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Antibiotic-Resistant Urinary Tract Infection in a Bahamian Woman: A Case Report

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Abstract

Bacterial resistance to antibiotics is becoming a major public health challenge in the Bahamas. Indiscriminate use of antibiotics by medical practitioners is a major contributor to this problem. We describe a 53-year-old woman who presented with symptoms of a urinary tract infection. Empiric treatment with first- and second-line antibiotics, namely trimethoprim-sulfamethoxazole and ciprofloxacin, respectively, were ineffective in clearing the infection. After culture and sensitivity testing via minimum inhibitory concentration analysis, nitrofurantoin proved to be the only effective oral antibiotic.

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Introduction

Minor injuries, such as abrasions, may still lead to death, even in this age of modern medicine. Health literature and the media have highlighted cases of morbidity and mortality resulting from antibiotic resistance. Based on data from the Centers for Disease Control and Prevention, approximately 2 million people in the United States are affected by antibiotic-resistant illnesses annually, resulting in approximately 23,000 deaths [1].

A number of antimicrobial agents have proven ineffective against organisms such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*. The medical arena has also witnessed the emergence of resistant strains of tuberculosis, pulmonary and urinary tract pathogens, and sexually transmitted pathogens, including *Treponema pallidum* and *Neisseria gonorrhoeae* [2]. The indiscriminate use of antibiotics in medical practice has been a major factor contributing to this crisis. Other factors include premature discontinuation of antibiotic regimens by patients, use of expired antibiotics, and antibiotic use in livestock farming.

Due to the decline in the effectiveness of currently available antibiotics, it is of utmost importance that physicians establish good prescribing habits in both outpatient and inpatient settings. Physicians must invest greater effort to prevent further diminution of the effectiveness of these life-saving drugs, thereby preventing a global healthcare catastrophe. The following describes a case of antimicrobial resistance to two drugs commonly used to treat urinary tract infections (UTIs), namely trimethoprim-sulfamethoxazole (TMP-SMX) and ciprofloxacin.

Case description

A 53-year-old woman presented to the Family Medicine Clinic with mild generalized abdominal pain and urinary frequency. She reported having symptoms for several weeks that had progressed over the previous few days, prompting her to seek care. She denied having any dysuria, lower back pain, or fever. Although there was no reported incontinence, she stated that she passed urine more frequently to avoid an accident. The patient's past medical history included a diagnosis of pre-diabetes in the previous year, and she admitted being compliant with metformin and acarbose. Additionally, she had two normal spontaneous vaginal deliveries and never had any surgeries.

On examination, the patient was afebrile with mild suprapubic tenderness and no tenderness of the lumbar region. Auscultation of the heart and lungs was normal, and there were no neurological deficits. A urine dipstick was equivocal and revealed no obvious abnormalities except trace leukocyte esterase and trace blood. Investigations were ordered, including a complete blood count, glycated hemoglobin levels (HbA1c), and a comprehensive metabolic panel. A midstream urine for microscopic examination and culture and sensitivity testing was also ordered. Additionally, an ultrasound scan of the kidneys, urethra, and urinary bladder (KUB) was requested and a follow-up appointment was scheduled for the following week.

The following results of the investigations were reviewed upon the patient's return to the clinic: white blood cell count 5.3 K/UL (4.8–10.8 K/UL), hemoglobin 13.7 g/dL (12.0–16.0 g/dL), hematocrit 44.3% (36%–47%), platelets 287 K/UL (140–420 K/UL), HbA1c 6.0% (4.5%–6.0%), BUN 14 mg/dL (7–18 mg/dL), creatinine 0.7 mg/dL (0.6–1.3 mg/dL), and the KUB scan revealed no abnormalities. Abnormal findings were confined to the midstream urine results. A urine dipstick analysis demonstrated positive nitrite and 1+ leucocyte esterase. Microscopic examination of the urine showed the presence of bacteria and 25–50 white blood cells per high-powered field. A urine culture showed greater than 100,000 col/mL of mixed coliform species. The patient was diagnosed with chronic cystitis and was prescribed a course of oral TMP 160 mg/SMX 800 mg (twice daily for 14 days).

On follow-up 3 weeks later, the patient reported no resolution of the suprapubic tenderness or urinary frequency. Another urine culture was ordered and showed no change in the colony count of coliform bacteria. The patient was switched to ciprofloxacin 500 mg twice daily for 1 week. Upon completion of the course of antibiotics, the patient returned to the clinic and reported persistence of the suprapubic pain, new-onset dysuria but no fever, and increased urinary frequency. A third midstream urine sample was sent for analysis. Culture and sensitivity testing were performed, revealing greater than 100,000 col/mL of *Escherichia coli*. Minimum inhibitory concentration testing showed resistance to ampicillin, cefotaxime, ceftazidime, tetracycline, and TMP-SMX, minimal susceptibility to ciprofloxacin and ceftriaxone, and significant susceptibility to nitrofurantoin. A prescription for nitrofurantoin 100 mg orally twice daily for 7 days was given to the patient. A follow-up urine culture was obtained after the 7 days of treatment with nitrofurantoin. Upon return to clinic on day fourteen post-therapy, the patient remained asymptomatic and the follow-up urine culture was negative.

