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OUTCOME OF ASYMPTOMATIC CALICEAL CALCIUM NEPHROLITHIASIS

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ABSTRACT: To evaluate the utility of extensive treatment of asymptomatic caliceal calcium stones, we reviewed the outcome of 76 untreated patients (pts). Forty-eight (63.1%) remained symptom-free throughout a follow-up of 60±38 months. However, 28 (24 m, 4 f), almost all of them with a history of kidney stones, experienced a symptomatic event: the cumulative probability was 39% at five years and 51% at ten. In 14 pts the event was colicky pain leading to passage of the stone, and 14 pts (18.4%) required ESWL or urological interventions. In the symptomatic patients, the stone size was the only predictive factor. In the patients requiring ESWL or endoureteral removal, the stones grew with time (6.9±2.1 to 10.8±4.1 mm, p<0.01); 13 of the 17 stones smaller than 8 mm, were passed spontaneously but only one of the 11 stones larger than 8 mm (76.5 vs 9.1%, p<0.01).

These data suggest that an expectant strategy is still justified and reasonable in many cases and that ESWL is to be preferred to deal with stones sited in the upper or middle calyx, growing larger than 8 mm, particularly in males with recurrent calcium stone disease.

KEY WORDS: *Urinary calculi, Calcium stones, Prognosis*

INTRODUCTION

Extracorporeal shock wave lithotripsy (ESWL) has radically changed the treatment of urinary stones (1).
ESWL is one of the most impressive examples of the contribution that modern technology can make to medical practice. It results in a significant reduction in morbidity, invasiveness, discomfort and cost of the treatment of stones (1). These features have induced many urologists to use ESWL also to treat symptom-free caliceal stones causing neither discomfort nor urinary tract obstruction. The aim is the prevention of future episodes of pain, urinary tract obstruction and infection. However, these problems can be caused by the ESWL procedure itself, which is not free from other risks or complications (2). Moreover, undue use of ESWL in all patients with caliceal urolithiasis increases the social costs.
Consequently, in clinical practice, the question arises whether to treat the asymptomatic caliceal calcium stone with ESWL or simply to wait.
In the present study we evaluated the occurrence of symptomatic events in untreated patients with caliceal calcium stones. The natural history of asymptomatic stones has been recently viewed (3), but there is still no definite answers to this dilemma. In an attempt to obtain more details about the risk of unfavourable events and to detect predictive features, we investigated the outcome of patients with caliceal calcium stones.

METHODS

Seventy-six patients (46 males and 30 females, aged 42±12 yrs) with asymptomatic caliceal stones were selected from an overall population of 506 primary calcium stone formers followed up in the stone clinics in Pisa and Casale Monferrato during the period 1985-1994. To enter the study, patients had to have been asymptomatic for at least six months after identification of the stone by radiographic and ultrasonographic methods.
Patients with primary hyperparathyroidism or hypercalcemia were excluded as were patients with infectious, cystine or uric acid stones.
At baseline we recorded the age, sex, body mass index (BMI) of each patient, and the size, number and site of the stones; stones were measured again at the end of the observation period.
At the time of entry to the stone clinic, patients were studied to detect any risk factors for calcium stone disease, namely hypercalciuria (urinary calcium excretion >4 mg/kg b.w.), hyperuricosuria (urinary uric acid excretion >700 mg/24 h), hyperoxaluria (urinary oxalate excretion >42 mg/24 h) and hypocitraturia (urinary citrate excretion <320 mg/24 h). In all the patients, fluid therapy and dietary measures were suggested and in some cases drugs were prescribed to correct the urinary abnormalities.
The number of stones already passed, and details of ESWL, surgical or endoureteral procedures were obtained from the patients' records.
For each patient the time spent from the diagnosis till the symptomatic event leading to passage of the stone, ESWL or urological interventions was recorded. Patients who remained symptom-free were censored at the time of the last sonographic or X-ray check.
Statistical analysis was done using the Kaplan-Meier time-to-event survival curve, analysis of variance (one-way ANOVA), Chi-square test, Chi-square for linear trend, Student's t-test for paired and unpaired data. All results are given as mean ± standard deviation.
Differences were considered statistically significant when $p<0.05$.

RESULTS

In our series, 48 of the 76 patients (63.1%) remained

asymptomatic throughout a follow-up of 60±38 months (Fig. 1). Twenty-eight (36.8%) experienced a clinical event within 33±22 months of identification of the stone. The cumulative probability of a symptomatic event was 39% at five years and 51% at ten (Fig. 1). In half the cases (14 pts) it was a renal colic leading to passage of the stone and in the other half ESWL (11 pts) or endoureteral removal (3 pts) were required. Symptomatic events requiring treatment occurred only in 18.4% of the patients: gross hematuria in two cases, persistent loin pain in one, migration of stones in the pelvis in eight, and ureteral obstruction in four. In all these patients treatments were successful, with no major complications; only two patients required re-treatment with ESWL.

