubbles” in his urine. A urine culture was never obtained.

1. Which one of the following is true regarding UTIs in general or more specifically in this patient?

- The yearly incidence in men younger than 50 years is 100 per 10,000
- A urine culture was unnecessary before starting antibiotics
- The patient should receive antibiotics for 3 days
- Dysuria is an uncommon symptom in men with UTIs
- Escherichia coli* was the most likely culprit bacteria for his UTIs

Urinary tract infections are uncommon in men because of the longer length of the male urethra, antibacterial properties of prostatic fluid, and less frequent periurethral colonization in men. The incidence in men younger than 50 years is approximately 5 to 8 per 10,000 per year. The incidence of UTIs in men increases with age, and the lifetime prevalence is estimated at 13,000 to 14,000 per 100,000 adult men.<sup>1</sup> Although most community-acquired UTIs in women can be treated empirically with antibiotics without the need for a urine culture, a urine culture should always be obtained when a male patient presents with a suspected UTI. Simple UTIs (eg, cystitis in women) can be treated with 3 days of antibiotics<sup>2</sup>; however, UTIs in men are considered “complicated” by definition and warrant at least 7 days of antibiotic therapy. Dysuria is the most frequent presenting symptom of UTIs in both men and women.<sup>1,3,4</sup> Most UTIs are caused by gram-negative organisms from the colon that colonize the periurethral skin. *E coli* is the most common cause of UTIs in both sexes.

On examination, the patient appeared pale and cachectic. Cervical, axillary, and inguinal lymph nodes were not palpable. His abdomen was scaphoid with marked right lower quadrant tenderness without rigidity, guarding, or rebound tenderness. An ill-defined mass was palpable in the right lower quadrant. There was no tenderness in the cos-

tovertebral angle. On auscultation, bowel sounds were normoactive. Laboratory studies yielded the following results (reference ranges provided parenthetically): hemoglobin concentration, 11.9 g/dL (13.5-17.5 g/dL); mean corpuscular volume, 78.3 fL (81.2-95.1 fL); white blood cell count,  $15.9 \times 10^9/L$  ( $3.5-10.5 \times 10^9/L$ ) with 85% neutrophils; and creatinine level, 1.1 mg/dL (0.9-1.4 mg/dL). Urinalysis revealed 21 to 30 white blood cells per high-powered field, 3 to 10 red blood cells per high-powered field, no casts, and numerous bacteria. A clean-catch, midstream urine specimen showed no bacterial growth.

2. A history of which one of the following would not increase this patient's risk of recurrent UTIs?

- Diabetes mellitus
- Cystoscopy
- Benign prostatic hyperplasia
- Colovesical fistula
- Tobacco use

Urinary tract infections in men, especially if recurrent, warrant a search for an underlying structural abnormality, such as an enlarged prostate, colovesical fistulas associated with colonic malignancy or inflammatory bowel disease, and congenital malformations of the urogenital tract. Instrumentation of the urinary tract (eg, during a cystoscopy or catheterization) can result in UTIs in both men and women. Conditions that suppress immune function (eg, diabetes mellitus, infection with human immunodeficiency virus) can also predispose men to recurrent UTIs. Furthermore, uncircumcised men with poor hygiene and men who partake in unprotected sexual intercourse are also at increased risk of recurrent UTIs.<sup>1,3</sup> Although tobacco use is a risk factor for urothelial malignancies, it is not associated with an increased risk of UTIs. The site of the infection in the urinary tract can offer a clue to the underlying predisposing condition.

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See end of article for correct answers to questions.

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Infections of the upper urinary tract (eg, pyelonephritis) are typically caused by obstructive uropathy from a calculus or a tumor. In contrast, infections of the lower urinary tract (eg, cystitis, urethritis) are often the result of a sexually transmitted infection. The organism causing the UTI can also provide some insight into the underlying predisposition. Gram-negative bacteria such as *E coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* are often found in patients with anatomic obstruction.<sup>5-7</sup> One study suggested that approximately 24% of patients with a stone were infected with a urease-splitting organism.<sup>8</sup> In contrast, organisms such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Ureaplasma urealyticum*, or *Trichomonas vaginalis* are typically sexually transmitted infections.<sup>5-7</sup> Yeast (eg, candidal) infections might suggest underlying immunosuppression such as that which occurs with diabetes or corticosteroid use.<sup>5-7</sup> Catheterization results in a higher prevalence of resistant organisms, including *Pseudomonas* species and rare gram-negative organisms.<sup>9</sup>

In our patient, computed tomography of the abdomen and pelvis showed thickening of the cecum and terminal ileum with inflammatory stranding in the adjacent peritoneal fat. A fistulous communication was noted between a loop of terminal ileum and the dome of the urinary bladder.