Discussion

This case highlights the growing problem of multidrug-resistant bacterial infections in the Bahamas. Unfortunately, this case is not unique, as other authors have documented similar findings. [3, 4] Although bacterial resistance to antibiotics has been well recognized for over a decade, the number of Bahamian patients affected is currently unknown. This article focuses exclusively on UTIs resistant to two commonly prescribed drugs. Coliform species are the most common pathogens isolated from

positive urine cultures in both the outpatient and inpatient settings in the Bahamas. Historically, the overwhelming majority of presentations were uncomplicated and easily treated with oral antibiotics. However, in the primary care setting today, UTIs are becoming increasingly difficult to treat; some documented cases have even progressed to urosepsis, requiring patients to be hospitalized for intravenous management. In cases requiring hospitalization, urinary tract pathogens have been resistant to treatment with oral TMP-SMX and/or ciprofloxacin. Understanding both the mechanisms of action of the drugs and the mode by which bacteria develop resistance to them may be the best approach to mitigating this problem.

The alarming global increase in resistance to TMP-SMX [5-7] has serious public health implications given that TMP-SMX is the first-line treatment for uncomplicated UTIs in the Bahamas. TMP and SMX act synergistically to impede two important phases of nucleic acid and protein biosynthesis in bacteria, thus disrupting the folate synthesis pathway [8]. TMP inhibits thymidine, an essential precursor for the formation of DNA, by inhibiting the enzyme dihydrofolate reductase, which is responsible for the conversion of dihydrofolate to tetrahydrofolate. SMX exerts its action by competing with para-aminobenzoic acid, thus impeding its conversion to dihydrofolic acid. Several mechanisms are responsible for the acquisition of bacterial resistance to TMP-SMX, including the development of drug-resistant genes, plasmid-coded dihydrofolate reductase, and dihydropteroate synthetase [9].

As in the above case, it has been noted that ciprofloxacin-resistant bacteria are also sometimes resistant to TMP-SMX and other antibiotic agents [10]. Ciprofloxacin is a second-generation fluoroquinolone with broad-spectrum antibiotic activity. It inhibits two essential bacterial enzymes, DNA gyrase and topoisomerase IV, thereby preventing the unwinding of the DNA strand [11]. Bacteria acquire resistance to fluoroquinolones via diverse and elaborate mechanisms. Correia et al. reported that the principal means involve one or a combination of target-site gene mutations that alter the drug-binding affinity of target enzymes [12]. Alternative mechanisms of resistance include mutations resulting in increased efflux or decreased uptake of drugs, thereby reducing intracellular levels of fluoroquinolones and acquisition of plasmid-encoded resistance genes, leading to the formation of target protection proteins, drug-modifying enzyme, or multidrug efflux pumps.

One antibiotic that is currently being used to tackle the resistance problem in the primary care setting in the Bahamas is nitrofurantoin. Introduced in 1953, it has been proven very effective in the treatment of uncomplicated UTIs [13, 14]. A company called Nostrum Laboratories recently acquired the rights to produce nitrofurantoin, and consequently, the drug's price has increased tremendously. Though the high cost of such an effective antibiotic may appear to be a disadvantage, one major benefit is that fewer people have access to it, thus maintaining its status as a last resort for UTI treatment. Nitrofurantoin is readily absorbed in the gut and is effective against a range of both gram-positive and gram-negative bacteria, including Enterobacteriaceae. Because of the multiplicity of its mechanisms of action, bacteria are less resistant to this drug compared with other antibiotics. Nitrofurantoin inhibits ribosomal proteins, which impedes DNA and RNA production and cell wall synthesis, causing bacterial cell death. Despite the development of resistance to other drugs, nitrofurantoin remains an effective option against UTIs in the Bahamas.

Conclusion

This case represents an unfortunate predicament encountered daily in clinical practice. The emergence of multidrug-resistant bacteria is a foreseeable public health challenge in the Bahamas. Clinicians must recognize the existence of bacterial resistance to empirical antibiotics prescribed for the treatment of

uncomplicated UTIs to reduce the dissemination of resistance. Although TMP-SMX and ciprofloxacin have been used as first-line treatments for UTIs, their efficacy is rapidly declining. Fortunately, nitrofurantoin, which is less widely used by clinicians because of the high price, remains an effective option as a drug of last resort. More effort is required in directing policies regarding antibiotic prescribing, and their inappropriate and unnecessary administration should be strongly discouraged.

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