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Stone culture retrieved during percutaneous nephrolithotomy: is it clinically relevant?

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Abstract Stone culture has been frequently investigated following percutaneous nephrolithotomy (PNL) in the last decade. We aimed to crucially define the clinical role of stone culture in modifying the treatment plan in patients with postoperative sepsis. Between June 2012 and April 2013, a total of 79 consecutive PNL procedures were included. Perioperative data were prospectively maintained. Preoperative urine sample, retrieved stone fragments and postoperative nephrostomy tube urine sample were cultured and antibiotic sensitivity tests were performed. The occurrence of at least two of the systemic inflammatory response syndrome (SIRS) events during their inpatient stay was diagnostic of SIRS. The antibiotic regimen utilized and its modifications were reported. The preoperative culture was positive in 26 patients (32.9 %). The culture of stone fragments showed significant bacterial growth in 23 (29.1 %) cases. Significant growth on stone culture was significantly associated with the presence of preoperative urinary catheters and positive preoperative urine culture ($P = 0.001$, 0.006 respectively). Postoperative culture was positive in only six patients (7.6 %). SIRS was diagnosed in the first postoperative day in 12 patients (15.2 %). Leukocytosis was the only predictor of SIRS. Neither preoperative culture, stone culture nor postoperative culture was predictor of SIRS. Stone culture was positive in four patients with SIRS. Stone culture changed the treatment plan in only one patient. Our data do not support the routine implementation of stone culture in the PNL workup, as it did not indicate a change of antibiotic regimen in most of the cases.

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Introduction

Percutaneous nephrolithotomy (PNL) has been widely accepted as a minimally invasive procedure in the treatment of renal stones. Post-PNL, urinary tract infection and its sequelae have been shown to be 35 %, fever 21–32 % [1] and septicemia 0.3–4.7 % [2]. Two mortalities were reported out of five cases that had sepsis in a series of 318 patients [3]. In another series of 700 PNL patients, six mortality cases (0.8 %) were reported out of nine that developed sepsis [4]. Many publications have investigated factors that might contribute to the development of postoperative infection, and hence to be preoperatively identified and probably treated to decrease such complications and mortality. Previous ipsilateral PNL and paraplegia were reported to be risk factors [2]. Long operative time, longer postoperative hospital stay [5], female sex, diabetes mellitus [6] and preoperative endotoxin level [7] were also reported as contributing factors.

Both preoperative and stone cultures were suggested as potential factors to predict postoperative UTI and its sequelae. The role of preoperative urine culture has been investigated in many series and failed to identify patients who developed sepsis post-PNL and ureteroscopy [8–10]. In a series of mini-PNL, similar morbidity and septic complications were reported among patients with positive and negative preoperative urine culture despite adequate preprocedure culture-based treatment [6]. Furthermore, Korets et al. [11] concluded that even appropriately treated preoperative UTI might not prevent infected urine post-PNL.

Collecting renal pelvis urine and stone fragments for cultures may be recommended to identify the offending organism in patients at risk for sepsis, particularly those with a large stone burden requiring multiple access tracts [11]. Although the role of stone culture in the prediction of perioperative septic events is well documented [10, 12, 13], its role in directing postoperative antibiotic regimen and patient management is to be confirmed [1]. This study was conducted to prospectively assess the clinical role of stone culture in improving patient outcome and modifying the treatment plan.

Patients and methods

After obtaining institutional review board and ethical committee approval, eligible patients were enrolled in the study. We included all patients having stones as eligible for PNL with the exclusion of patients having urinary diversion, patients on preoperative antimicrobial therapy, pediatric patients, tubeless PNL and cases with intraoperative laser fragmentation, as stone fragments could not be collected for culture. Patients with positive preoperative urine culture were not excluded from this study and received their antibiotics according to culture sensitivity. Patient's baseline data, stone criteria and perioperative parameters were prospectively collected. Routine laboratory and radiologic assessments were performed. Preoperative midstream urine sample was taken for culture and antibiotic sensitivity. In patients with a nephrostomy tube fixed for drainage purposes prior to PNL, cultures were collected from the nephrostomy tube. Significant growth was defined as more than 100×10^3 colony forming units.

