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Original Article

An Outbreak of Postoperative Rapidly Developing and Multidrug-Resistant *Klebsiella Pneumoniae* Urosepsis Due to a Contaminated Ureteroscope

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Abstract

Introduction: Outbreaks caused by microorganisms contaminating the inside of rigid ureteroscopes are extremely rare. Some of these outbreaks, especially those caused by multidrug-resistant (MDR) infections, can cause serious problems, even death. Among these serious infections, we have no data about *Klebsiella pneumoniae* outbreaks caused by rigid ureteroscopes and their management and consequences.

Aim: We aimed to report the outcomes of an outbreak of rapidly developing MDR *K. pneumoniae* urosepsis linked to rigid ureteroscopy (URS).

Materials and methods: Data for 68 patients who had ureteroscopic lithotripsy (URS-L) operations using the same ureteroscope were retrospectively reviewed. Among them, 17 patients with postoperatively developing urosepsis were included in the study. Samples were taken from the operating room, camera heads, endoscopes, and ancillary instruments for culture workup. *K. pneumoniae* was produced in a swab culture obtained from the water inlet channel of the ureteroscope.

Results: All patients had sepsis signs that developed within hours (2-7 hours). MDR *K. pneumoniae* was detected in the urine cultures of all patients. It was sensitive only to amikacin, tigecycline, colistin, and netilmicin. All patients were treated with tigecycline (100 mg intravenous daily). It was observed that *K. pneumoniae* growth continued without any symptoms in the first and fourth weeks of follow-up in 4 patients. These patients were accepted as colonization; no additional treatment was given.

Conclusions: In the case of rapidly developing urosepsis after the URS procedure in a patient, instruments, devices, and endoscopes should be immediately checked for contamination to prevent the emergence of an outbreak.

Keywords

Klebsiella pneumoniae, ureteroscopes, ureteroscopy, urosepsis

INTRODUCTION

Rigid ureteroscopes are widely used for diagnosing and treatment of stone disease, strictures, and ureteric tumours. Although the risk of device-related transmission of infection is very low, various outbreaks can occur if attention is lacking. Rigid ureteroscopes can be contaminated with microorganisms from body fluids. The multiple, narrow lumens in ureteroscopes make the cleaning of rigid ureteroscopes a complex task. Shortcomings and errors during the disinfection process could lead to the survival of pathogens. Microorganisms that remain after insufficient disinfection may form a biofilm layer inside the instruments. After this stage, there is a risk of cross-contamination between patients. In order to re-use the same ureteroscope, the device must be completely disinfected.

It was reported that among various endoscopes, the flexible ones especially host more pathogens and they cause outbreaks.[1,2] However, outbreaks caused by microorganisms contaminating the inside of rigid ureteroscopes are extremely rare.[3] Some of these outbreaks, especially those caused by multidrug-resistant (MDR) infections, can cause serious problems, even death. Among these serious infections, we have no data about *Klebsiella pneumoniae* outbreaks caused by rigid ureteroscopes and their management and consequences.

We report an outbreak of MDR *K. pneumoniae* urosepsis linked to rigid ureteroscopy (URS), along with a discussion of outbreaks caused by endoscopes (cystoscopes, rigid ureterorenoscopes, and flexible ureteroscopes) commonly used in endourological procedures.

AIM

We think that the present study will contribute to the literature and will guide our colleagues in clinical practice. To our best knowledge, this is the first report of an outbreak of *K. pneumoniae* due to a contaminated ureteroscope.

MATERIALS AND METHODS

Study design

In order to publish the patient data used in the study, data usage permission was obtained from the hospital management (date: 23.10.2020). Informed consent was provided by all patients to share their individual data. Data of 68 patients who underwent ureteroscopic lithotripsy (URS-L) operation using the same ureteroscope between November 2018 and February 2019 were retrospectively reviewed. Among them, 17 patients with urosepsis were included in the study. Patients' demographic characteristics, underlying diseases, date and type of surgeries, clinical evaluations, and treatment outcomes were recorded.