Comparison of the event and the no-event patients showed *that the former* were almost exclusively male and younger. No relationship was found with the size or number of stones at baseline, but the lower pole seemed to be the prevalent site in patients remaining symptom-free (Tab. I). Most patients with a history of stone passages were in the event group: the more stones they had passed, the higher prevalence of events (Tab. II).

Stone size was the only predictive factor of the outcome of symptomatic patients. In the treated patients the stone was larger at the outcome than in the patients who passed their stones (Tab. III). In other words the stones grew significantly bigger only in the group who experienced events not leading to stone passage (Tab. III). In the event group, 13 of the 17 stones smaller than 8 mm were passed compared to only one out of 11 stones larger than 8 mm (76.5 vs 9.1%, p<0.01).

The prevalence of the classic risk factors in the 76 patients at baseline were: hypercalciuria 48.6%, hyperuricosuria 40.0%, hyperoxaluria 14.5 and hypocitraturia 18.0%. No significant differences were observed between event and no-event stone patients.

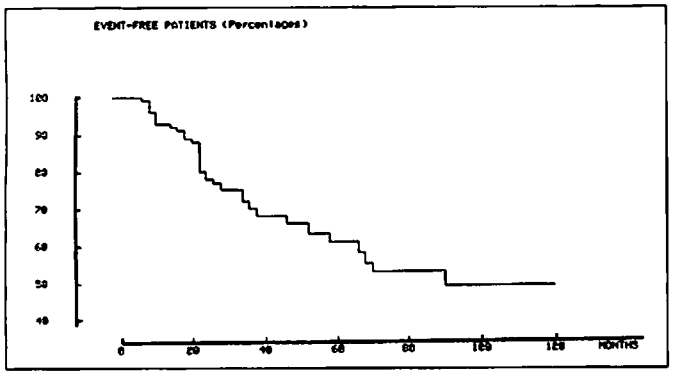

Fig. 1 - Probability of symptomatic events in patients with caliceal calcium stones.

Table I - Baseline data for patients with calcium stones with or without a symptomatic event in the follow-up

	No event	Event	
Male/female	22 / 26	24 / 4	* *
Age, years	45 ± 12	37 ± 10	§ §
B M I, kg/m²	24.7 ± 3.3	26.2 ± 4.4	n.s.
Stone size, mm	7.1 ± 3.0	6.2 ± 1.8	n.s.

	No event No. (%)	Event No. (%)
Number of stones		
– 1	31 (64.6)	19 (67.8)
– 2	14 (29.2)	7 (25.0)
– ≥3	3 (6.2)	2 (7.2)
Site of the stones (calyx)		
– Upper/middle	14 (50.0)	14 (50.0)
– Lower	34 (70.8)	14 (29.2)
– Multiple	2 (50.0)	2 (50.0)

*** p<0.01 (X^2 test); § § p<0.01 (Student's t-test)*

Table II - Historical data at identification of calcium stone formers with or without clinical events. Top: number of patients (percentage) with no previous stones, or with history of stones passed or requiring ESWL or urological treatments. Bottom: number of patients (percentage) with different numbers of stones passed in the past

	No event No. (%)	Event No. (%)
History of		
– No stone	14 (73.7)	5 (26.2)
– Stone passed	9 (37.5)	15 (62.5)
– Treatments	25 (75.7)	8 (24.7)

Chi-square: 9.94, p<0.01

No. previous stones		
0	32 (76.2)	10 (23.7)
1-2	12 (48.0)	13 (52.0)
≥3	4 (44.4)	5 (55.5)

Chi-square for linear trend: 5.92, p<0.05

Table III - Changes in stone size in the patients remaining asymptomatic, or with a clinical event resulting in spontaneous passage or requiring ESWL or urological treatment

	No event	Event	
		Stone passed	Stone treated
Stone size, mm			
at identification	7.1 ± 3.0	5.5 ± 1.1	6.9 ± 2.1
at outcome	7.5 ± 3.0	6.0 ± 1.2	10.8 ± 4.1 ***
t-test (paired)	n.s.	n.s.	p<0.01

**** p<0.001 vs "No event" and "Stone passed" groups (ANOVA)*

Discussion

Medical therapy is the first choice in uric acid stone disease, using alkalinizing agents, allopurinol and fluid. This is not the case for calcium stones. Detection and correction of the risk factors for calcium stone disease is very important to prevent their recurrence and growth but unfortunately it cannot dissolve them (4, 5).

Therefore, in clinical practice, after identification of a caliceal calcium stone, the question arises whether to treat it or not. Although ESWL is relatively safe, especially in patients with a single caliceal calcium stone, resulting in good stone clearance and minimal discomfort (6), indiscriminate ESWL treatment of these stones is still debated.