**3. Which one of the following is the most likely diagnosis in this patient?**

- a. Acute appendicitis
- b. Lymphoma
- c. Crohn disease
- d. Behçet disease
- e. Ulcerative colitis

Acute appendicitis is unlikely given the recurrent nature of the symptoms. The cachexia and weight loss suggest a chronic illness and would be compatible with lymphoma; however, the absence of lymphadenopathy and lymphocytosis argue against this diagnosis. Crohn disease follows a bimodal age distribution, with the first peak between ages 15 and 30 years, which is compatible with this patient's presentation. Additionally, the recurrent abdominal pain, nausea, vomiting, and weight loss, along with the ileal thickening on computed tomography and an enterovesical fistula, could all be related to Crohn disease. Although similar to Crohn disease in some aspects, ulcerative colitis is unlikely because it does not affect the small intestine, is only a mucosal process, and does not cause fistulas. Although Behçet disease, a vasculitis that typically manifests with recurrent oral and genital ulcerations, is a possibility, it is unlikely in the absence of the ocular manifestations and arthritis that typically accompany this disease. The most likely diagnosis in this young man with evidence of terminal ileal thickening and an enterovesical fistula is Crohn disease.

After blood cultures were obtained, the patient was administered levofloxacin and metronidazole to cover enteric pathogens likely to cause UTIs in the setting of an enterovesical fistula. These organisms include gram-negative bacteria such as *E coli*, *Klebsiella* species, and *Proteus* species, as well as anaerobic organisms such as *Pseudomonas* and *Clostridium* species.

**4. Which one of the following is the next best test to confirm the diagnosis?**

- a. Cystoscopy
- b. Colonoscopy
- c. Esophagogastroduodenoscopy
- d. Capsule endoscopy
- e. No further evaluation; initiate treatment

Cystoscopy might demonstrate the fistulous opening but is unlikely to provide any further diagnostic information. Colonoscopy would be useful to assess the activity, extent, and severity of the disease. In addition, biopsy specimens could be obtained during colonoscopy, providing histologic confirmation of the diagnosis. Crohn disease can affect the upper gastrointestinal tract; however, this patient has no symptoms to suggest upper gastrointestinal tract involvement, making an upper endoscopy relatively low yield. Capsule endoscopy is unlikely to add further diagnostic information over that provided by enterography. Further, in a patient with active intestinal inflammation and obstructive symptoms (ie, abdominal pain, nausea, and vomiting), capsule retention proximal to the area of inflammation is a risk. Therapy for Crohn disease often requires the use of immunosuppressive medications; therefore, the diagnosis should be confirmed with tissue biopsy, and diagnoses of atypical infections and malignancy should be excluded before initiating treatment.

Colonoscopy showed a stricture in the region of hepatic flexure with associated mucosal edema, ulceration, and nodularity. There was a fistulous opening in the area. Biopsy specimens showed active chronic colitis with inflammatory polyps. Cytomegalovirus and acid-fast stains were negative.

