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Original Research Article

The Endourological Management of Renal and Ureteric Matrix Calculi: Soft Stones with Hard Outcome

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Abstract

Background: Matrix calculi are rare calculi accounting for 1-2% of all urinary stones. Due to atypical clinical presentation and imaging characteristics, these constitute diagnostic and therapeutic challenges. **Material and Methods:** We conducted a retrospective review of patients from Jan 2010 to December 2020 at a large tertiary care teaching hospital. The patients of renal/ureteric matrix calculi who were managed at our institute were included for study analysis. Demographic parameters (clinical profile, imaging characteristics), and surgical outcomes were analysed. **Results:** 40 patients (1.14%) were found to have matrix stones. The mean age of presentation was 38.81± 15.34 years (range 7-78). The male: female ratio was 2.33:1. Most common presenting symptoms were flank pain (47.5%) followed by UTI (25%). Recurrent urolithiasis was the most common predisposing factor (22.5%). The mean stone size was 2.52 ±0.83 cm. Most cases were managed with endo-urological procedures (PCNL/URS). The mean age of presentation, stone size, operative time and hospital stay was significantly higher in females ($p<0.05$). Minor complications (mostly Clavein grade 1 and 2) were observed in 10 patients (25%). The stone free rate in immediate postoperative period and at 3 months were 85% and 87.5%. The mean follow up period was 16.55 + 2.38 months (range 12-20). **Conclusion:** The matrix calculi are rare calculi accounting for 1.14% of upper urinary tract stones. Minimally invasive procedures (PCNL/URSL) are safe and primary treatment modality with acceptable stone-free rates (87.5%). However, overall surgical outcomes are poorer than crystalline stones. In short these "soft stones have hard outcome".

Keywords: Urinary Calculi, Urinary Tract Stones, Crystalline Stones.

Introduction

Matrix calculi are rare urinary calculi first described by Gage and Beal in 1908[1]. They account for only 1-2% of all urinary stones[2,3]. These stones were also called previously as fibrinomas, albumin calculi and colloid calculi[3-5]. Due to a typical clinical presentation and radiographical characteristics, these stones constitute diagnostic and therapeutic challenges in clinical practice[3]. While, normal urinary stones are more common in males (male to female ratio of 2-3:1) matrix stones are 2-3 times more commonly encountered in females[6,7]. These stones have tendency to grow to larger sizes at presentation due to absence of alarming symptoms (hematuria,dysuria) and also may re-grow rapidly after surgical removal[5,8]. Due to their sticky and gelatinous nature (**Figure 1**) they can adapt to the shape of renal pelvis/ ureter leading to complete obstruction presenting as acute renal insufficiency[9-11]. Matrix calculi have high proteinaceous component (average: 65%, range: 42-84%) compared to normal brittle calcigerous calculi (2.5% matrix)[2,5]. Hence they are usually radiolucent/ faintly radio-opaque on plain radiography[9-11]. There is paucity of literature about urinary matrix calculi and no standard guidelines are available about management. The objectives of our study were to evaluate clinical trends and outcomes of patients of matrix calculi who presented at our centre.