In this retrospective study, 36.8% of the patients selected experienced a symptomatic event. Half these events were renal colic leading to passage of the stone. This favourable and resolutive event is much more frequent when the stone is smaller than 8 mm. When the stone is larger, urinary tract obstruction is much more probable requiring ESWL or other treatments, as previously reported (7).

The higher the number of previous stone passages, the greater are the chances of a clinical event, but the growth of the stone is the main risk factor associated with obstructive uropathy requiring treatment.

This occurred in 14 of the 76 patients in this series, with calcium caliceal stone at baseline. In all cases, the lithotripsy (or endoureteral removal) was successful. It thus follows that, when an extensive treatment strategy is employed for asymptomatic caliceal stones, about 80% of the treatments should be unneccessary within a five-year period.

As a rule, a treatment is well indicated when the expected benefits exceed the risks and the costs.

The costs of frequent monitoring for untreated patients are also present in ESWL treated patients to assess the clearance of stone fragments and the absence of complications, and to check the effectiveness of medical treatment for the prevention of recurrences.

In caliceal calcium stone patients the benefit of ESWL consists in the prevention of a symptomatic event; the risks include hematuria, pain due to stone fragment passage, or those connected with analgesic or antibiotic therapy, with the invasive procedure employed in case of ureteral obstruction, or re-treatments. Major complications, like perinephric or retroperitoneal hemorrhage, are rare (2), and early reports of an increased prevalence of arterial hypertension in ESWL treated patients are far from demonstrated (8, 9).

In the years before ESWL, patients with small asymptomatic caliceal stones did not undergo surgery and "watching and waiting" was largely accepted (10). Our data suggest that this approach is still reasonable in many cases. However, for stones in the upper or middle calyx, growing larger than 8 mm, prophylactic ESWL may be indicated because of the high risk of a symptomatic event not followed by passage of the stone and for the high ESWL free stone rates (11). However, in our opinion, the decision whether or not to treat patients with asymptomatic stones is also affected by non-clinical aspects such as occupational, socio-economic or psychological factors. In these cases, the final decision is the patient's but the physician *must make* patients aware of the risks, advantages and probable outcomes of the different approaches.

In conclusion, caliceal calcium stones can remain asymptomatic in about 61% of patients at five years. In the case of a symptomatic event, the stone size is a prime factor in the outcome: the stone is more likely to be passed if it is smaller than 8 mm. Stones larger than 8 mm can cause urinary tract obstruction requiring removal.

These data suggest that an expectant strategy is still justified and reasonable but ESWL has to be preferred for stones growing larger than 8 mm, particularly when sited in the upper or middle calyx and in male patients with recurrent calcium stones. This approach could reduce the social costs and the potential risks or complications of extensive ESWL treatments although a prospective study is needed to define the precise risks and benefits of ESWL in patients with asymptomatic caliceal calcium stones.

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References

1. Goldman HL, Resnick MI, Buck AC. The history of urinary lithiasis and its treatment. In: Wickham JEA, Buck AC, eds. Renal tract stones. Metabolic basis and clinic practice. New York: Churchill Livingstone, 1990; 3-18.
2. Krysiewicz S. Complications of renal extracorporeal shock wave lithotripsy reviewed. Urol Radiol 1992; 13: 139-45.
3. Glowacki LS, Beecroft ML, Cook RJ, Pahl D, Churchill DN. The natural history of asymptomatic urolithiasis. J Urol 1992; 147: 319-21.
4. Churchill DN. Medical treatment to prevent recurrent calcium urolithiasis. Mineral Electrolyte Metab 1987; 13: 294-304.
5. Goldfarb S. Dietary factors in the pathogenesis and prophylaxis of calcium nephrolithiasis. Kidney Int 1988; 34: 544-55.
6. Drach GW, Dretler S, Fair W, et al. Report of the United States Cooperative Study of extracorporeal shock wave lithotripsy. J Urol 1986; 135: 1127-33.
7. Ueno A, Kawamura T, Ogawa A, Takayasu H. Relation of spontaneous passage of ureteral calculi to size. Urology 1977; 10: 544-6.
8. Williams GM, Kaude JV, Newman RC, Peterson JC, Thomas WC. Extracorporeal shock-wave lithotripsy: long-term complications. A J R 1988; 150: 311-5.
9. Yokoyama M, Shoji F, Yanagizawa R, et al. Blood pressure changes following extracorporeal shock wave lithotripsy for urolithiasis. J Urol 1992; 147: 553-8.
10. LeRoy AJ. Diagnosis and treatment of nephrolithiasis: current perspectives. A J R 1994; 163: 1309-13.
11. Pearle MS, Clayman RV. Outcome and selection of surgical therapies of stones in the kidney and ureter. In: Coe FL, Favus MJ, Pak CYC, Parks JH, Preminger GM, eds. Kidney stones. Medical and surgical management. Philadelphia: Lippincott-Raven 1996; 709-55.

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