# Multibacterial Growth From a Surgical Renal Stone Culture: A Case Report and Literature Review

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Urinary calculi may harbor bacteria, and this may lead to deleterious events during stone fragmentation and removal. The isolation of such bacteria from surgically extracted calculi allows for the specific tailoring of antimicrobial therapy. Here, we describe a case involving percutaneous stone removal from which the stone culture demonstrated growth of five different microorganisms. The results of this culture prompted a change in the antibiotic coverage, resulting in a more targeted treatment and improved patient care.

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**KEY WORDS**

Stone culture • Urinary tract infection • Nephrolithiasis

Despite the use of culture-specific or broad-spectrum antibiotic therapy prior to surgical removal of upper tract nephrolithiasis, certain patients still develop postoperative sepsis. Some have reported that preoperative voided urine cultures from these patients may not be reflective of the bacterial environment within the stone that is to be treated.[1] Manipulating the stone during attempts at removal and fragmentation may liberate these organisms into the bloodstream, heightening the risk of sepsis or systemic inflammatory response syndrome (SIRS). Thus, prescribing antimicrobial therapy that will eradicate the organism in the urine and provide broad-spectrum coverage for the potentially different bacteria harbored within the stone is desired. Furthermore, performing a stone culture may identify organisms that are not covered by initial antibiotic therapy, providing an opportunity to institute earlier targeted therapy.[2] Here we present a unique case in which a patient with a large renal stone was subjected to percutaneous nephrostolithotomy (PCNL) in which the stone culture demonstrated avid growth of five different bacterial strains, four of which were not identified in the preoperative urine culture.

## Case Report

A 48-year-old white woman developed left flank pain, dysuria, fever, and chills. She was healthy other than a history of a left renal stone 10 years prior for which she underwent shock wave lithotripsy. Urinalysis demonstrated pyuria and bacteriuria. A non–contrast-enhanced computed tomography scan of the abdomen and pelvis demonstrated a staghorn stone occupying her left kidney with associated moderate hydronephrosis and perinephric stranding. She was initially administered ceftriaxone intravenously, and an internalized ureteral stent was inserted. Her clinical status rapidly improved. Urine culture demonstrated growth of *Escherichia coli* sensitive to trimethoprim-sulfamethoxazole, which she took orally prior to stone removal. She underwent PCNL during which all stone was removed. The stone was composed of magnesium ammonium phosphate and calcium carbonate phosphate. The stone culture demonstrated growth of five different multidrug-resistant bacteria: *E coli*, *Pseudomonas* species, *Enterococcus* species, and two different strains of *Enterobacter cloacae* (Table 1). The patient's antibiotic regimen was changed to amikacin to reconcile the results of her stone culture, which differed from those of her urine culture, and she had

*The stone culture technique that we employed involved washing the stone surface with sterile water, crushing the stone with a sterile mortar and pestle, mixing the pulverized stone with 1 mL of trypticase soy broth, and streaking the resulting "stone paste" onto blood agar and MacConkey agar plates.*

**TABLE 1**

**Stone Culture Results**

| Drug | *Pseudomonas* | *Enterococcus* | *Escherichia coli* | *Enterobacter cloacae #1* | *Enterobacter cloacae #2* |
|---|---|---|---|---|---|
| Amikacin | S | NT | S | S | S |
| Ampicillin | NT | S | NT | NT | NT |
| Aztreonam | R | NT | S | R | I |
| Carbenicillin | NT | NT | NT | NT | NT |
| Cefoxitin | R | NT | S | R | R |
| Ceftazidime | S | NT | S | R | R |
| Ciprofloxacin | R | R | R | R | R |
| Erythromycin | NT | R | NT | NT | NT |
| Ofloxacin | R | NT | S | S | I |
| Keflin | I | S | R | R | R |
| Macrodantin | S | S | R | R | R |
| Mezlocillin | I | S | R | R | R |
| Piperacillin | S | S | R | R | R |
| Tobramycin | R | S | S | I | R |
| Trimethoprim/ Sulfamethoxazole | R | NT | S | R | R |
| Vancomycin | S | NT | NT | NT | NT |
| Vibramycin | R | NT | NT | NT | NT |
| Oxacillin | R | NT | NT | NT | NT |

I, intermediate; NT, not tested; R, resistant; S, sensitive.

an uneventful recovery. The stone culture technique that we employed involved washing the stone surface with sterile water, crushing the stone with a sterile mortar and pestle, mixing the pulverized stone with 1 mL of trypticase soy broth, and streaking the resulting "stone paste" onto blood agar and MacConkey agar plates. The agar plates were examined for bacterial growth after 24 to 48 hours. For gram-positive colonies that have grown on blood agar, a wet mount, catalase test, coagulase test, esculin agar slants, and salt broth were used for speciation. For gram-negative colonies that grew on MacConkey agar, an API-20E test kit was used for speciation. The various bacteria were then freshly inoculated onto blood or MacConkey agar, and antibiotic sensitivity was determined using the Kirby-Bauer method.