Material and methods

We retrospectively reviewed database of patients who underwent some surgical management- percutaneous nephrolithotomy (PCNL) or ureteroscopic lithotripsy (URSL) for upper urinary tract (renal/upper ureteric) matrix calculi at a tertiary care teaching hospital from Jan 2010 to December 2020. The institutional ethical committee exempted our study for requiring any formal ethical approval as it was retrospective and all procedures were carried out as per Declarartion of Helinski after obtaining informed consent from patients. The definitive diagnosis of matrix calculi was based on radiological imaging-non contrast computerized tomography (NCCT) of abdomen (Figure 2), intra-operative findings (Figure 3 and 4) and infrared spectroscopic stone analysis. We excluded patients with anomalous kidney, active urinary tract infection (UTI), uncorrected coagulopathy, pregnancy, incomplete data or lost to follow-up. All procedures (PCNL or URSL) were performed by expert urologists at our institute under either spinal anesthesia or general anaesthesia. Baseline demographic features (age, sex, BMI), stone characteristics (size, location, laterality, Guy's stone score) total operative duration, postoperative complications (according to Clavien-Dindo classification), hemoglobin drop, stone clearance rate and hospital stay were analysed[12,13]. Success after procedure was defined as either stone free status or the presence of clinically insignificant residual fragments <3 mm on follow-up. Nephrostomy tube was removed after 48-hours after confirming stone clearance. The confirmation of complete stone clearance was done based on nephrostogram (Figure 5) or Non-Contrast CT KUB performed at 48 hours after surgery. The ureteral stent was removed after 2-weeks. All patients were given 4-6 weeks of antibiotic course. Follow up imaging was done with USG/NCCT KUB at 3 and 12-months post-operatively to see residual/recurrent stone.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 21.0 software (IBM Co., Armonk, NY, USA). Discrete categorical data were expressed as number and percentage. Continuous data were expressed as mean ± standard deviation. Categorical variables were analyzed using Pearson Chi-square test or Fisher's exact

test. Continuous variables were compared between the two groups (males and females) using independent samples Student's t-test or Mann-Whitney U test. A p-value < 0.05 was considered as statistically significant.

Results

More than 3500 patients underwent upper urinary tract stone surgery in above mentioned period out of which only 40 patients (1.14%) were found to have matrix stones. The baseline demographic characteristics are depicted in **Table 1.**

Table 1: Baseline patient demographics and stone characteristics

Parameter	Overall (N=40)	Male (N=12)	Female (N=28)	P value
Age (Years) Mean ± SD	38.81± 15.34	28.52±14.5	43.22±16.24	<0.01*
BMI (Mean ± SD)	23.81± 1.73	22.32±1.65	24.46±1.9	0.04*
Presenting Symptoms:				
Flank Pain	19	6	13	
Recurrent UTI	10	3	7	
Obstructive Uropathy	4	1	3	
EPN	1	0	1	
Asymptomatic	6	2	4	
Predisposing Factors:				
Recurrent Stone former	9	3	6	
Previous stone surgery	5	2	3	
Chronic Renal Failure	3	1	2	
Urinary Obstruction (PUJO, Ureteric stricture)	2	1	1	
Co-morbidities				
Diabetes	4	1	3	
Morbid Obesity	2	1	1	
Steroid Use	2	0	2	
Stone location				
Calyceal	6	2	4	
Pelvic	9	3	6	
Pelvicalyceal	16	5	11	
Upper ureter	3	1	2	
Mid and lower ureter	6	1	5	
Stone size (cm)	2.52±0.83	2.23±0.89	2.65±0.78	0.04*
Hounsfield Unit (HU) Mean±SD	545±130	538±123	549±121	0.54
Urine Culture				
Sterile	12	4	8	
Proteus mirabilis	7	2	5	
E. Coli	9	3	6	
Pseudomonas	3	1	2	
Klebsiella	2	0	2	
Others	3	1	2	
Polymicrobial	4	1	3	
Presence of hydronephrosis	14	3	11	<0.01*
Guy's stone score	2.3±0.44	2.2±0.42	2.4±0.45	0.08
*Statistically Significant, S.D: Standard Deviation, UTI: Urinary tract infection, EPN: Emphysematous pyelonephritis, PUJO: Pelviureteric obstruction				