**5. Which one of the following is true about this patient's disease?**

- a. Organ systems outside of the gastrointestinal tract are never affected
- b. Once the patient recovers, he will develop lifelong immunity to the disease
- c. He should abstain from cigarette smoking because it increases his risk of a disease flare
- d. He should use nonsteroidal anti-inflammatory drugs regularly because they are protective against disease flares
- e. This specific form of inflammatory bowel disease poses no increased risk of colon cancer

Approximately 25% of patients with inflammatory bowel disease develop extraintestinal manifestations.<sup>10</sup> These manifestations include joint disease (eg, sacroiliitis, ankylosing spondylitis), ocular involvement (eg, iritis, episcleritis, uveitis), skin involvement (eg, erythema nodosum, pyoderma gangrenosum), and biliary involvement (eg, primary sclerosing cholangitis). These manifestations often correlate with the activity of the disease, with the exception of primary sclerosing cholangitis and ankylosing spondylitis. The clinical course of Crohn disease is highly variable, but most patients have recurrent episodes of symptomatic disease interspersed with periods of remission. Cigarette smoking increases the risk of Crohn disease flares as well as the severity of the disease. Thus, patients should be counseled to discontinue tobacco smoking. Nonsteroidal anti-inflammatory drug use can precipitate disease flares, and patients should be counseled against their use as well. Patients with substantial colonic involvement by ulcerative colitis or Crohn disease are at increased risk of colon neoplasia after having the disease for 8 to 10 years. Colorectal surveillance is required in these patients.

Given the extent of disease and the colonic stricturing, a surgical consultation was obtained for this patient. He underwent repair of the colovesical fistula with resection of the terminal ileum, cecum, and ascending colon with ileo-ascending colonic anastomosis. After the operation, his symptoms completely resolved, and he was dismissed from the hospital 1 week later. Subsequently, he began receiving medical therapy for maintenance of Crohn remission.

## DISCUSSION

Urinary tract infections are uncommon in men, with an incidence of 5 to 8 per 10,000 per year in men aged 21 to 50 years.<sup>4</sup> In contrast, the incidence among young women is thought to be 30 times higher. This difference between the 2 sexes is attributable to the longer male urethra, antibacterial substances in prostatic fluid, and a lower incidence of urethral colonization in men because of differences in the periurethral environment. This has led to the idea that all UTIs in men should be considered complicated and warrant investigation for an underlying predisposition. Recurrent UTIs in men require at minimum a urologic evaluation because an underlying etiology is likely.<sup>4,11</sup> Screening for immunologic disorders that might increase the risk of infection (eg, diabetes, infection with human immunodeficiency virus, corticosteroid use, hematologic malignancies) is also advised.

Many conditions can predispose men to UTIs. Obstruction (eg, benign prostatic hyperplasia, stones, traumatic strictures, urogenital malignancy) can lead to urinary stasis and an increased risk of infection. Instrumentation of the

urinary tract performed for a wide variety of reasons (eg, evaluation of voiding, during hospitalization) is another risk factor that is independent of sex. As many as 25% of hospitalized patients have been reported to have a urinary catheter inserted at some point during hospitalization. A quarter of these patients go on to develop UTIs. As is the case with any recurrent infection, an underlying immunosuppressed state should be considered.<sup>1,3,4</sup> Finally, the possibility of an abnormal fistulous communication between the gastrointestinal tract and the urinary tract should be suspected, whether resulting from an ulcerating neoplasm, diverticulitis, or Crohn disease.

Crohn disease is an important consideration in patients with recurrent UTIs when no other cause is ascertained. Most commonly, UTIs in these patients are the result of direct extension of inflammation from a contiguous loop of inflamed bowel. In addition to the classic symptoms of a UTI (eg, dysuria, frequency, urgency), these patients often report pneumaturia (ie, "bubbles" in the urine) and occasionally note fecaluria.<sup>12</sup> These symptoms could be the first manifestation of Crohn disease in an otherwise healthy adult.

The clinical symptoms of UTIs in men are similar to those seen in women and include dysuria, urgency, and frequency. These symptoms have a positive predictive value of 75% for a UTI in men.<sup>13</sup> Although suprapubic pain suggests a diagnosis of cystitis, flank pain is suggestive of pyelonephritis. Other symptoms that may alert the physician to alternative etiologies include milky discharge and pruritus in gonococcal urethritis, perineal pain with cloudy urine in acute prostatitis, and a history of pneumaturia or fecaluria in patients with enterovesical or colovesical fistulas.