## Discussion

The development of a urinary tract infection is one of the most common postoperative complications associated with removal of upper urinary tract stones; this occurs in one-third of patients undergoing PCNL.[3] This places patients at risk for developing sepsis and SIRS, which can be fatal. It is also not uncommon for patients with a sterile preoperative urine culture to develop a postoperative infection after stone removal or fragmentation. Indeed, it has been demonstrated that urinary calculi can harbor bacteria.[4] Moreover, Charton and associates documented a 35% incidence of bacteriuria after PCNL in patients who had a sterile preoperative urine culture, suggesting that these organisms could have been liberated during the surgical procedure. All patients were found to have struvite stones.[5] Similarly, in a group of patients undergoing ureteroscopic stone removal, Mariappan and Loong reported that 25 of 75 patients had positive stone cultures, and 12 patients developed bacteremia with 7 exhibiting features of SIRS.[6]

Other investigations have demonstrated that metabolic stones, in addition to infection stones, can harbor bacteria.[7-12] This suggests that calculi of any composition can liberate bacteria during attempts at removal or fragmentation. In a large study involving 215 patients subjected to removal of renal or ureteral stones, Hugosson and colleagues noted that positive stone cultures were found in both infection and metabolic stones.[11] A total of 64 patients (30%) demonstrated bacterial growth in their stones: 71% of infection stones and 21% of metabolic stones were found to be infected. Some patients had more than one microorganism cultured from their stone, but the authors did not elaborate further on this topic.

Bacteria that reside within urinary calculi may differ significantly from the bacteria that are present in voided urine, thereby potentially evading the initial antibiotic coverage. Margel and colleagues reported on 75 patients undergoing PCNL.[1] A total of 17 had bacterial colonization in both their preoperative urine and surgical stone samples, and 6 demonstrated pathogens that differed in each specimen. Seventeen patients developed postoperative SIRS; in 13 of these patients, the antibiotic coverage was changed according to the stone culture results with subsequent clinical improvement in each case. On univariate analysis (multivariate analysis not performed), the only factor that predicted the development of SIRS was a positive stone culture. Similarly, Ma and associates found that, on multivariate logistic regression analysis, positive stone culture was the strongest predictor of postoperative SIRS, which developed in 21 of 66 patients undergoing PCNL.[13] A positive stone culture was present in 49%. Fourteen of the 21 patients with SIRS were treated with antibiotics based on their stone culture, and all recovered uneventfully. In another study, Mariappan and colleagues found that a positive stone or renal pelvic urine culture in patients undergoing PCNL was associated with a fourfold relative risk of severe systemic infection.[2] These investigator demonstrated similar findings in a cohort of patients subjected to ureteroscopic stone removal.[6]

Many investigators have reported on the specific bacterial species isolated from stone cultures after surgical stone removal (Table 2).[1,2,6-12,14-16] These studies have shown that the most common organisms found in these cultures are *E coli*, *Proteus* species, *Enterococcus, Klebsiella* species, and *Staphylococcus* species. Fungal organisms such as *Candida albicans* may also reside in stones.[10,15,16] The spectrum of bacteria differs somewhat among pure metabolic stones, pure infection stones, and mixed metabolic/infection stones (Table 3).

## Conclusions

Our case was certainly unique in that it represents the most bacterial species ever isolated from a surgically removed upper urinary tract stone. The role of stone culture is not clearly defined; however, it may be advisable during removal of large volume upper tract stones as it may permit more targeted antimicrobial therapy and perhaps avert some of the consequences of SIRS or sepsis. This will need to be verified with a randomized, controlled study, which to date has not been done. In addition, certain patients undergoing surgical removal of smaller upper tract stones may benefit from such testing, and the profiles of such patients will need to be determined. ■