Table 2: Comparison of intra-operative and peri-operative parameters

Parameter	Overall (n=40)	Male (n=12)	Female (n=28)	P value
Type of Procedure				
PCNL	33	10	23	0.72
URSL	7	4	3	
Total operating time (minutes)				
PCNL	83.3± 18.2	75.4±17.6	86.7±18.8	0.01*
URSL	46.9±13.0	45.5± 12.7	47.8± 13.2	0.62
Stone free rate-N (%)				
On 2nd post-op day	34 (85%)	11 (91.7%)	23 (82.1%)	0.003*
After 3 months	35 (87.5%)	11 (91.7%)	24 (85.7%)	0.002*
At 12 months	32(80%)	10 (83.3%)	22 (78.6%)	0.01*
Hemoglobin drop (g/dl)	0.88±0.21	0.85±0.17	0.89±0.22	0.45
Mean creatinine rise (mg/dl)	0.91±0.25	0.81±0.21	0.96±0.28	0.09
Hospital stay (days)	2.5±0.5	2.4±0.4	2.9±0.5	0.002*
Clavein-Dindo Classification				0.03
Grade 1				
Fever	3	1	2	
Pain	2	1	1	
Nausea/vomiting	1	0	1	
Grade 2				
Urinary tract infection	1	0	1	
Bleeding requiring transfusion	1	0	1	
Grade 3				
Bladder clot evacuation	1	1	0	
Grade 4				
Urosepsis	1	0	1	

The mean age of presentation was 38.81± 15.34 years (range 7-78). The male: female ratio was 2.33:1. Most common presenting symptoms were flank pain (47.5%) followed by UTI (25%). Recurrent urolithiasis was the most common predisposing factor (in 22.5% patients). The mean stone size was 2.52 ±0.83 cm. Co-morbidities (diabetes, morbid obesity and steroid use) was present in 8-cases (20%). The urine culture revealed growth of micro-organisms in 28 (70%) patients. The intra-operative and postoperative details are depicted in **Table 2**. Most cases were managed with endourological procedures (PCNL/URS). On comparison of data the mean age of presentation, stone size, operative time and hospital stay was significantly higher in females ($p<0.05$). Stone clearance rate was also significantly poorer in females than males. (85.7% versus 91.7%, $p<0.05$). Minor complications (mostly Clavein grade 1 and 2) were observed in 10 patients (25%). The stone free rate in immediate postoperative period and at 3 months were 85% and 87.5%. The mean follow up period was 16.55 $\pm$ 2.38 months (range 12-20).

Table 3: Brief description of previous study related to matrix calculi

S.No	Author, Year	Country	Sample size (N) (F:M)	Mean Age (Range)	Predisposing factors	Surgical Modalities Used (No. of patients-Modality)
1.	Beltrami et al[5], 2014	Italy	9 9:0	50 (4-69)	Recurrent UTI Previous Stone surgery	6 –PCNL 1 - PCNL +RIRS+SWL 1 -RIRS+PCNL 1 - Multidisciplinary approach
2.	Shah HN et al[2] 2008	India	17 1.83:1	44.3 (26-71)	Recurrent UTI Previous Stone surgery Chronic Renal Failure	All patients PCNL
3.	Rowley MW et al[6] 2008	USA	9 3.5:1	47.8 (26 mo-70)	Recurrent UTI Previous Stone surgery Chronic Renal Failure Smoking	8 –PCNL 1 -PCNL+SWL
4.	Bani-Hani AH et al[3] 2005	India	5 2:3	70 (63-78)	UTI Previous Stone surgery	2 –Open Pyelolithotomy 2 -PCNL 1 - URSL+PCNL
5.	Stoller ML et al[7] 1994	USA	5 1.5:1	50.8 (23-64)	Recurrent UTI Stones former Previous Stone surgery Urinary obstruction	4 –PCNL 1 -Open Nephrolithotomy
6.	Present Study 2018	India	40 2.33:1	38.81 (7-78)	Recurrent UTI Stones former Previous Stone surgery Chronic Renal Failure Urinary obstruction	33 –PCNL 5 -URSL 2 -PCNL+URSL
PCNL: Percutaneous nephrolithotmy, URSL: Ureteroscopic Lithotripsy, RIRS: Retrograde Intra-renal Surgery						

