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Bladder stones after bladder augmentation are not what they seem

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Summary

Introduction
Bladder and renal calculi after bladder augmentation are thought to be primarily infectious, yet few studies have reported stone composition.

Objective
The primary aim was to assess bladder stone composition after augmentation, and renal stone composition in those with subsequent nephrolithiasis. The exploratory secondary aim was to screen for possible risk factors for developing infectious stones.

Study design
Patients treated for bladder stones after bladder augmentation at the present institution between 1981 and 2012 were retrospectively reviewed. Data were collected on demographics, surgeries and stone composition. Patients without stone analysis were excluded. Stones containing struvite, carbonate apatite or ammonium acid ureate were classified as infectious. The following variables were analyzed for a possible association with infectious bladder stone composition: gender, history of cloacal exstrophy, ambulatory status, nephrolithiasis, recurrent urea-splitting urinary tract infections, first vs recurrent stones, timing of presentation with a calculus, history of bladder neck procedures, catheterizable channel and vesicoureteral reflux. Fisher's exact test was used for analysis.

Results
Of the 107 patients with bladder stones after bladder augmentation, 85 met inclusion criteria. Median age at augmentation was 8.0 years (follow-up 10.8 years). Forty-four patients (51.8%) recurred (14 multiple recurrences, 143 bladder stones). Renal calculi developed in 19 (22.4%) patients with a bladder stone, and 10 (52.6%) recurred (30 renal stones).

Overall, 30.8% of bladder stones were non-infectious (Table). Among patients recurring after an infectious bladder stone, 30.4% recurred with a non-infectious one. Among patients recurring after a non-infectious stone, 84.6% recurred with a non-infectious one ($P = 0.005$).

Compared with bladder stones, renal stones were more likely to be non-infectious (60.0%, $P = 0.003$). Of patients with recurrent renal calculi after an infectious stone, 40.0% recurred with a non-infectious one.

No clinical variables were significantly associated with infectious stone composition on univariate ($\geq$0.28) or bivariate analysis ($\geq$0.36).

Discussion
This study had several limitations: it was not possible to accurately assess adherence with bladder irrigations, and routine metabolic evaluations were not performed. The findings may not apply to patients in all clinical settings. While stone analysis was available for 3/4 of the stones, similar rates of incomplete stone analyses have been reported in other series.

Conclusions
In patients with bladder augmentation, 1/3 of bladder stones and >1/2 of renal stones were non-infectious. Furthermore, an infectious stone does not imply an infectious recurrent stone and no known clinical variables appear to be associated with stone composition, suggesting that there is a possible metabolic component in stone formation after bladder augmentation.

Table Stone composition of bladder and renal stones in patients with augmented bladders.

Stone composition	Bladder stones (n = 143) (%)	Renal stones (n = 30) (%)
Infectious stones	**99 (69.2%)**	**12 (40.0%)**
Struvite	79 (55.2%)	11 (36.7%)
Pure carbonate apatite	15 (10.5%)	1 (3.3%)
Pure ammonium acid ureate	2 (1.4%)	0 (0.0%)
Mixed stones with calcium phosphate	4 (2.8%)	0 (0.0%)
Non-infectious stones	**44 (30.8%)**	**18 (60.0%)**
Calcium phosphate	41 (28.7%)	14 (46.7%)
Pure calcium oxalate	0 (0.0%)	4 (13.3%)
Uric acid	3 (2.1%)	0 (0.0%)

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Introduction

Bladder and renal stones are common in patients with bladder augmentation [1—6]. Calculi occurring in this population are primarily thought to be infectious; this is largely based on series of adults with spinal cord injuries reporting that virtually all bladder and renal calculi are struvite [7,8]. Therefore, extrapolating these findings to children with augmentation cystoplasty may be inappropriate. Small case series of children with augmented bladders show that a significant proportion of stones are non-infectious [1—4,9—15]. In addition, it is believed that, to date, no published reports exist on the composition of renal calculi in this population. Metabolic abnormalities may play a significant role in stone formation, particularly in non-infectious stones.

The primary aim of this study was to assess bladder stone composition after bladder augmentation, and renal stone composition in those with subsequent renal stones. The secondary exploratory aim was to screen for possible risk factors for developing infectious stones.