**TABLE 2**

**Upper Tract Surgical Stone Series and Stone Culture Results Since 1980**

| Study | Number of Patients | Number of Positive Stone Cultures N (%) | Most Common Organisms Isolated (%) |
|---|---|---|---|
| Korets R et al[16,a] | 198 | 33 (16)<br>33 positive stone cultures in 204 PCNLs | 39 total microorganisms cultured<br>*E coli* – 9 (23)<br>*Enterococcus* – 9 (23)<br>*Klebsiella* – 7 (18) |
| Margel D et al[1] | 75 | 36 (48) | *Enterococcus* – 13 (36)<br>*E coli* – 10 (27)<br>*Klebsiella* – 4 (11) |
| Mariappan P et al[2] | 54 | 19 (35) | *E coli* – 5 (26)<br>Coagulase-negative *Staphylococcus* – 5 (26)<br>*Proteus* – 4 (21)<br>*Enterococcus & S faecalis* – 1 (1.4) |
| Mariappan and Loong[6] | 73 | 25 (34) | *E coli* – 17 (68)<br>*Proteus* – 5 (20)<br>*Klebsiella* – 2 (8.0) |
| Dewan B et al[12,a] | 70 | 33 (47) | 38 total microorganisms cultured<br>*Acinetobacter* – 13 (34)<br>*Klebsiella* – 11 (29)<br>*E coli* – 4 (11) |
| Gault MH et al[10] | 207 | 12 (5.8) | *Pseudomonas* – 4 (33)<br>Coagulase-negative *Staphylococcus* – 2 (17)<br>*E coli* – 1 (8.3)<br>*Proteus* – 1 (8.3)<br>*Staphylococcus* & *Enterococcus* – 1 (8.3) |
| Bratell S et al[8] | 80 | 42 (53) | *E coli* – 14 (33)<br>*U urealyticum* – 6 (14)<br>*P mirabilis* – 5 (12) |
| Hugosson J et al[11,a] | 215 | 64 (30) | 85 total microorganisms cultured<br>*E coli* – 21 (25)<br>*Proteus* – 17 (20)<br>*Staphylococcus* – 8 (9.4) |
| McCartney AC et al[7] | 24 | 10 (42) | *E coli* – 2 (20)<br>*Pseudomonas* – 2 (20)<br>*P mirabilis* & *E coli* – 2 (20) |
| Fowler JE Jr[15] | 16 | 17/22 (77)<br>22 total stone specimens as some patients had bilateral procedures | *P mirabilis* – 9 (53)<br>*P aeruginosa* – 2 (12)<br>*P mirabilis & S marcescens* – 2 (12) |
| Lewi HJ et al[9] | 63 | 24 (38) | *E coli* – 9 (38)<br>*P mirabilis* – 7 (29)<br>*P mirabilis* & *E coli* – 5 (21) |
| Dajani and Shehabi[14] | 122 | 20 (16) | *E coli* – 6 (30)<br>*Pseudomonas* – 5 (25)<br>Coagulase-positive *Staphylococcus* – 3 (25) |

[a]In some stone cultures, more than one microorganism was cultured. This is why the total number of microorganisms does not equal the number of positive stone cultures.
PCNL, percutaneous nephrostolithotomy.