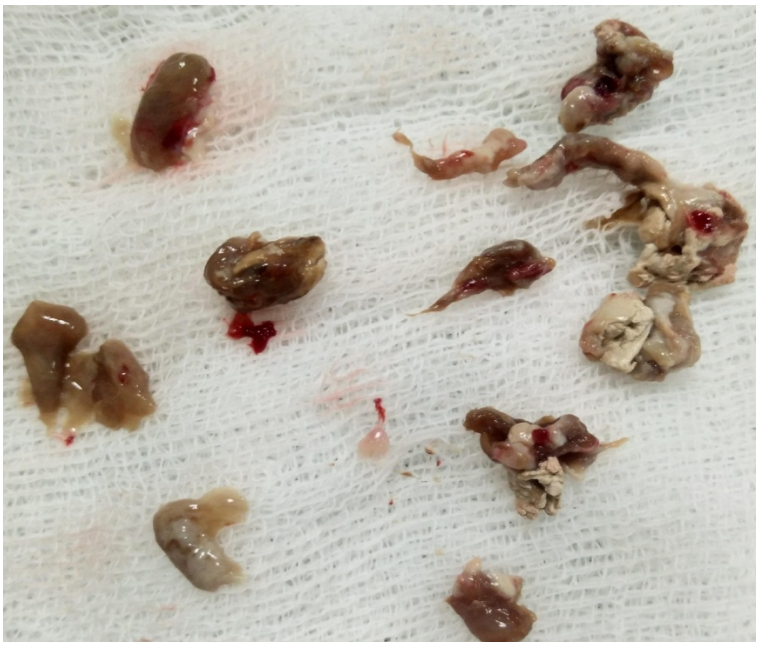

Figure 1: Clinical image depicting soft gelatinous nature of matrix stones

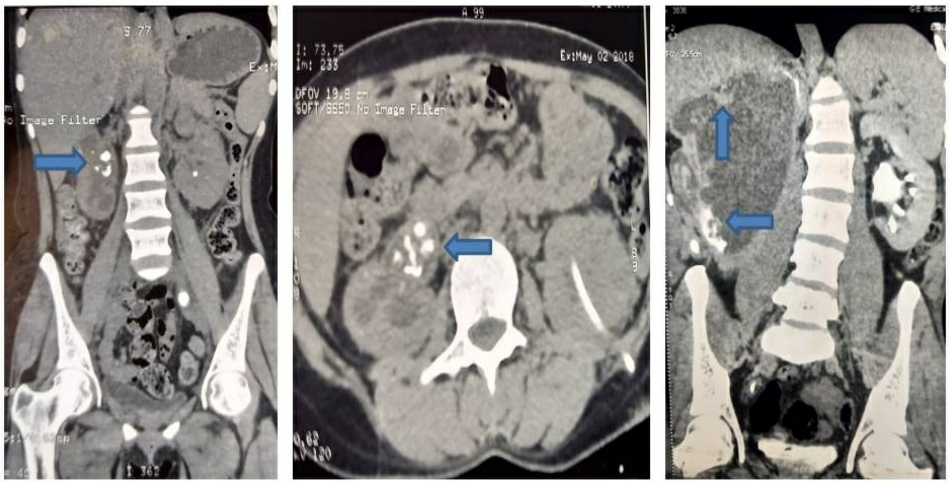

Figure 2: Non contrast CT scan image showing irregular radio-densities in right upper ureter (blue arrow)

