Kaohsiung Journal of Medical Sciences (2012) **28**, 322–326

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ORIGINAL ARTICLE

Comparison of secondary signs as shown by unenhanced helical computed tomography in patients with uric acid or calcium ureteral stones

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Received 22 April 2011; accepted 20 June 2011
Available online 18 April 2012

KEYWORDS
Secondary sign;
UHCT;
Ureteral stone;
Uric acid stone

Abstract Unenhanced helical computed tomography (UHCT) has evolved into a well-accepted diagnostic method in patients with suspected ureterolithiasis. UHCT not only shows stones within the lumen of the ureter, it also permits evaluation of the secondary signs associated with ureteral obstruction from stones. However, there we could find no data on how secondary signs might differ in relation to different compositions of ureteral stones. In this study, we compared the degree of secondary signs revealed by UHCT in uric acid stone formers and in patients forming calcium stones. We enrolled 117 patients with ureteral stones who underwent UHCT examination and Fourier transform infra-red analysis of stone samples. Clinical data were collected as follows: age, sex, estimated glomerular filtration rate (eGFR), urine pH, and radiological data on secondary signs apparent on UHCT. The uric acid stone formers had significantly lower urine pH and eGFR in comparison to calcium stone formers, and on UHCT they also had a higher percentage of the secondary signs, including rim sign (78.9% vs. 60.2%), hydroureter (94.7% vs. 89.8%), perirenal stranding (84.2% vs. 59.2%) and kidney density difference (73.7% vs. 50.0%). The radiological difference was statistically significant for perirenal stranding ($p = 0.041$). In conclusion, we found that UHCT scanning reveals secondary signs to be more frequent in patients with uric acid ureteral stones than in patients with calcium stones, a tendency that might result from an acidic urine environment.

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1607-551X/$36
doi:10.1016/j.kjms.2011.11.013

Introduction

Investigation by unenhanced helical computed tomography (UHCT) has evolved into a well-accepted alternative to the use of intravenous urography (IVU) in patients with acute flank pain and suspected ureterolithiasis [1]. Many studies have investigated the efficacy of UHCT in the diagnosis of ureteral stone disease, and have demonstrated that UHCT is more sensitive than other imaging methods for the detection of ureteral stone disease in adults [2,3]. Its most important disadvantage is the high radiation dose [4]. However, two important advantages of UHCT are the short duration of examination and the absence of contrast medium administration [2,5]. UHCT not only detects the ureteral stone, but also demonstrates renal and extrarenal pathologies (secondary signs) associated with the stone [6].

Detection of secondary signs associated with a ureteral stone can provide data on the degree of the ureteral obstruction [5,7–9]. In this study, we evaluated secondary signs associated with ureteral stones, such as hydroureter proximal to the stone, perinephritic stranding, the tissue rim sign, and kidney density difference.

Various stone compositions may induce different chemical stimulation and then cause different tissue reaction in the urinary tract. We found no data on how secondary signs might differ according to the different compositions of ureteral stones. In this study, we compared the percentage of secondary signs apparent on UHCT in calcium stone formers with that in uric acid stone formers.

Material and method

From January 2007 to March 2011, 117 patients with a ureteral stone who underwent UHCT and stone analysis were enrolled into our study. The clinical data collected were: age, sex, renal function, and urine pH; the radiological data were the secondary signs of urolithiasis apparent on UHCT. The stone samples were collected after ureteroscopic lithotripsy or spontaneous passage. All the stones were sent for analysis by Fourier transform infrared spectroscopy. Renal function was evaluated with estimated glomerular filtration rate (eGFR) using the modification of diet in renal disease (MDRD) formula. All cases of ureteral stone were diagnosed on UHCT and confirmed by stone samples. The secondary signs included the tissue rim sign, hydroureter, perirenal stranding and renal density difference between affected and non-affected kidneys. Exclusion criteria included bilateral renal disease, percutaneous nephrostomy drainage, and ureteral stent insertion before stone removal. Patients with stone components other than calcium or uric acid were also excluded from the study.