Materials and methods

A retrospective, IRB-approved, single-center study of patients treated for bladder stones after bladder augmentation at the present institution between 1981 and 2012 was performed. Data on demographics, surgeries, stone cultures and stone composition (determined by infrared spectroscopy at a single laboratory, Beck Analytical Services, Indianapolis, Indiana) were collected. Patients without stone analysis were excluded. Stones containing struvite, carbonate apatite or ammonium acid ureate (AAU) were classified as infectious [16]. Stones were similarly managed regardless of composition [6]. Stone cultures were sent, based on surgeon preference. Stone-free status was confirmed by kidney, ureters and bladder (KUB) X-ray and renal bladder ultrasound (RBUS) at 2—6 months after stone surgery. Individuals with >1 recurrence were classified as having multiple recurrences. Routine follow-up included serial, typically annual, physical examination, serum chemistry, KUB and RUBS.

The following variables were analyzed for a possible association with infectious bladder stone composition: gender, history of cloacal exstrophy, ambulatory status, nephrolithiasis, recurrent urea-splitting UTIs during follow-up (two or more UTIs per year), first vs recurrent stones, timing of presentation with a calculus, history of bladder neck procedures, catheterizable channel and VUR. Cloacal exstrophy predisposes patients to short bowel syndrome, which may increase overall stone risk and affect stone composition [17,18]. A UTI was defined as a positive catheterized urine culture in a symptomatic patient. Timing of presentation was classified based on time after augmentation and age after augmentation. Late presentation was defined as $\geq$6 years after augmentation, which was the median time of presentation with any stone (either first or recurrent, range 5 months—30.6 years). Timing of presentation based on age was classified in two ways: as a stone developing in adolescence (14—18 years old) or adolescence/young adulthood (14—21 years old). Bladders with bladder neck procedures and catheterizable channels may empty inefficiently. Routine cystography was not performed after augmentation. Any grade of VUR (yes/no) was assessed on any available cystourethrogram or videourodynamics study performed after augmentation. Analysis of VUR was restricted to patients with cystogram data. Timing of detected VUR was classified as pre-stone (from augmentation to 1 year prior to first bladder stone), peri-stone (between 1 year prior and 1 year after first bladder stone) and post-stone ($\geq$1 year after bladder stone). For bladder stones, VUR data was available in 75%, 63% and 75% of cases during pre-stone, peri-stone and post-stone timeframes, respectively (mean 71%).

For renal stones: gender, recurrent urea-splitting UTIs and VUR were analyzed as possible risk factors for infectious composition. VUR data was available in 47%, 54% and 77% of cases during pre-stone, peri-stone and post-stone timeframes, respectively (mean 59%). VUR may allow trapped mucus to become a stone nidus in the collecting system [19].

Fisher's exact test was used for analysis. Variables with a $P < 0.4$ on univariate analysis were included in a multivariate analysis. A critical $P = 0.05$ was used (Stata 10.1).

Results

Population characteristics

Of the 720 patients in the institutional augmentation database, 107 (14.9%) developed bladder calculi. Of these, 85 patients (79.4%) met inclusion criteria by having a stone analysis available (Table 1). Forty-seven patients (55.3%) were female, 57.6% had a neuropathic bladder secondary to myelomeningocele, and 7.0% had cloacal exstrophy. Overall, 55.3% of patients were non-ambulatory. Median age at augmentation was 8.0 years (range 2.4—22.8) and median follow-up was 10.8 years (range 1.8—32). The most common bowel segments used for augmentation were ileum (82.4%) and sigmoid (11.8%). Others were augmented with ureter (1.2%) or composite segments, either ileocecum (2.4%) or stomach/ileum (1.2%). A catheterizable channel was created in 84.7%. Bladder neck procedures were performed in 68.2% (bladder neck reconstruction in 41.2%, bladder neck sling only in 18.8%, artificial urinary sphincter in 5.9% and bladder neck closure in 2.4%). Eighteen patients (21.2%) had recurrent UTIs with urea-splitting organisms. No patients had bladder or renal stones prior to augmentation.

Bladder stones

Of the 85 patients treated for a bladder stone, 44 (51.8%) recurred (14 had multiple recurrences), for a total of 143 stones available for analysis. Overall, 30.8% of bladder stones were non-infectious (Table 2). Two-thirds of these were pure calcium phosphate stones. Others were mostly mixed calcium phosphate/oxalate stones, with a median calcium phosphate content of 65% (range 22—90%). No pure calcium oxalate bladder stones were observed. Three uric acid stones (2.1% of all bladder stones) were noted: two pure and one combined with calcium oxalate. Infectious