Intervention

At the time of anesthesia, a single dose of third-generation cephalosporin was given for patients with negative urine culture. For patients with positive culture, the antibiotic was given according to the culture and sensitivity test 48 h prior to intervention. PNL was performed according to standard technique [14]. An open-tip ureteric catheter was inserted, and then fluoroscopic-guided access was established and dilated to 30 Fr using Alkan's dilators. An Ampletz sheath was placed and all cases were done using a rigid nephroscope. Stone disintegration was done as indicated using an ultrasonic and/or pneumatic lithotriptor. A nephrostomy tube was routinely placed at the end of the procedure. The retrieved stone fragments were cultured and antibiotic sensitivity tests were performed. On the first operative day, the nephrostomy tube urine sample was cultured and antibiotic sensitivity tests were performed. A control film X-ray/NCCT was performed and the nephrostomy tube was removed accordingly; then the ureteric catheter was removed the day after. The hemoglobin level was routinely checked on the first postoperative day. Patients with positive preoperative culture continued the same antibiotic regimen for 3 days. In those with negative culture, oral ciprofloxacin was prescribed routinely for 5 days.

The occurrence of at least two systemic inflammatory response syndrome (SIRS) events during their inpatient stay was diagnostic of SIRS. The criteria were defined as a temperature <36 or more than 38 °C, heart rate more than 90 beats/min, respiratory rate more than 20/min and WBCs < 4.000 or more than 12.000/mm^3 [15]. If a patient developed SIRS, he was put under strict observation and the antibiotic was upgraded empirically into combination IV therapy including the preoperatively provided antibiotic together with aminoglycoside. If the preoperative antibiotic was aminoglycoside, imipenem was added till the patient stabilized or postoperative cultures became available.

Statistical analysis

The data were collected using SPSS version 16 (Chicago, IL, USA). Patient and stone characteristics as well as operative variables that might affect the occurrence of SIRS in addition to culture results were evaluated using univariate analysis (Chi-square test for categorical variables and independent sample *t* test for continuous variables).

Results

Between June 2012 and April 2013, a total of 79 consecutive PNL procedures that met the inclusion criteria were included. Patients' perioperative and stones' criteria are illustrated in Table 1. The preoperative culture was positive in 26 patients (32.9 %) (Fig. 1a). *E. coli* were the causative organisms in half of the patients. Culture of stone fragments showed no growth in 56 (70.9 %) cases, while bacterial growth was detected in 23 (29.1 %) cases. Grown organisms included *E. coli* in nine, Klebsiella in three, yeast in three, *Enterococcus faecalis* in two, *E. cloacae* in two, *Pseudomonas aeruginosa* in two, *Proteus* in one and *Alcaligenes faecalis* in one. Significant growth on stone culture was significantly associated with the presence of preoperative urinary catheters (three double pigtail stents or seven nephrostomy tubes) (10/23 $P = 0.001$) and positive preoperative urine culture (15/23 $P = 0.006$). Postoperative culture was positive only in six patients (7.6 %). SIRS was diagnosed on the first postoperative day in 12 patients (15.2 %). Preoperative leucocytosis was the only predictor of SIRS. Neither preoperative culture, stone culture nor postoperative culture was a predictor of SIRS Table 2.

