

Increased prevalence of simple renal cysts in patients with gout

Eduardo Massato Hasegawa · Ricardo Fuller ·
Maria Cristina Chammas · Filipe Martins de Mello ·
Claudia Goldenstein-Schainberg

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Abstract The aim of this study was to determine the prevalence of simple renal cysts in gout patients and evaluate associated risk factors for its development. Hundred and forty-six patients followed at our outpatient Gout Unit and 47 sex- and age-matched healthy kidney donors who had undergone routine renal ultrasonography, using a static gray scale and real-time B-mode units with a 3.5- or 5.0-MHz transducer, were evaluated for the presence of renal cysts. Demographic and clinical characteristics of gout patients were evaluated considering possible risk factors for the occurrence of simple renal cysts such as age, male gender, hypertension, and renal impairment. The prevalence of simple renal cyst was 26.0 % in gout patients and 10.6 % in control group ($P = 0.045$). Gout patients with simple renal cysts presented less renal lithiasis than those without this complication (5.2 vs 25.9 %; $P = 0.003$) in spite of an overall higher frequency of renal stones in gout patients compared to control group (20.5 vs. 6.3 %, $P = 0.025$). The presence of simple renal cyst in gout was not associated with previously reported factors such as age ($P = 0.296$), male predominance ($P = 0.688$), hypertension ($P = 0.314$), and renal impairment ($P = 0.254$). Moreover, no association with disease duration ($P = 0.843$) or tophi ($P = 0.616$) was observed. In conclusion, gout patients have an increased

prevalence of simple renal cysts associated with a lower occurrence of nephrolithiasis. Whether renal cysts have any protective effect in the development of nephrolithiasis in gout remains to be determined.

Keywords Simple renal cysts · Gout · Renal ultrasonography · Renal lithiasis

Introduction

Gout is a clinical metabolic disease caused by an inflammatory response to monosodium urate crystals, which may occur in people with hyperuricemia [7, 28]. Several renal disorders have been described in gout such as uric acid urolithiasis, involvement of blood vessels, and glomerular, tubular and interstitial tissues injury [3, 7, 30], but there are no data in the literature regarding the occurrence of simple renal cysts in this disease.

In the general population, the presence of simple renal cysts is frequently an incidental finding on renal ultrasonography with a prevalence varying from 4.2 to 41 % [11, 21, 25, 26, 31, 34, 35, 37, 42]. Although their natural history is not completely understood, they are considered benign lesions and usually remain untreated [35, 37]. Sometimes, however, they may increase in size and number, mainly in young subjects when rapid progression may occur [37].

The occurrence of simple renal cyst has been related to male gender and aging [12, 25, 26, 36, 37, 42], with increased prevalence especially among people older than 70 years of age, in whom it may reach 50 % [27]. An association of the presence of simple renal cyst with hypertension and decreased renal function has also been reported [2, 12, 31, 36]. Eventually, patients with simple renal cysts and hypertension have increased release of

E. M. Hasegawa · R. Fuller · F. M. de Mello (✉) ·
C. Goldenstein-Schainberg
Disciplina de Reumatologia,
Faculdade de Medicina da Universidade de São Paulo,
Av. Dr. Arnaldo 455, sala 3142, São Paulo,
SP 01246-903, Brazil
e-mail: filipimello@hotmail.com

M. C. Chammas
Division of Radiology, Faculdade de Medicina
da Universidade de São Paulo, São Paulo, Brazil

rennin from the affected kidney, and blood pressure normalization after surgical removal or decompression of the cyst by aspiration has been described [4, 43].

In patients with gout and hyperuricemia, some forms of autosomal polycystic kidney disease have been described [8, 23, 38]. These diseases are a heterogeneous group of disorders characterized by genetic mutations that induce abnormal epithelial proliferation and differentiation in the kidney, leading to formation of fluid-filled cysts in the renal parenchyma [16]. Hence, this mechanism is much different from that of simple renal cyst formation. Nevertheless, the occurrence of simple renal cyst in gout has not been investigated. Therefore, we sought to determine the prevalence of simple renal cyst in patients with gout and its possible association with clinical parameters.

Subjects and methods

Medical charts of 146 consecutive patients regularly followed at our outpatient gout clinic and 47 age- and sex-matched healthy kidney donors (control group) were retrospectively reviewed. All patients met the American College of Rheumatology classification criteria for gout [41]. Arterial hypertension was defined in accordance with the JNC 7 report [13], diabetes mellitus according to the American Diabetes Association classification criteria [1], dyslipidemia according to the ATP III guidelines [18], and decreased renal function if glomerular filtration rate was under 60 ml/min/1.72 m² body surface area. Due to the fact that serum uric acid and uric acid excretion present high levels of variability during disease course and suffer great influence of external factors such as diet and medication [22], their measurements were not considered for the current study. All patients were adequately treated for gout with uricosuric agent (benzbromarone) or xanthine oxidase inhibitor (allopurinol).

Patients and controls were subjected to renal ultrasonography and evaluated by experienced radiologists using real-time B-mode units with a 3.5- or 5.0-MHz transducer.

