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ORIGINAL ARTICLE

Therapy and Prevention of Postoperative Urosepsis of Ureter Endoscopic Lithotripsy for “Non-infection”[△]

Jun Shen^{1, 2}, Fa Sun², Fang-min Chen², Zhi-ping Wu²,
and Sheng-wen Li^{1, 3*}

¹Medical Center, Tsinghua University, Beijing 10084, China

²Department of Urology, the Affiliated Hospital of Guizhou Medical University, Guiyang 550004, China

³Department of Urology, the First Hospital of Tsinghua University, Beijing 100016, China

Key words: lithotripsy; non-infection; ureter; urosepsis

Objective To analyze the risk factors causing postoperative urosepsis in ureter endoscopic lithotripsy without infection preoperatively, in order to make a more effective and safer preventive and therapeutic strategy.

Methods From January 2010 to January 2015, 5 ureteral calculus patients undergoing ureter endoscopic lithotripsy with holmium laser were retrospectively enrolled in this clinical study. These patients suffered urosepsis postoperatively confirmed by the clinical presentations and laboratory results, while they had no infection in their blood and urine preoperatively. Without delay, 5 patients were treated by anti-inflammation and anti-shock.

Results The vasopressor drug was stopped gradually after 12-36 hours. The body temperature was recovered to normal in 2 or 3 days, and the blood and urine test results were not abnormal in 7 days. At last, 5 patients were all cured.

Conclusions Stone and operation themselves are potential factors to cause urosepsis after ureter endoscopic lithotripsy. Especially for patients who had not presented infection preoperatively, careful preparation preoperatively, corrective manipulation, low pressure irrigation, drainage and controlling time during operation, and early diagnosis, appropriate treatment postoperatively are the key to cure and prevent urosepsis.

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RECENTLY, the patients with upper urinary tract lithotripsy are mostly treated by interventional endourological techniques, such as ureteroscopy lithotripsy (URL), flexible URL (FURL), and percutaneous nephrolithotripsy (PCNL), which have the advantages of minimal invasion, fast recovery, and so on. Among them, ureteroscopy is more microinvasive and convenient to treat ureteral calculus. However, some complications caused by ureteroscopy are happened from time to time. Urosepsis was the most serious complication which mortality rate reached up to 28.3%-41.1%.¹ In this study, we summarized 5 cases presented urosepsis postoperatively, in order to make a more effective and safer preventive and therapeutic strategy.

PATIENT AND METHODS

Patients

From January 2010 to January 2015, more than 2000 patients were treated with ureter endoscopic lithotripsy with holmium laser at the Affiliated Hospital of Guizhou Medical University. There were 24 patients without infection in their blood and urine before operation, but 5 patients aged between 36 and 69 years (mean age: 47 ± 13.14 years) presented urosepsis postoperatively, including 3 males and 2 females. There were unilateral ureteral calculus in 4 cases and bilateral ureteral calculus in 1 case. The stones were located in the upper and middle of the ureter. Moderate to severe dilation/hydronephrosis appeared in urinary tract above stone. All patients felt swelling pain inconspicuously. One case was accompanied with type 2 diabetes mellitus. Two cases who had caught unclear chill and fever were accompanied with lower back swell feeling. Preoperatively, the results of routine blood test and routine urine test were normal. These 5 patients did not use antibiotics, and their vital signs were all steady preoperatively.

Three patients underwent URL under transurethral local anesthesia, and the other two underwent URL with general anesthesia. The procedure was done using a ureteroscopy (8.0/9.8 Fr, Storz, Germany) with holmium laser for 60-150 minutes. During the operation, the hard stones were found and pyuria appeared in 2 cases immediately after the stones were broken through. The pyurias were extracted for urine culture. Postoperatively, 5 Fr double J stent (Cook, USA) was put on 5 patients respectively, without catheter for continuous drainage, and they were taken with routine anti-infective therapy. From 1 to 4 hours after surgery, 5 cases showed chill, high fever, palpitation, polypnea, and dysphoria. Two of them yelled for swell pain on their hemi-back and waist of operation. One of them

showed delirious speech. Five cases presented temperature up to 39°C - 41°C , blood pressure down to 90/60 mm Hg-80/50 mm Hg, heart rate up to 110-130 beats per minute. All the values of hemoglobin and platelet decreased, but the values of C-reactive protein and procalcitonin increased obviously. White blood cell (WBC) count decreased in 3 cases and increased in 2 cases obviously, and percentage of neutrophil granulocyte increased. Two patients showed hepatic impairment. In all the cases, the diagnosis was urosepsis based on the clinical feature and physical examinations.