Patients with positive stone culture could be classified into three distinct groups. The first group included 11 patients in whom both the preoperative as well as stone

Table 1 Patients' perioperative and stone's criteria

Patients' demographics	
Age (median; range)	52 (18–72)
Sex (*n*; %)	
Male	34 (43)
Female	45 (57)
Preoperative serum uric acid (mg/dl) (median; range)	6.4 (2.6–10.8)
Preoperative WBCs count (10^3/cc) (median; range)	8.1 (2.6–19.6)
Diabetes mellitus (*n*; %)	11 (13.9)
Stone's and renal criteria	
Previous intervention for renal stone (*n*; %)	
Open surgery	14 (17.7)
PNL	10 (12.7)
ESWL	4 (5)
Kidney side (*n*; %)	
Right	39 (49.4)
Left	40 (50.6)
Stone location (*n*; %)	
Proximal ureter	5 (6.3)
Renal pelvis	22 (27.8)
Pelvicalyceal	26 (32.9)
Calyceal	26 (32.9)
Preoperative hydronephrosis (*n*; %)	47 (59.4)
Preoperative stent/nephrostomy (*n*; %)	10 (12.7)
Duration in days (median; range)	(2–48)
Stone disintegration (*n*; %)	
No	5 (6.3)
Pneumatic	5 (6.3)
Ultrasound	46 (58.2)
Combined	22 (29.1)

cultures yielded the same organism (5 *E. coli*, 2 *Klebsiella*, 1 *Proteus*, 1 *E. faecalis*, 1 *E. cloacae*, 1 *P. aeruginosa*). Postoperatively, of these patients, imipenem was continued in six, third-generation cephalosporin in two (according to culture in 1 and empirically because of multi-drug resistance in 1), quinolones in one, amoxicillin/clavulanate in one and aminoglycoside in one as the preoperative antibiotic. In this group, four patients had stone cultures with the same antibiotic sensitivity as the preoperative culture. Another patient had a stone culture that showed multi-drug resistance. These five patients did not develop SIRS. Cultures of the remaining six patients provided different antibiotic sensitivity for the grown organism. Five of them had no change in the antibiotic therapy as the patients were clinically stable with no evidence of SIRS. In the remaining patient, SIRS developed and the antibiotic was changed empirically from imipenem to imipenem and aminoglycoside. The patient was well controlled on this combination. Interestingly, stone culture was available a day later and revealed antibiotic sensitivity to aminoglycoside (Fig. 1b).

The second group included eight patients with negative preoperative culture, while the stone culture was positive for *E. coli* in four, yeast in two, *E. cloacae* in one and *P. aeruginosa* in one. All these patients received third-generation cephalosporins preoperatively and six of them were clinically stable. Two patients developed SIRS in the first postoperative day. Both patients were upgraded empirically into third-generation cephalosporin with aminoglycoside. Unfortunately, both patients had persistent clinical manifestations. A day later, stone cultures were available and yielded *E. coli* growth sensitive to aminoglycoside in one patient and the combination continued without change; his clinical syndrome was controlled on the 3rd day. In the other patient, the stone culture yielded imipenem and we changed the combination antibiotic therapy accordingly. The patient was well controlled within 2 days (Fig. 1c). The last group comprised four patients in whom the stone culture yielded different organisms (*Klebsiella*, *E. faecalis*, yeast, *A. faecalis*) compared with (*E. coli* in 3 and *E. cloacae* in 1) in the preoperative cultures. Of these patients, postoperatively three were maintained on imipenem and one on aminoglycoside. Three patients were clinically stable and did not require to change the antibiotic, though stone cultures yielded different antibiotic sensitivity in two and multi-drug resistance in the third. The fourth patient developed SIRS and the antibiotic was upgraded empirically up to a combination of imipenem and aminoglycoside and was well controlled on this combination. Interestingly, stone culture was available a day later and revealed antibiotic sensitivity to imipenem (Fig. 1d). The remaining eight patients who developed SIRS had negative stone culture and were well controlled on empirical antibiotic upgrading.