The tissue rim sign was defined as visualization of annular soft tissue immediately adjacent to the segment of the ureter surrounding the stones [10–12]. Hydroureter was defined as the presence of unilateral ureteral dilatation at a certain level below which the caliber was normal, and by visualization of the continuation of the proximally dilated ureter to the renal pelvis. Perinephric fat stranding was defined as increased density or stranding in the surrounding perirenal adipose tissue as a result of inflammation secondary to ureteral stones [8,13]. Renal density difference was evaluated as the asymmetric density decrease in Hounsfield units (HU) between the affected and non-affected kidneys [8,14–17].

The patients were divided into two groups: those with a calcium stone and those with a uric acid stone. The clinical and radiological data were compared between the two groups. Continuous variables (age, GFR, urine pH) are expressed as mean ± standard deviation, and were compared using the Student t test or Mann–Whitney test. Categorical data (rim, hydroureter, perirenal stranding, kidney density difference) are expressed as percentages, and were compared using the χ^2 test or Fisher's exact test where appropriate.

Results

The mean age of these 117 patients was 54.83 ± 12.68 years (range, 18–84), with a male-to-female ratio of 81:36. Thirty-six patients (30.8%) had a history of recurrent stone. Eighty-eight patients (75.2%) had a clinical history of hematuria, with more than five red blood cells in each high-power field on urine examination. The mean urine pH was 5.92 ± 0.60 (range, 5.0–7.5). The mean eGFR was 77.66 ± 29.47 (range, 13.79–160.41). Concerning radiological data, secondary signs were present on UHCT as follows: rim sign in 74 patients (63.2%), hydroureter in 106 (90.6 %), perirenal stranding in 74 (63.2%) and kidney density difference in 63 (53.9%). The stone analysis showed that 98 patients (83.8%) were calcium stone formers and 19 (16.2%) were uric acid stone formers (Table 1).

On reviewing the clinical data from the two groups with ureteral stones of different composition, it was apparent that urine pH and eGFR were significantly lower in the uric acid stone formers than in the calcium stone formers. The radiological data showed the uric acid stone formers to have a higher percentage of secondary signs on UHCT in comparison to calcium stone formers, including rim sign (78.9% vs. 60.2%), hydroureter (94.7% vs. 89.8%), perirenal stranding (84.2% vs. 59.2%), and kidney density difference (73.7% vs. 50.0%). The radiological difference was statistically significant for perirenal stranding ($p = 0.041$) (Table 2).

Discussion

In patients with suspected renal colic, kidney–ureter–bladder (KUB) plain x-ray film and ultrasound (US) may be the least expensive and most easily accessible imaging modalities. However, if needed and available, UHCT can be considered a better alternative than IVU, because it has a higher diagnostic accuracy and, as it is more effective, faster, less expensive and less risky than IVU, a better economic impact [6,18,19]. The direct costs of UHCT and IVU are nearly identical. However, indirect costs are much lower for UHCT; this is because the technique saves examination time and, when performed immediately, makes an initial abdominal plain film (KUB) and sonography unnecessary [20]. The sensitivity and specificity of UHCT and IVU were, respectively, 94.1 and 94.2%, and 85.2 and 90.4% [6,21,22]. CT scanning is a noninvasive technique that provides greater density discrimination between different

Table 1 Demographic and clinical characteristics of 117 patients with a ureteral stone.

Patient characteristic	
Age (y)	54.83 ± 12.68 (18–84)
Male:female	81:36 (69.2%:30.8%)
Stone composition	
Calcium	98 (83.8)
Uric acid	19 (16.2)
Recurrent stone formation (%)	36 (30.8)
Hematuria (%)	88 (75.2)
Urine pH	5.92 ± 0.60 (5.0–7.5)
eGFR	77.66 ± 29.47 (13.79–160.41)
Secondary sign seen on UHCT	
Tissue rim	74 (63.2)
Hydroureter	106 (90.6)
Perirenal stranding	74 (63.2)
Kidney density difference	63 (53.9)
Body mass index (kg/m^2)	25.54 ± 2.42 (18–38)