Methods

After ureter endoscopic lithotripsy with holmium laser, the 5 patients presented early uncomfortable symptoms such as waist pain, chill, and so on, some steps were taken to monitor vital signs, speed up the infusion, indwell urinary catheter in order to prevent urine reflux, gather urine for examination, observe the change of urine, and at the same time, blood routine and biochemical test were examined urgently. We immediately took antishock and supporting therapy, including clearing airway, inhaling oxygen, establishing two-path transfusion, and correcting acid-base disturbance. We adjusted infusion speed and volume according to vital signs, central venous pressure, and urine volume. Once urosepsis was confirmed, 200-400 ml fresh plasma were supplied for the patients, even 2 U homotype concentrated red blood cells (CRBC) were given to 2 serious cases. Under the condition of elevated blood pressure and sufficient blood volume, low dose of dopamine was infused via micro-pump, which could keep hemodynamics steady and increase kidney blood perfusion. At the same time of antishock, routine antibiotics could be substituted by the third generation of cephalosporin e.g. piperacillin/tazobactam, or the fourth generation of quinolone antibiotics, or even directly replaced by carbapenem antibiotics e.g. imipenem/cilastatin. Blood culture was examined when the patients' temperature exceeded 39°C . Urine culture and drug sensitive test were also made in time, which could be taken as a guide of drug used or rechoose.

RESULTS

After standard treatment, 5 patients with urosepsis recovered gradually, manifesting vital signs were steady and urine volume got normal. The vasopressor drugs were stopped gradually after 12-36 hours. The body temperature was recovered to normal in 2-3 days, and the blood and urine tests results were not abnormal in 7 days. If 3 consecutive days of urinalysis were normal, then their

antibiotics could be stopped. The test results of blood culture were: 4 cases (-); urine culture: 5 cases all (+), 1 case for *Klebsiella pneumonia*, 1 case for *Pseudomonas aeruginosa*, 3 cases for *Escherichia coli*.

DISCUSSION

In accordance with China Urology Disease Diagnosis and Treatment Guidelines (2014 edition),² it should be diagnosed as urosepsis when bacteremia caused by urinary tract infection or clinically suspected sepsis, was accompanied with clinical signs and symptoms of systemic inflammatory response syndrome. Serious urosepsis is diagnosis when the septic patient has multiple organ failure. In this study, we analyzed the possible causes, therapy and prevention methods about urosepsis after URL in patients without preoperative infection.

Pathogenesis

Firstly, complete stone obstruction is one of the causes of postoperative urosepsis. Some patients with unilateral ureteral calculi had tolerated to pains caused by long-term chronic obstruction and infection. Once complete obstruction, pyuria above stone was cut off just like autonephrectomy, which could make a false negative of WBC in urine test. Renal pelvic pressure might not be increased suddenly for the time being, and inside bacteria and endotoxins were in the state of rest. A lot of pyuria was observed to pour out when the stone was broken up by endoscopic lithotripsy with holmium laser. For avoiding interference to surgical field, some urologists would add up flush water to go on lithotripsy, which could lead to increase renal pelvic pressure, make germs and toxin into blood, trigger body to occur inflammatory response uncontrolled, give rise to a series of inflammatory mediator cascade release, and make autoimmune disorder or immunity paralysis.³ Meanwhile, it could result in vascular endothelial cells damage, induce mechanism of intravascular coagulation disorder, and then embody microcirculation ischemia and organs dysfunction.⁴ Two cases in this group were found to have pyuria in the course of lithotripsy. The operators neglected the small stone, and went on flushing water for lithotripsy. Although the operators crushed residual calculi and implanted double J stent for drainage within 15 minutes, the patients presented symptoms of infection. Secondly, bacteria and intertoxin are encapsulated in stones. A large number of bacteria and endotoxins around calculus were motivated and released to blood during lithotripsy, while the count of WBC was not increased preoperatively. Tenke *et al*⁵ reported that bacterial

resistance and toxicity in calculus were stronger than that of floating bacteria in urine. Although it was found that the renal pelvic urine was clear without pyuria, the patients showed toxic and infective symptoms after surgery 1-3 hours in 3 cases, which was testified by the positive results of urine culture postoperatively. The last but not least, inter-operative perfusion pressure is too high persistently. The normal renal pelvic pressure is 5-7 cmH₂O. The urination will be reduced when renal pelvic pressure is over 40 cmH₂O. The discharge of blood urea nitrogen and creatinine will be decreased.⁶ Some researchers indicated that the probability of postoperative fever would be increased when the renal pelvic high pressure (≥ 40 cmH₂O) was persistent for a period of time (≥ 60 seconds).⁷ Unlike to percutaneous nephrolithotripsy and FURL, URL is one-way about inlet and outlet without protecting and supporting of sheath, which can make renal pelvic pressure go up promptly and make bacteria and endotoxin go into blood during perfusion surgery.⁸