Discussion

PNL has become a common surgical intervention for patients with renal stone disease [16]. PNL is a surgical procedure that is associated with injury of the renal parenchyma, together with high pressure in the irrigation fluid causing disruption of the vascular, lymphatic and urothelial barrier, all of which may facilitate direct access of the bacteria and its toxin to the blood stream. Furthermore, stone manipulations may end up with release of endotoxins to blood [17]. The incidence of a single individual SIRS event, notably fever, is common after PNL and was reported in 21–32 % of the patients [1, 5]. In the majority of patients, fever is transient and recovery is spontaneous with conservative measures. The occurrence of SIRS events was inconsistently reported among the published series, ranging from 9.8 to 37 % [1, 10, 11]. Less frequently, SIRS may progress to sepsis and even septic shock. The incidence of clinically significant sepsis post-PNL was reported to be 0.3–4.7 %

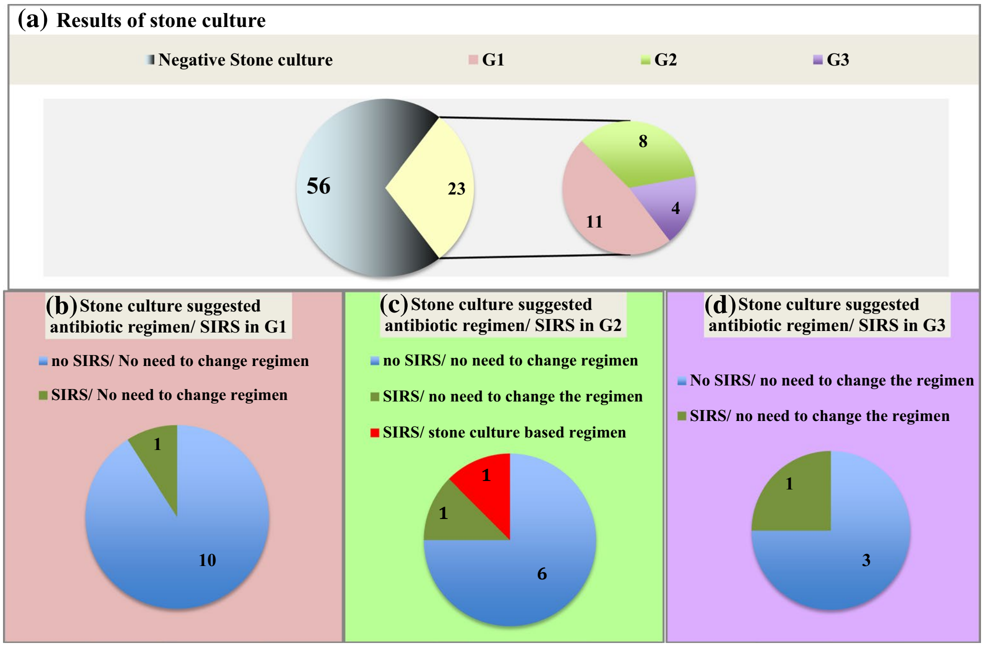

Fig. 1 **a** Results of stone culture. For positive stone culture grouping: *G1* preoperative and stone cultures yielded the same organism; *G2* negative preoperative culture; *G3* preoperative and stone cultures yielded different organisms. **b–d** Stone culture suggested antibiotic regimen and occurrence of SIRS among positive stone culture groups (*G1–3*)

Table 2 Analysis for potential SIRS predictors

	No. of SIRS	SIRS	*P* value
No of procedures	67	12	
Mean age (±SD in years)	52 ± 11.4	49.8 ± 12.3	0.5
Mean baseline serum uric acid (±SD in mg/dl)	6.4 ± 2	6.8 ± 1.5	0.4
Mean preoperative WBCs count (±SD in 1000/cc)	7.9 ± 2.8	10.1 ± 3.9	0.019
Sex; no (%)			0.7
Male	41.8)	6 (50)	
Female	39 (58.2)	6 (50)	
Diabetes mellitus; no. (%)	7 (10.4)	4 (33.3)	0.06
Previous stone surgery; no. (%)	25 (37.3)	2 (16.7)	0.2
Preoperative stent/nephrostomy; no. (%)	7 (10.4)	3 (25)	0.13
Positive preoperative MSUC; no. (%)	21 (31.3)	5 (41.7)	0.5
Positive stone culture; no. (%)	19 (28.4)	4 (33.3)	0.7
Positive postoperative NTUC; no. (%)	6 (9)	0 (0.0)	0.5
Bilateral renal stones; no (%)	6 (9)	2 (16.7)	0.6
Operative stone disintegration; no. (%)	62 (92.5)	12 (100)	1
Preoperative hydronephrosis; no. (%)	39 (58.2)	8 (66.7)	0.7

[2, 5]. Lewis et al. [3] reported 0.6 % mortality secondary to post-PNL sepsis. In this investigation, the incidence of SIRS was 15 %, but neither clinically significant sepsis nor perioperative mortality was reported.