Sepsis was defined as identification of two or more systemic inflammatory response syndrome criteria (temperature <36°C or >38°C; white cell count >12000 or <4000/mm^3; respiratory rate >12/min or $PaCO_2$ <32 mmHg; heart rate >90/min;), in addition to known or suspected infection.[4] Comorbidities of patients were evaluated according to the Charlson Comorbidity Index (CCI).[5]

Preoperative prophylaxis and disinfection protocol

All patients were evaluated with urine culture prior to URS. If the culture was positive, appropriate treatment was given according to the antibiogram and a negative culture was seen. Antibiotic prophylaxis was administered with a third-generation cephalosporin (a single dose of 1 gram intravenous ceftriaxone 1 hour before surgery).

The disinfection protocol in our hospital was as follows: opening of all joint points on the ureteroscopes, washing with tap water and immersing in two-component high-level disinfection solution (Discleen Endo PAA® Base and Discleen Endo PAA® Activator, Bochemia, Liberec, Czech Republic) for 5 min. A final rinse with sterile water was executed to clean solution residues.

Patient evaluations

Patients with suspected postoperative urosepsis were assessed with physical examination, complete blood count, C-reactive protein (CRP), serum biochemical analysis, coagulation tests and urinalysis, midstream urine culture and blood culture/antibiogram tests. All patients were evaluated with computed tomography to exclude potential complications such as pyonephrosis, renal or perirenal abscess.

Investigation of the source of the outbreak

The Infection Control Committee was consulted about the situation. Samples were taken from the operating room, camera heads, endoscopes, and ancillary instruments for culture study. Swabs from environmental samples were enhanced in trypticase lineage broth (TSB) for 7 days at 37°C. These samples were filtered through a 0.2-mm cellulose membrane filter. Disinfectants and soaps were transferred to TSB-containing neutralizers (3% Tween, 80.3% saponin, 0.1% histidine, 0.1% cysteine). The enriched TSB samples were then cultured on Columbia and MacConkey plates. All channels of the ureteroscope were irrigated with sterile saline solution (20 ml) and samples were collected by swabbing the channel ends. Then 10 ml of the flashing solution samples were filtered and neutralized. Filters and swabs were processed in the same way. The identification of pathogen species and their susceptibility profiles were performed in an automated manner by the VITEK 2 system.

In a swab culture obtained from the water inlet channel of the ureteroscope, *Klebsiella pneumoniae* was produced.

After this finding, it was understood that this was an outbreak and that the sterile solution had not been passed through all the holes in the endoscope at high pressure. The endoscope was removed from use. After that, no other cases were detected. The Infection Control Committee identified the source of contamination as a patient colonized with *K. pneumoniae* who had URS performed prior to the outbreak and was hospitalized in the intensive care unit.

Statistical analysis

Continuous variables are shown as mean ± SD and categorical variables are shown as numbers and percentages. The SPSS 22.0 (IBM, NY, USA) program was used for calculations.

RESULTS

Ureteroscopic lithotripsy was performed due to upper ureter stones for 7 patients, lower ureter stones for 3 patients, middle ureter stones for 1 patient and renal pelvis stones for 6 patients. Their mean age was 40.7±16.2 years. Eleven (65%) of the patients were male and 6 (35%) were female. The mean body mass index was 24.8±4.9 kg/m^2. Six of the patients had one or more comorbidities; 3 patients had diabetes mellitus (DM), 2 patients had hyperlipidemia, and 1 patient had myocardial infarction (MI), cerebrovascular occlusion (CVO), and peptic ulcer. The mean CCI score was 1.0±1.2. Among the patients, 5 (3 women, 2 men) had preoperative DJ stent, and 1 male patient had percutaneous nephrostomy. Within this time period, 68 patients were operated with the contaminated endoscope and 17 of these patients (25%) were infected with MDR *K. pneumoniae*.

All patients had sepsis signs that developed within hours (2-7 hours). All patients were treated in the urology department; no patient required admission into the critical care unit.

White blood cell (WBC) count and CRP values were high in all patients. The mean WBC was 13.4±2.2×10^3 µL (range 10.5–18) and the mean CRP was 301.3±23.5 mg/L (range 280–350) **(Table 1)**.

On CT imaging, no pathology requiring drainage such as hematoma, abscess or perirenal collection was observed in any patient. Of all 17 patients, 10 had JJ stents and 7 had ureter catheters. Ureteral catheters were removed 1 day after the operation and DJ stents were removed under local anesthesia after positivity of urine cultures.