Data are represented as *n* (%) or mean ± SD (range). eGFR = estimated glomerular filtration rate using the modification of diet in renal disease (MDRD) formula.

tissues than plain x-ray. Ready access to the picture archive and communication system (PACS) allows all the specialists involved in care of a patient to interpret the radiological report with the benefit of images. In addition, NHCT is able to detect various additional renal and extrarenal pathologies, demonstrating not only the urinary tract calculi but also the secondary signs associated with ureteral stones [10,23,24]. Secondary signs are indicators of ureteral duct obstruction. A stone may not be easily identified for a number of reasons, such as small size, low attenuation, respiratory movement, volume averaging, paucity of retroperitoneal fat, confusion with a phlebolith, or recent passage. Also, the identification of stones may be difficult in patients with phleboliths along the course of the ureter. The visualisation by CT of secondary signs of an obstructed ureter is helpful in making the diagnosis of ureteral stone. When no stone is detected in the presence of secondary signs, then previously passed stones, pyelonephritis, and causes of obstruction other than stones should be considered.

Hydroureter, which is the most common secondary sign of ureteral stones, has been detected with CT in 69–83% of adult patients, and in 73% of a pediatric population. Perirenal stranding was defined as increased density in the surrounding perirenal adipose tissue as a result of inflammation secondary to ureteral stones (Fig. 1). It has been found in 36–82% of adult patients, and at a lower rate in the pediatric population [25]. The tissue rim sign appears as a result of inflammation and edema in the ureteral wall surrounding the stones (Fig. 2). This sign has been reported to have high specificity in distinguishing ureteral stones from phleboliths. A soft tissue rim sign around a calcific focus is an important indicator of a ureteral stone, whereas a comet tail sign suggests a phlebolith (a calcified venous thrombosis), a radiological mimic of a ureteral stone [11]. The tissue rim sign has been detected in 34–76% of patients with a ureteral stone [26].

In stone disease, a decrease in renal density may be observed secondary to the ureteral obstruction. For the present study, the renal parenchymal density was measured in the upper, middle, and lower portions of each kidney, and a mean value calculated. The difference between the mean values of the affected and non-affected kidneys was used to predict the presence of an acutely obstructing ureteral stone. Several studies have suggested that a renal parenchymal density difference of 5 HU or greater between an acutely obstructed and an unobstructed kidney can be a valuable secondary sign that the acute obstruction is the result of a ureteral stone. A density difference of 5 HU or more has been detected in 24–95% of patients [27]. In the minority of patients with a ureteral stone in whom the renal parenchymal density difference is less than 5 HU, combining other secondary signs may be helpful.

The sensitivity of each secondary sign in predicting the presence of an acute obstructing ureteral stone was as

Table 2 Comparison of clinical and radiological data between patients with a calcium ureteral stone and those with a uric acid stone.

	Calcium stone (*n* = 98)	Uric acid stone (*n* = 19)	*p*
Location of stone			
Upper ureter	32 (32.7%)	6 (31.6%)	0.557
Mid ureter	25 (25.5%)	7 (36.8%)	
Lower ureter	41 (41.8%)	6 (31.6%)	
Tissue rim (%)	59 (60.2%)	15 (78.9%)	0.193
Hydroureter (%)	88 (89.8%)	18 (94.7%)	0.690
Perirenal stranding (%)	58 (59.2%)	16 (84.2%)	0.041*
Kidney density difference ≥5 HU	49 (50.0%)	14 (73.7%)	0.078
Age (y)	53.73 ± 12.83	60.53 ± 10.42	0.032*
eGFR	84.52 ± 25.94	43.31 ± 17.86	<0.001*
Urine pH	6.03 ± 0.57	5.37 ± 0.44	<0.001*
BMI (kg/m^2)	25.89 ± 3.40	25.74 ± 2.73	0.857

Data are represented as *n* (%) or mean ± SD (range).
*Statistically significant, $p < 0.05$. eGFR = estimated glomerular filtration rate using modification of diet in renal disease (MDRD) formula; HU = Hounsfield unit.