## TABLE 3

### Upper Tract Surgical Stone Series Reporting Results of Both Metabolic and Infection Stone Cultures Since 1980

| Study | Metabolic Stones With Positive Stone Culture (%) | Infection Stones With Positive Stone Culture (%) | Mixed Stones With Positive Stone Culture (%) | Most Common Organisms Isolated (%) |
|---|---|---|---|---|
| Dewan B et al[12] | 47 (33/70) | | | 38 total microorganisms cultured |
| | | | | *Acinetobacter* – 13 (34) |
| | | | | *Klebsiella* – 11 (29) |
| | | | | *E coli* – 4 (11) |
| | | | | *S aureus* – 4 (11) |
| | | | | *U urealyticum* – 2 (5.3) |
| | | | | *E faecalis* – 2 (5.3) |
| | | | | *Pseudomonas* – 1 (2.6) |
| | | | | *M morganii* – 1 (2.6) |
| | | NR | | |
| | | | NR | |
| Gault MH et al[10] | 4.3 (9/207) | | | *Pseudomonas* – 2 (22) |
| | | | | *E coli* – 1 (11) |
| | | | | *Proteus & Citrobacter* – 1 (11) |
| | | | | Coagulase-negative *Staphylococcus* – 1 (11) |
| | | | | *Enterococcus* & Coagulase-negative *Staphylococcus* – 1 (11) |
| | | | | α-hemolytic *Streptococcus* – 1 (11) |
| | | 10 (3/30) | | *Pseudomonas* – 2 (67) |
| | | | | Coagulase-negative *Staphylococcus* – 1 (33) |
| | | | NR | |
| Bratell S et al[8] | 25 (10/40) | | | *E coli* – 6 (60) |
| | | | | *U urealyticum* – 2 (20) |
| | | | | *Klebsiella* – 1 (10) |
| | | | | *S epidermidis* – 1 (10) |
| | | 77 (24/31) | | *E coli* – 7 (29) |
| | | | | *Proteus* – 5 (21) |
| | | | | *U urealyticum* – 3 (13) |
| | | | | *U urealyticum, E coli, S epidermidis,* & diphtheroid rod – 3 (13) |
| | | | | *Proteus, Klebsiella, & Citrobacter* – 2 (8.3) |
| | | | | *Klebsiella* – 1 (4.2) |
| | | | | *Klebsiella & E coli* – 1 (4.2) |
| | | | | *S epidermidis* – 1 (4.2) |
| | | | 67 (6/9) | *Enterococcus* – 2 (40) |
| | | | | *U urealyticum* – 1 (20) |
| | | | | *E coli* – 1 (20) |
| | | | | *S aureus* – 1 (20) |
| Hugosson J et al[11,a] | 21 (32/153) | | | 45 total microorganisms |
| | | | | *E coli* – 14 (31) |
| | | | | *Staphylococcus* species – 7 (16) |
| | | | | *Streptococcus* – 3 (6.7) |
| | | | | *Proteus* – 2 (4.4) |
| | | | | *U urealyticum* – 2 (4.4) |
| | | | | *Enterococcus* – 2 (4.4) |
| | | | | *Enterobacter* – 1 (2.2) |
| | | | | *Pseudomonas* – 1 (2.2) |
| | | | | *Klebsiella* – 1 (2.2) |
| | | 71 (27/38) | | 34 total microorganisms |
| | | | | *Proteus* – 15 (44) |
| | | | | *Pseudomonas* – 5 (15) |
| | | | | *E coli* – 4 (12) |
| | | | | *Enterococcus* – 3 (8.8) |
| | | | | *Enterobacter* – 2 (5.9) |
| | | | | *Klebsiella* – 2 (5.9) |
| | | | | *U urealyticum* – 2 (5.9) |
| | | | | *Staphylococcus* species – 1 (2.9) |

**TABLE 3** (*Continued*)

| Study | Metabolic Stones With Positive Stone Culture (%) | Infection Stones With Positive Stone Culture (%) | Mixed Stones With Positive Stone Culture (%) | Most Common Organisms Isolated (%) |
|---|---|---|---|---|
| | | | 29<br>(5/17) | 6 total microorganisms<br>*E coli* – 3 (50)<br>*Staphylococcus* species – 2 (33)<br>*Klebsiella* – 1 (17) |
| McCartney AC et al[7] | 24<br>(4/17) | | | *E coli* – 2 (50)<br>*S aureus* – 1 (25)<br>*Pseudomonas* – 1 (25) |
| | | 86<br>(6/7) | | *Proteus & E coli* – 2 (33)<br>*Pseudomonas* – 1 (17)<br>*Proteus* – 1 (17)<br>*Klebsiella* – 1 (17)<br>*Proteus & S faecalis* – 1 (17) |
| | | | NR | |
| Fowler JE Jr[15] | NR | | | |
| | | 77<br>(17/22) | | *Proteus* – 9 (53)<br>*Pseudomonas* – 2 (12)<br>*Klebsiella* – 2 (12)<br>*Serratia* – 1 (5.9)<br>*Proteus & E coli* – 1 (5.9)<br>*Proteus & Serratia* – 1 (5.9)<br>*Proteus & Candida* – 1 (5.9) |
| | | | NR | |
| Lewi HJ et al[9] | 22<br>(10/46) | | | *E coli* – 7 (70)<br>*Proteus* – 1 (10)<br>*Klebsiella* – 1 (10)<br>*S faecalis* – 1 (10) |
| | | 82<br>(14/17) | | *Proteus* – 6 (43)<br>*Proteus & E coli* – 5 (36)<br>*E coli* – 2 (14)<br>*Proteus & Pseudomonas* – 1 (7.1) |
| | | | NR | |
| Total | Metabolic Stones | | | 116 total organisms<br>*E coli* – 34 (29)<br>*Staphylococcus* – 14 (12)<br>*Klebsiella* – 14 (12)<br>*Acinetobacter* – 13 (11)<br>*U urealyticum* – 6 (5.1)<br>*Pseudomonas* – 5 (4.3)<br>*Streptococcus* – 5 (4.3)<br>*Enterococcus* – 4 (3.4)<br>*Proteus* – 3 (2.6) |
| | | Infection Stones | | 98 total organisms<br>*Proteus* – 36 (37)<br>*E coli* – 13 (13)<br>*Pseudomonas* – 10 (10)<br>*Proteus & E coli* – 8 (8.2)<br>*Klebsiella* – 6 (6.1)<br>*U urealyticum* – 5 (5.1)<br>*Staphylococcus* – 3 (3.1)<br>*Enterococcus* – 3 (3.1)<br>*U urealyticum, E coli, S epidermidis, &* diphtheroid rod – 3 (3.1)<br>*Enterobacter* – 2 (2.1)<br>*Proteus, Klebsiella, & Citrobacter* – 2 (2.1) |
| | | | Mixed Stones | 11 total organisms<br>*E coli* – 4 (36)<br>*Staphylococcus* – 3 (27)<br>*Enterococcus* – 2 (18)<br>*Klebsiella* – 1 (9.1)<br>*U urealyticum* – 1 (9.1) |