While there was no growth in blood culture in any patient, MDR *K. pneumoniae* proliferated in urine cultures of all patients **(Table 2)**. In the antibiogram study, it was sensitive only to amikacin, tigecycline, colistin, and netilmicin. The bacteria were even resistant to carbapenem. With the recommendation of the Infection Control Committee, all patients were treated with tigecycline (100 mg intravenous daily). Patients were discharged after urine culture sterilization and WBC/CRP values normalized.

Table 1. Demographics and clinical characteristics of the patients

Parameters	n=17
Age, (years) (mean±SD)	40.7±16.2
Sex, n (%)	
Male	11 (65%)
Female	6 (35%)
BMI, (kg/m^2) (mean±SD)	24.8±4.9
CCI score, (mean±SD)	1.0±1.2
WBC, ×10^3 µL (mean±SD)	13.4±2.2
CRP, mg/L (mean±SD)	301.3±23.5
Comorbidities, n (%)	
DM	3 (17.6%)
MI	1 (5.9%)
CVO	1 (5.9%)
Peptic ulcer	1 (5.9%)
Hyperlipidemia	2 (11.8%)
Stone location, n (%)	
Lower ureter	3 (17.6%)
Middle ureter	1 (5.9%)
Upper ureter	7 (41.2%)
Renal pelvis	6 (35.3%)
Surgery, n (%)	
Rigid URS-L	17 (100%)
Preoperative drainage	
dj stent	5 (29.4%)
Nephrostomy	1 (5.9%)
Patients operated with contaminated endoscopes	68
Patients infected with MDR *K. pneumoniae* from contaminated endoscopes	17 (25%)

BMI: body mass index; WBC: white blood cells; CRP: C-reactive protein; CCI: Charlson comorbidity index; URS-L: ureterorenoscopic lithotripsy

It was observed that *K. pneumoniae* growth in urine continued without any symptoms in the first and fourth weeks of follow-up in 4 patients. These patients were accepted as colonization; no additional treatment was given.

DISCUSSION

Standard endoscopes used in endourology carry the risk of contamination because they are used repeatedly for patients. Therefore, they must be decontaminated before use for the next patient. Decontamination processes include pre-cleaning, cleaning, disinfection, rinsing, drying and storage steps. Errors and deficiencies in decontamination processes lead to the survival of pathogens and cross-con-

Table 2. Case definitions, treatments, and outcomes of patients identified during the outbreak

Case No	Age/sex	Indication	Urosepsis onset (hour)	Fever attacks (number)	Positive culture	Tigecycline time (day)	Status
1	68/M	ureteral stone	5	5	urine	14	recovered
2	45/F	ureteral stone	6	4	urine	14	recovered
3	52/M	ureteral stone	5	6	urine	14	colonization
4	37/F	ureteral stone	2	5	urine	14	recovered
5	25/M	ureteral stone	3	4	urine	10	recovered
6	41/M	ureteral stone	5	7	urine	14	colonization
7	22/F	ureteral stone	3	6	urine	11	recovered
8	29/M	ureteral stone	7	4	urine	13	recovered
9	55/M	ureteral stone	5	5	urine	14	recovered
10	62/M	diagnostic	3	3	urine	14	colonization
11	43/F	ureteral stone	4	4	urine	11	recovered
12	32/F	ureteral stone	5	3	urine	10	recovered
13	21/M	ureteral stone	3	2	urine	10	recovered
14	35/M	ureteral stone	2	4	urine	14	colonization
15	41/M	ureteral stone	3	6	urine	10	recovered
16	48/M	ureteral stone	5	7	urine	14	recovered
17	36/F	ureteral stone	7	4	urine	10	recovered

tamination between patients. If this is not noticed, outbreaks can occur.