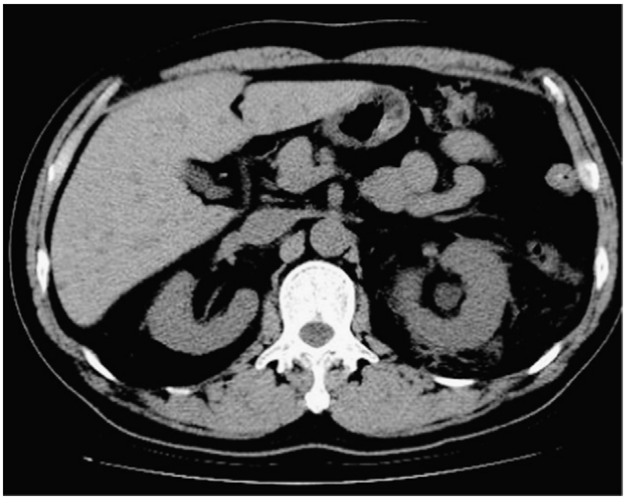

Figure 1. In a 55-year-old male patient, left perinephritic edema and fat stranding secondary to ureteral stone is seen. Additionally, ipsilateral hydronephrosis is observed.

follows: hydroureter, 90%; perinephric stranding, 82%; tissue rim sign, 77%; and parenchymal density difference, 89%. The specificity of each secondary sign was as follows: ureteral dilatation, 93%; perinephric stranding, 93%; tissue rim sign, 92%; and parenchymal density difference, 100% [9,28,29]. The odds ratio for the frequency of the tissue rim sign with stones versus tissue rim with phleboliths was 31:1 [29].

When using unenhanced CT to help diagnose acute flank pain, if neither a ureteral stone nor an indeterminate but suspicious calcification is observed, then secondary signs of obstruction are important for diagnosis. Comparison with the periureteric area on the opposite side facilitates the diagnosis. The results of the present study form the basis of an imaging algorithm that can be used when interpreting unenhanced CT images of patients with acute flank pain. Single secondary sign may not present in every case on the UHCT scan, but the combined effect of multiple secondary signs may greatly increase the detection rate of radiological diagnosis of ureteral stone by UHCT.

Figure 2. In a 48-year-old female patient, ureteral wall thickening (tissue rim sign) secondary to a stone in the left middle ureter is observed.

The different composition of ureteral stones and the resulting different chemical stimulation may cause different tissue reactions. In the present study, we also looked at the percentage of secondary signs associated with different stone compositions. The results show that uric acid stones cause a higher percentage of secondary signs than calcium stones. It is difficult to explain the mechanism for this difference. Urine pH is one possible cause of urothelial stimulation. The urine of uric acid stone formers is acidic than that of calcium stone formers. The acidic environment causes a stronger tissue reaction within and surrounding the ureteral wall. The other possibility is that uric acid stone formation is linked with the metabolic syndrome [30]; because obese patients have more fat tissue surrounding the ureter, UHTC will show a greater periureteral tissue reaction to the stone in such patients.

Our study does have limitations. The percentage of uric acid stone formers among our study participants was low, so there were insufficient uric acid stone patients in comparison with calcium stone formers. Observations from other groups with a high prevalence of uric acid stone formation are needed.

In conclusion, UHCT is the best tool for the diagnosis of urinary stone disease. It is especially valuable in patients allergic to contrast medium, and also in those with poor renal function because it provides images not only of the urinary system but also of peritoneal and retroperitoneal soft tissue. UHCT not only shows stones within the lumen of the ureter, but also permits evaluation of the secondary signs associated with ureteral obstruction by stones. Identification of secondary signs supports the diagnosis of ureteral stones and contributes to the evaluation when there is difficulty in stone diagnosis. Uric acid stone formers have a higher percentage of secondary signs on UHCT in comparison with calcium stone formers.

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