Initial evaluation consists of a urinalysis with microscopy, preferably on a clean-catch, midstream specimen. A positive Gram stain is 90% sensitive and 80% specific for infection.<sup>1</sup> It should be noted that a negative urine Gram stain, particularly on unspun urine, does not rule out a UTI. The sensitivity and specificity of uncentrifuged urine is 94% and 90%, respectively, when 100,000 colony-forming units (CFUs) per milliliter are isolated.<sup>13</sup> The degree of pyuria is an extremely useful tool with a sensitivity of 85% to 90% if greater than 10 white blood cells per milliliter are present on urinalysis. Dipstick tests (eg, leukocyte esterase, nitrite) are specific but not sensitive for diagnosis. The criterion standard for diagnosis is a urine culture with sensitivities. The exact number of bacteria necessary to diagnose a UTI in men is controversial: some advocate treatment for any man with bacteriuria regardless of the number, others recommend treatment for greater than 10,000 CFUs, and still others advise treatment for greater than 100,000 CFUs (using spun or unspun urine). For patients presenting with recurrent UTIs, appropriate evaluation with urologic

testing, cross-sectional imaging, testing for acquired or inherited immunodeficient conditions (eg, immunoglobulin deficiency, lymphoma, diabetes, infection with human immunodeficiency virus) should be pursued on the basis of the suspected predisposing condition.

Treatment recommendations are based largely on studies conducted in women, children, and those of advanced age, with little or no literature on young men. The decision to treat young men can be challenging, especially because they might be symptomatic without findings on urinalysis or the required number of CFUs on urine culture. Treatment decisions should be based on the organism and sensitivities when available. For uncomplicated infections, trimethoprim-sulfamethoxazole and fluoroquinolones are the first-line agents. The duration of treatment is typically 7 to 10 days but may need to be extended when the prostate is involved or when the specific organism identified merits more aggressive treatment.<sup>2,4</sup>

#### REFERENCES

1. Cunha B. Urinary tract infection, males. *eMedicine*. Updated October 19, 2009. <http://emedicine.medscape.com/article/231574-overview>. Accessed March 10, 2011.
2. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med*. 2002;113(suppl 1A):5S-13S.
3. Griebing T. Urinary tract infection in men. In: Litwin MS, Saigal CS, eds. *Urologic Diseases in America*. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Washington, DC: US Government Printing Office, 2007, NIH Publication No. 07-5512 (pp 623-645).
4. Hummers-Pradier E, Ohse AM, Koch M, et al. Urinary tract infection in men. *Int J Clin Pharmacol Ther*. 2004;42(7):360-366.
5. Chamberlain NR. Bladder, kidney, and prostate. In: Chamberlain NR, ed. *The Big Picture: Medical Microbiology*, 1st ed. New York, NY: McGraw-Hill; 2009:341-346.
6. Orenstein R, Wong ES. Urinary tract infections in adults. *Am Fam Physician*. 1999;59(5):1225-1234, 1237.
7. Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. *Clin Infect Dis*. 2004;38(8):1150-1158.
8. Qaader DS, Yousif SY, Mahdi LK. Prevalence and etiology of urinary stones in hospitalized patients in Baghdad. *East Mediterr Health J*. 2006;12(6):853-861.
9. Ko MC, Liu CK, Woung LW, et al. Species and antimicrobial resistance of uropathogens isolated from patients with urinary catheter. *Tohoku J Exp Med*. 2008;214(4):311-319.
10. Monsen U, Sorstad J, Hellers G, et al. Extracolonic diagnoses in ulcerative colitis: an epidemiological study. *Am J Gastroenterol*. 1990;85:711-716.
11. Lipsky BA. Urinary tract infections in men: epidemiology, pathophysiology, diagnosis, and treatment. *Ann Intern Med*. 1989;110(2):138-150.
12. Heyen F, Ambrose N, Allan R, Dykes P, Alexander-Williams J, Keighley M. Enterovesical fistulas in Crohn's disease. *Ann R Coll Surg Engl*. 1989;71(2):101-104.
13. Wiwanitkit V, Udomsantisuk N, Boonchalermvichian C. Diagnostic value and cost utility analysis for urine Gram stain and urine microscopic examination as screening tests for urinary tract infection. *Urol Res*. 2005;33(3):220-233.

**Correct Answers: 1. e, 2. e, 3. c, 4. b, 5. c**