Few studies have reported on outbreaks caused by endoscopes used in endourological procedures. Wendelboe et al. reported a *Pseudomonas aeruginosa* outbreak associated with outpatient cystoscopy in 23 patients over a 4-month period. *P. aeruginosa* was detected in both blood and urine cultures of patients. Seventeen of the cases had urinary tract infections (UTI) alone, 2 of them had bacteremia alone, and 4 of them had UTI plus bacteremia.[6] Jimeno et al. reported a *Salmonella* spp. outbreak caused by a cystoscope in four patients who underwent cystoscopy within a 2-month period. They achieved eradication of the outbreak by the intensification of the cystoscope cleaning and disinfection protocol.[7] Koo et al. reported an outbreak of MDR New Delhi metallo-β-lactamase *K. pneumoniae* and *E. coli* UTIs caused by the camera head in 5 patients who underwent cystoscopy. The outbreak was controlled after disinfecting the camera head with ethylene oxide and use of a single-use camera sheath.[8]

To date, four outbreaks caused by ureteroscopes were reported. Chang et al. determined an outbreak of ertapenem-resistant *Enterobacter cloacae* UTIs. In their study, pulsed-field gel electrophoresis (PFGE) analysis revealed that all 15 isolates (patients) and three isolates (ureteroscope) shared a common pattern with minor variance. The pathogen could not be eliminated until ethylene oxide was added to the sterilization protocol.[3] Kayabas et al. reported an outbreak of *P. aeruginosa* UTI caused by inadequately disinfected surgical devices (cystoscopes, ureteroscopes, resectoscopes, forceps, and nephroscopes) after various endourological procedures.[9] Mansour et al. reported another *P. aeruginosa* UTI in 10 patients who underwent a URS procedure 24 to 72 hours before. This outbreak was due to the use of inadequately disinfected water. In their hospital, an ultraviolet disinfection system was used for bladder irrigation water. This system failed to disinfect the water and an outbreak occurred.[10] Kumarage et al. reported an outbreak of MDR *P. aeruginosa* UTIs linked to flexible URS. The risk factors identified included surface cuts, stretching and puckering of the outer cover in both ureteroscopes, absence of bedside cleaning, overnight delay between ureteroscopy and decontamination, inadequate drying after decontamination, and non-traceability of connector valves. After removing these two ureteroscopes, they did not encounter any more cases of MDR *P. aeruginosa*.[11]

Outbreaks after cystoscopy or URS may be caused by the environment in which the procedure is performed or by the assistant medical staff, in addition to endoscopic instruments. Pena et al. reported an outbreak of carbapenem-resistant *P. aeruginosa* in 59 patients who had cystoscopy within a 1.5-year period and they saw that this outbreak resulted from contamination of the cystoscopy room via an unsealed drain with PFGE analysis.[12]

High-level disinfection solutions are recommended for the decontamination of endoscopes.[13] Glutaraldehyde, ortho-phthalaldehyde, peracetic acid/hydrogen peroxide, and electrolyzed acid are the main high-level disinfectants used. In our clinic, we use a peracetic acid-based two-component liquid disinfection agent (Discleen Endo PAA®). Although we decontaminated in accordance with the dilution and time instructions of the company that produc-

es the disinfection fluid, our experience of this outbreak suggested that there could be a mistake caused by assistant medical staff. The source of the outbreak was the fact that the water inlet channel of the ureteroscope was not sufficiently flushed with disinfection fluid. As a result, even if the ureteroscope was kept in disinfection fluid for a sufficient time, the water inlet channel remained contaminated. For disinfection of the endoscopes, assistant medical staff needs specific training including cleaning, high-level disinfection, and sterilization procedures. The outbreak we experienced was due to the lack of training about disinfection rules and the inability to authorize specific staff about this issue.

In addition to causes due to contamination of endoscopic devices and lack of sterilization, the main risk factors for the development of urosepsis include causes linked to immune system suppression like HIV and AIDS, corticosteroid intake, organ transplantation, cancer and cancer treatments; advanced age, diabetes mellitus, fecal incontinence (inability to control bowel movements), female gender, immobility, incomplete urinary drainage or urinary retention, polycystic renal disease, pregnancy, surgeries or urinary tract surgeries, stone or benign prostate growth, urethral stenosis or catheter use for urinary tract obstruction, and urinary drainage due to other causes. Diabetes mellitus is perhaps a predominant disease among these predisposing causes. The incidence of urosepsis increases in patients with long duration and severe DM. High blood glucose and defective host immune factors increase the predisposition to infection. Additionally, hyperglycemia increases intracellular calcium levels and interacts with actin causing neutrophil function disorder and resulting in diapedesis and phagocytosis. Vaginal candidiasis and vascular disease play roles in recurrent infections. A recent meta-analysis assessing 13 studies (5 prospective) including 5597 patients reported that postoperative urosepsis development risk was 5.0% after ureteroscopy used for urinary system stone disease treatment. Advanced age, DM, ischemic heart disease, preoperative stent insertion, positive urine culture, and long operation duration were found to be associated with postoperative urosepsis development risk.[14] We think comorbid diseases in our patients with DM, MI, and CVO contributed to the development and progression of the urosepsis tableau.