Many reports have suggested potential factors as a predictors of SIRS following PNL including female sex, *Diabetes mellitus* [6], *Paraplegic patients* [2] and presence of anatomical renal abnormalities [18]. Although positive preoperative urine culture has been reported as a predictor of overall complications during PNL [19], its role in predicting septic complications is debatable. Most of the studies denied its predictive ability [8, 10, 12, 20, 21] with only two studies showing that preoperative culture is predictive of postoperative sepsis [13, 22]. The limited predictive ability of preoperative culture may be due to the hypothesis that infection might be isolated proximal to calcular obstruction with no way down to the bladder with high false negative results. Leukocytosis is an indicator for the body immune response against infection. In the current cohort, a significant association between SIRS and preoperative leukocytosis was demonstrated. In a recent report, leukocytosis was identified as a significant predictor of postoperative sepsis in patients with colorectal cancer [23]. Notably, Bozkurt et al. [24] denied the value of postoperative leukocytosis in sepsis prediction among PNL patients.

In the last decade, the value of stone culture was raised and repeatedly studied in the urologic literature. The culture of stone fragments revealed significant bacterial growth in 3–50 % of the patients subjected to PNL according to different investigators [10, 12, 13, 22]. Stone culture revealed significant bacterial growth at a rate lower than preoperative urine culture in some reports [13, 22] and higher in others [10, 12]. Most of the investigators agreed that stone culture is highly predictive of septic events after PNL [8, 10, 12, 20, 22]. This was explained by the release of endotoxin from stones upon intraoperative stone manipulation. On the other hand, Korets et al. [11] denied this significant association, as it was not maintained on multivariate analysis. This matched with our experience. Similarly, Cadeddu et al. [25] found no correlation between post-PNL fever and stone composition, either infectious or non-infectious.

We believe that the clinical impact of the stone culture results in directing the treatment plan is far more important than its predictive value. In this experience, among the 12 patients (15 % of the patients' cohort) who developed SIRS, stone culture was available in only 4 (5 % of the patients' cohort). Moreover, stone culture antibiotic sensitivity was clinically useful in only one patient (1 % of the patients' cohort). SIRS develops usually in the first few hours following the procedure, while stone culture is usually available within 48 h after the procedure; this make the urologists in charge obliged to upgrade the antibiotics empirically till the culture results became available. Critical analysis of other reports showed similarly that stone culture was clinically relevant in changing the treatment plan and antibiotic policy in <5 % of the examined populations [10, 12, 13]. The possible advantage of this study is that it focuses on the clinical utility of this type of laboratory investigation rather than on its theoretical predictive ability. It also raises the cost-effectiveness of stone culture. The current study is limited by the small sample size, which did not allow recording of significant perioperative septic events. Also, it is limited by the absence of an appropriate cost analysis. Further studies are warranted to investigate the best antibiotic to be used empirically for negative preoperative culture, cultures with multi-drug resistance [26] or those who develop septic complications despite appropriate preoperative culture till postoperative cultures became available.

In conclusion, our data do not support the routine implementation of stone culture in the PNL work as a result of the stone culture and antibiotic sensitivity came out and did not dictate change of regimen in most of the cases. Post-PNL sepsis usually occurs in the early postoperative time and broad-spectrum antibiotics are usually prescribed and rarely stone culture result that would come 2–3 days later makes change. More attention should be directed to preoperative leukocytosis as a potential predictor of postoperative sepsis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards All human studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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