Therapy

Early detection and effective treatment are the key points to treat urosepsis. Once patients appear chill, high fever and so on after operation, urosepsis should be considered firstly. Some measures to clarify a diagnosis should be used such as getting blood/urine routinely and biochemical test urgently, getting blood culture, urine culture and drug sensitivity test when we take active resuscitation and supporting therapy. The antibiotics should be replaced by the more effective drugs immediately. The third-generation cephalosporin or piperacillin/tazobactam or carbapenems are recommended to use according to China Urology Disease Diagnosis and Treatment Guidelines (2014 edition). Chen *et al*⁹ reported that resistance bacteria for imipenem or cilastatin could not be found in urine tract infection, which included *Escherichia coli* (50%), *Proteus vulgaris*, *Enterococcus faecalis*, and *Klebsiella pneumonia*. In this study, the less serious cases were treated with piperacillin/tazobactam or the third-generation cephalosporin, or added moxifloxacin; the serious cases were treated with imipenem cilastatin directly. Kumar *et al*¹⁰ indicated that effective antibiotics were to be used as soon as possible; otherwise survival rate was reduced by 8% for each 1 hour delay. After diagnosis is confirmed, fresh frozen plasma 200-400 ml will be supplied for the patients, which can replenish the colloid, increase a lot of antibodies, and enhance the effect of antibacterial and remove toxins in the body together with antibiotics. CRBC are infused based on the levels of oxyhemoglobin saturation (SPO₂), hemoglobin, and hematocrit. Two severe cases in this group were

supplied 2 U CRBC respectively, one of whom had a lower SPO₂ of 90% (oxygen inhalation) and 70 g/L hemoglobin, the other of whom was 69-year old, combined with diabetes, continuous high fever, polypnea, and a lower SPO₂ of 88% in spite that his hematocrit was 31%. It is better to transfer into Intensive Care Unit, if the patient's condition worsened.

Prevention

(1) Identification of patients: As to identifying patients preoperatively, especially the patients with potential risk complications such as diabetes, anemia, hypoproteinemia, immunosuppression and cancer patients who have gone through radiotherapy and chemotherapy, surgeons have to keep an eye on them because of old age, tender, and hypoimmunity, which easily suffer from urosepsis once the germs go into blood from urine.¹¹ One patient in our study had combined with type 2 diabetes (15 years). Although the results of examination showed no infection before operation and URL was a minimally invasive surgery, some severe symptoms of infection were still presented postoperatively. So these patients should be controlled their complications before URL. In addition, there are some special patients with unclear causes of chill, fever, and lower back ache, who are likely to together with pyonephrosis. Two cases in our study presented empyema above stone obstruction, though the WBC counts were normal preoperatively.

(2) Use of antibiotics: At present, it is a controversial issue that antibiotics should be used in the patients without any signs of infection before URL with holmiumlaser.¹²⁻¹⁴ According to the above analysis of the pathogenesis, the authors propose that the second-generation cephalosporin is used intravenously at 30 minutes before surgery; for the high-risk patients, the antibiotics should be given 1-3 days in advance; during operation, urologist can add to use antibiotics at a time when the lithotripsy time is more than 3 hours. The routine antibiotics should be used for the patients postoperatively, and stopped when the number of WBC is normal in re-examination routine urine.

(3) Control of the operation time: the shorter operation time, the less infection opportunity. In this study, the operation time of 3 cases was over 120 minutes, and 2 cases were less than 90 minutes. We consider that the operation is relatively safe in 90 minutes.

(4) Perfusion pressure control: Perfusion pressure is the direct force to increase the chances of infection, which can make intrapelvic pressure rise instantly, and prompt bacteria and endotoxin into the blood. The critical factor of preventing urosepsis is good control for perfusion pressure. The authors advocate that the operator adopts discontinuous low-pressure perfusion when endoscopic is placed

into ureter. The operator can take disconnected drainage for pelvic decompression at the same time of discontinuous perfusion, which is crucial in preventing urosepsis postoperatively. Especially in pyonephrosis during operation, the operator can take drainage by opening outlet valve completely, and ask an assistant for sucking with negative pressure drainage using 20 ml or 50 ml injector, which can discharge a lot of hydrops, germs, and endotoxin rapidly and decrease pressure of renal pelvic, so reduce chance of infection. If the stone is larger, we suggest that double J stent should be placed through the gravel channel for drainage firstly, and then phase II lithotripsy can be performed until inflammation is controlled completely.

(5) Indwelling ureteral stent and catheter: After lithotripsy, ureteral stent and catheter should be placed for continuous drainage, which can ensure postoperative upper urinary tract unobstructed, and prevent the urine reflux and easily observe and test urine volume. All the 5 cases in this group were placed double J stents but not catheters. Two cases of them showed waist distending pain, chill, high fever. By urethra catheterization, the operators found that one patient (65-year old) was extracted urine 700 ml, the other one (36-year old) was no more than 100 ml. There was a possible reason that ureteroscopic body pressed on vesical neck during operation leading to pain stimulation, which makes cystospasm or bladder out-flow obstruction, and then urine reflux. Two patients felt waist-ache alleviative after indwelling catheter. According to the strict enforcement of the preventive measures above, no one case has presented urosepsis in our hospital for nearly a year.

In conclusion, urosepsis is one of the serious complications after ureter endoscopic lithotripsy. Stone and operation themselves are potential factors to cause urosepsis postoperatively. Especially for patients who had not presented infection preoperatively, many doctors had often neglected to take preventively some antibiotics for them, or took some medicine but not for adequate duration. Therefore, preoperatively careful preparation can reduce the chance of serious infection postoperatively; corrective manipulation, low pressure irrigation, drainage and controlling time during operation are the effective ways to decrease the occurrence of urosepsis; early diagnosis and appropriate treatment postoperatively are the key to cure patients with urosepsis.

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