Many factors in the perioperative period cause disruptions of the immune system and increase the postoperative infection and sepsis development risk. After surgery, surgical stress induces a neuroendocrine response activating the central nervous system (CNS) and hypothalamic pituitary adrenal (HPA) axis suppressing the T cell response and cellular immunity for several days and affecting cytokine production to a clear degree. Additionally, postoperative pain and medications used are known to play a role in the immune system suppression.[15] Amodeo et al. showed a clear reduction in TNF-α, IL-2, IFN-γ, and lymphoproliferation in the early postoperative period with disrupted cell-mediated immunity. TNF-α and IFN-γ suppression continued for a period longer than 48 hours postoperatively while IL-2 and lymphoproliferation returned to normal trends. Additionally, while there was no negative correlation between morphine and cytokine production, they identified inverse correlations between age and morphine and between age and lymphoproliferation. We did not study factors evaluating the immune response in our study, but we think weakening or disruption of the postoperative immune response was an additional worsening factor in our urosepsis outbreak.

The present study has some limitations. The major limitation is that the study has a retrospective nature. Another potential limitation is that we did not investigate clonal analysis of *K. pneumoniae* isolates with PFGE analysis which can ensure that more effective control measures are taken to terminate the outbreak.

CONCLUSIONS

In the case of rapidly developing urosepsis after endourological procedures, it should be considered that the device used may be contaminated, in addition to patient-related factors. Necessary precautions should be taken in terms of disinfection and sterilization in order to prevent outbreaks.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Очаг послеоперационного быстроразвивающегося и полирезистентного *Klebsiella pneumoniae* уросепсиса из-за контаминации уретероскопа

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Резюме

Введение: Очаги, вызванные микроорганизмами, загрязняющими внутреннюю часть жёстких уретероскопов, крайне редки. Некоторые из этих очагов, особенно вызванные инфекциями с множественной лекарственной устойчивостью (МЛУ), могут вызывать серьёзные проблемы и даже смерть. Среди этих серьёзных инфекций у нас нет данных об очагах *Klebsiella pneumoniae*, вызванных жёсткими уретероскопами, лечении и последствиях.

Цель: Мы стремились сообщить об исходах очагов быстро развивающейся МЛУ K. pneumoniae уросепсиса, связанной с ригидной уретероскопией (УРС).

Материалы и методы: Ретроспективно проанализированы данные 68 пациентов, перенёсших операцию уретероскопической литотрипсии (УРС-Л) с использованием одного и того же уретероскопа. Среди них в исследование были включены 17 больных с развившимся в послеоперационном периоде уросепсисом. Образцы были взяты из операционной, головок камер, эндоскопов и вспомогательных инструментов для посева. *K. pneumoniae* продуцировали в культуре мазка, полученного из водозаборного канала уретероскопа.

Результаты: У всех пациентов были признаки сепсиса, которые развивались в течение нескольких часов (2-7 часов). МЛУ *K. pneumoniae* была обнаружена в посевах мочи у всех пациентов. Он был чувствителен только к амикацину, тигециклину, колистину и нетилмицину. Все пациенты получали тигециклин (100 мг внутривенно ежедневно). Было отмечено, что рост *K. pneumoniae* продолжался бессимптомно в течение первой и четвёртой недель наблюдения у 4 пациентов. Эти пациенты были приняты в качестве колонизации; никакого дополнительного лечения не проводилось.

Заключение: В случае быстро развивающегося уросепсиса после процедуры УРС у больного следует немедленно проверить инструменты, приборы, эндоскопы на предмет контаминации, чтобы не допустить возникновения очага.

Ключевые слова

Klebsiella pneumoniae, уретероскопы, уретероскопия, уросепсис