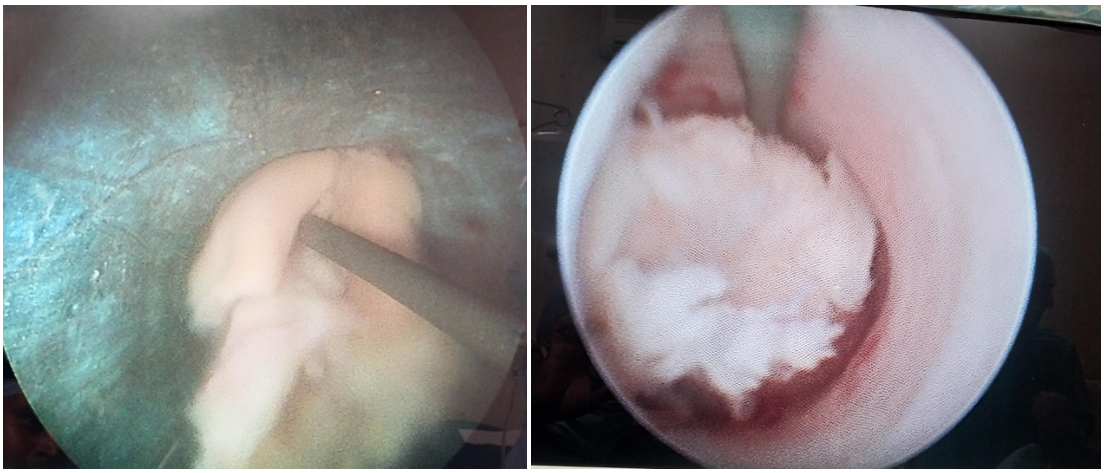

Figure 3 and 4: Intra-operative images of matrix calculi

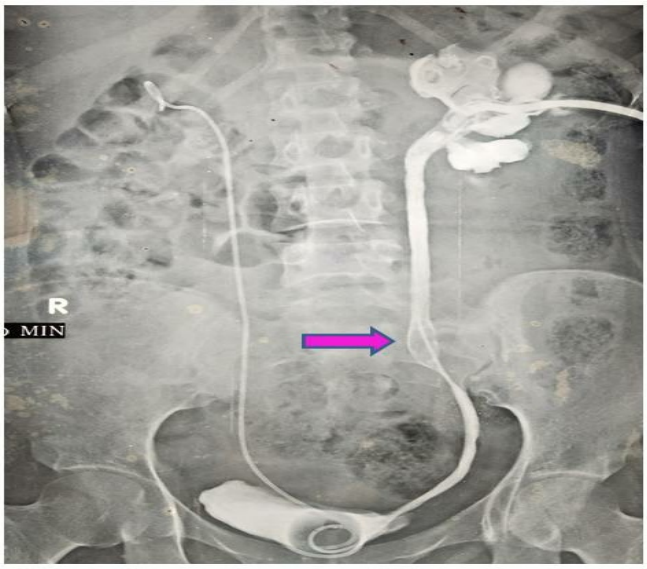

Figure 5: Nephrostogram image showing filling defect in mid-ureter (pink arrow)

Discussion

There is only limited published literature available on outcomes of matrix urinary calculi. A brief description is depicted in **table 3**. In previous studies the mean age of presentation is described as more than 45 years[2-6]. The mean age of presentation was less (38.81 years) in our study. With advancement in diagnostic imaging and increased patient awareness many cases are now diagnosed at an early age.

Stoller et al showed that matrix stones are three times more common in female population in contrary to epidemiology of crystalline renal stones[7]. Female predominance was also revealed in our patients (2.33:1).

The major predisposing factors for matrix calculi as also found in present study include previous stone surgery, recurrent stone formers, recurrent UTI (especially due to Proteus mirabilis/ Escherichia coli), chronic renal failure, proteinuria, urinary stasis etc[2-7].

Boyce and Garvey et al have demonstrated that matrix substance of both crystalline (calcigerous) and non-crystalline (matrix) calculi are closely related but not identical[14]. The matrix substance consists of approximately one-third mucopolysaccharide (a carbohydrate) and two-thirds mucoprotein (distinct from Tamm-Horsfall protein) by weight[14].