[a]In some stone cultures, more than one microorganism was cultured. This is why the total number of microorganisms does not equal the number of positive stone cultures.
NR, not reported.

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## References

1. Margel D, Ehrlich Y, Brown, N et al. Clinical implication of routine stone culture in percutaneous nephrolithotomy—a prospective study. *Urology.* 2006;67:26-29.
2. Mariappan P, Smith G, Bariol SV, et al. Stone and pelvic urine culture and sensitivity are better than bladder urine as predictors of urosepsis following percutaneous nephrolithotomy: a prospective clinical study. *J Urol.* 2005;173;1610-1614.
3. Cadeddu JA, Chen R, Bishoff J, et al. Clinical significance of fever after percutaneous nephrolithotomy. *Urology.* 1998;52;48-50.
4. Larsen EH, Gasser TC, Madsen PO. Antimicrobial prophylaxis in urologic surgery. *Urol Clin North Am.* 1986;13:591-604.
5. Charton M, Vallancien G, Veillon B, Brisset JM. Urinary tract infection in percutaneous surgery for renal calculi. *J Urol.* 1986;135:15-17.
6. Mariappan P, Loong CW. Midstream urine culture and sensitivity test is a poor predictor of infected urine proximal to the obstructing ureteral stone or infected stones: a prospective clinical study. *J Urol.* 2004;171:2142-2145.
7. McCartney AC, Clark J, Lewi HJ. Bacteriological study of renal calculi. *Eur J Clin Microbiol.* 1985;4:553-555.
8. Bratell S, Brorson JE, Grenabo L, et al. The bacteriology of operated renal stones. *Eur Urol.* 1990;17:58-61.
9. Lewi HJ, White A, Hutchinson AG, Scott R. The bacteriology of the urine and renal calculi. *Urol Res.* 1984;12:107-109.
10. Gault MH, Longerich LL, Crane G, et al. Bacteriology of urinary tract stones. *J Urol.* 1995;153:1164-1170.
11. Hugosson J, Grenabo L, Hedelin H, et al. Bacteriology of upper urinary tract stones. *J Urol.* 1990;143:965-968.
12. Dewan B, Sharma M, Nayak N, Sharma SK. Upper urinary tract stones & ureaplasma urealyticum. *Indian J Med Res.* 1997;105:15-21.
13. Ma K, Xu QQ, Huang XB, et al. Clinical implication of stone culture in percutaneous nephrolithotomy. [Article in Chinese] *Zhonghua Yi Xue Za Zhi.* 2010;90:222-224.
14. Dajani AM, Shehabi AA. Bacteriology and composition of infected stones. *Urology.* 1983;21:351-353.
15. Fowler JE Jr. Bacteriology of branched renal calculi and accompanying urinary tract infection. *J Urol.* 1984;131:213-215.
16. Korets R, Graversen JA, Kates M, et al. Post-percutaneous nephrolithotomy systemic inflammatory response: a prospective analysis of preoperative urine, renal pelvic urine and stone cultures. *J Urol.* 2011;186:1899-1903.

## MAIN POINTS

- Despite the use of culture-specific or broad-spectrum antibiotic therapy prior to surgical removal of upper tract nephrolithiasis, certain patients still develop postoperative sepsis. Some have reported that preoperative voided urine cultures from these patients may not be reflective of the bacterial environment within the stone that is to be treated.
- The development of a urinary tract infection is a common postoperative complication associated with removal of upper urinary tract stones; one-third of patients undergoing percutaneous nephrostolithotomy experience this occurrence, which places patients at risk for developing sepsis and systemic inflammatory response syndrome, which can be fatal.
- Prescribing antimicrobial therapy that will eradicate the organism in the urine and provide broad-spectrum coverage for the potentially different bacteria harbored within the stone is desired. In addition, performing a stone culture may help to identify organisms that are not covered by initial antibiotic therapy, providing an opportunity to institute earlier targeted therapy.