Bani-Hani et al proposed that the reason for the lack of calcifications in matrix calculi could be due to reduced urinary calcium excretion by the affected kidney[3]. These stones may silently grow to large sizes leading to obstructive uropathy and presenting with acute/chronic renal failure[6,9]. Four patients(10%) in present study also presented with symptoms of renal failure secondary to obstructive uropathty. Rarely, emphysematous pyelonephritis has been described in patients of matrix urolithiasis like one of our patients[15].

Matrix stones usually have different characteristics on imaging than crystalline stones. Pure matrix stones are radiolucent on plain roentgen films[16-18]. However, faint radio-opaque shadow may appear in presence of minute calcification[4-7]. NCCT scan is the gold standard imaging modality for diagnosing these stones. Matrix stones appear as non-enhancing soft tissue densities with or without irregular internal or peripheral rim calcification[4,16,17]. Measurement of the Hounsfield unit (HU) varies with mineralogical amount, composition, and

pattern of distribution in the matrix calculi[4,17]. The average HU in our study subjects were 545±130 which is low compared to crystalline stones.

Despite advances in radio-imaging techniques, definitive diagnose of matrix stones can only be established on surgical stone extractions and stone analysis[3,6,7]. No well-defined guidelines are available yet on management of matrix calculi and treatment has been extrapolated from retrospective studies.

Matrix calculi are usually larger in size and have less chance to pass spontaneously[5,8]. The average size of stones in present study was around 2.5 cm which is quite high. Extracorporeal shock wave lithotripsy (ESWL) is usually fruitless procedure for management of these stones due to the gelatinous nature, larger volume, lack of disruptable mineral contents and difficulty in fluoroscopic targeting of these stones[3,6]. In three of our patients there was history of failed stone clearance after ESWL performed at other centres.

Nowadays, minimally invasive endourological surgeries (PCNL/URSL) are standard, widely popular and effective surgical modality for management of renal/ureteric matrix calculi[2-6,18,19]. The safety of endourological procedures in managing matrix calculi was evident in the present study as well as there was little drop in haemoglobin(<1g/dl) and minimal rise in serum creatinine (<1 mg/dl).

The average stone clearance after PCNL at 3-months post-surgery was 87.5% in present study, which is inferior to that for normal crystalline stones (>95%)[20,21].

Few unique findings in present study that deserve special mention include-(a) More amount of contrast was required for delineation of stones and average radiation exposure time was high; (b) None of the modalities (pneumatic lithotripter/Ho-YAG laser were effective in successful disintegration of stones and use of triprong/biprong forceps with concomitant lukewarm saline flush was more effective in stone evacuation and clearance.

In our opinion, utilization of flexible nephroscope, triprong stone grasping forceps and lukewarm saline wash during PCNL are valuable manoeuvres for improving the surgical success rate and for diminishing the operative duration. Current knowledge about application of these facts is scant.

Most of the complications in present study were minor and were managed conservatively. Postoperative adjunctive procedure (bladder clot evacuation) was performed in 1 patient, while the nephrostomy catheter was maintained for an extra week in 2 patients. One patient with extensive matrix stones developed urosepsis in immediate postoperative period, which was managed successfully with intravenous antibiotics, ionotropic supports and supportive measures.

Our study has few limitations. The present series is a retrospective study and represents clinical data of a single centre only. We also lack long term data on outcome of these patients. However, to the best of our knowledge, the present study so far gives the largest comprehensive evaluation of demographic profile and outcomes of matrix calculi from a tertiary care centre. Prospective multicentre studies in future will help to provide insights into the patho-physiology, molecular genesis and metabolic abnormalities of this rare entity.

Conclusion:

The matrix calculi are rare calculi accounting for 1.14% of upper urinary tract stones. Minimally invasive procedures like PCNL and URSL are safe and primary treatment modality for matrix calculi with acceptable stone-free rate (87.5%). However, overall surgical outcomes (stone free rates and complications) are poorer than for normal crystalline stones. In short it can be

summarized that “soft stones have hard outcome”.

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