Patients with polycystic kidney disease were excluded from this analysis. Ultrasonographic criteria for the diagnosis of a simple renal cyst include the following: (1) spherical or ovoid shape, (2) absence of internal echoes, (3) presence of a thin, smooth wall that is separate from the surrounding parenchyma, and (4) enhancement of the posterior wall, indicating ultrasound transmission through the water-filled cyst [15].

For statistical comparison of categorical variables, chi-square and exact Fisher's tests were utilized, while continuous variables were assessed by Student's *t* test. A *P* value of less than 0.05 was considered statistically significant.

Results

The mean age of gout patients was 64.5 ± 11.0 years (range 26–88 years) similar to control group which was 63.2 ± 11.2 years (range 26–85 years) (*P* = 0.702). The percentage of male patients and controls was 89 and 85 %, respectively (*P* = 0.940). Mean disease duration was 17.5 ± 10.3 years.

Ultrasonographic evaluation revealed a total prevalence of simple renal cysts of 26 % (38/146) among gout patients, significantly higher compared to 10.6 % (5/47) for the control group (*P* = 0.045). The prevalence of renal lithiasis was also higher in the gouty group compared to controls (20.5 vs 6.3 %; *P* = 0.025).

As shown in Table 1, gout patients with renal cyst (*n* = 38) and without this complication (*n* = 108) had comparable frequencies of male gender (*P* = 0.688), hypertension (*P* = 0.314), diabetes mellitus (*P* = 0.162), decreased renal function (*P* = 0.254), dyslipidemia (*P* = 0.110), and tophi (*P* = 0.616). In contrast, the prevalence of nephrolithiasis was significantly lower in patients with simple renal cyst compared to those without this condition (5.2 vs. 25.9 %; *P* = 0.003). Of note, age (67.2 vs. 64.0 years; *P* = 0.296) and disease duration (17.3 vs. 17.9 years; *P* = 0.843) were similar in both groups.

Table 1 Clinical features of 146 gout patients with and without renal cysts

	With cyst (<i>n</i> = 38)	No cyst (<i>n</i> = 108)	Total (<i>n</i> = 146)	<i>P</i>
Age ^a	67.2 ± 8.1	64.0 ± 11.8	64.5 ± 11.0	0.296
Disease duration ^a	17.3 ± 9.3	17.9 ± 10.4	17.5 ± 10.3	0.843
Male gender ^b	35 (92.1)	95 (87.9)	130 (89.0)	0.688
Hypertension ^b	36 (94.7)	94 (87.0)	130 (89.0)	0.314
Dyslipidemia ^b	27 (71.0)	82 (75.9)	109 (74.6)	0.110
Diabetes mellitus ^b	11 (28.9)	18 (16.6)	29 (19.8)	0.162
Renal impairment ^b	15 (39.4)	30 (27.7)	45 (30.8)	0.254
Tophi ^b	19 (50.0)	47 (43.5)	60 (45.2)	0.616
Nephrolithiasis ^b	2 (5.2)	28 (25.9)	30 (20.5)	0.003

^a Mean ± SD in years

^b Number (percentage)

Discussion

We have reported for the first time an increased prevalence of simple renal cyst among gout patients associated with a lower frequency of renal lithiasis in the subjects that presented renal cysts.

Age matching was essential to determine that this parameter does not seem to be a major contributing factor for the presence of simple renal cyst in gout, in spite of previous reports of this association in the general population [12, 25, 26, 36, 37, 42]. Reinforcing these findings, gout patients with and without simple renal cyst had comparable ages minimizing therefore the relevance of this factor in the evaluated patient group.

The well-balanced gender distribution among patients with and without simple renal cyst rules out the possibility that the known male predominance of gout could have overestimated the frequency of this complication.

Additionally, hypertension and decreased renal function, previously recognized as linked with simple renal cysts in the general population, were not found to be associated with this complication in gout [10, 14, 15, 17]. Moreover, diabetes mellitus and dyslipidemia [14], comorbidities frequently observed in gout and often concurrently observed in gout patients with hypertension and impaired renal function, were also not associated with the presence of simple renal cyst in the present cohort.

The mechanisms involved in the development of simple renal cyst are not well understood, although it might be related to aberrant tubular growth secondary to increased workload of the remaining tubules after a loss of nephrons [12, 17]. In early renal disease, microscopic tubular dilatation may precede the development of simple renal cysts [5, 6]. In gout, however, both microtubular dilatation and aberrant tubular growth have not been reported, therefore, whether these renal alterations are also involved in the development of cysts in gout patients remains to be determined.

On the other hand, the comparable frequency of renal impairment in patients with and without simple renal cyst does not support the notion that this complication is secondary to nephron lesion associated with urate crystals deposition in the interstitium of the medulla and pyramids with surrounding giant cell reaction, characteristic to uric acid nephropathy [10]. Moreover, in the present series, longstanding disease and tophi do not seem to account for simple renal cyst occurrence, despite the fact that renal involvement in gout is related to disease duration [10, 19, 30].

We have confirmed previous reports of higher frequency of lithiasis in gout patients [20, 33]. In fact, the frequency of 20 % was three times more than normal controls. This finding may be directly related to serum urate

concentration and with amounts of urate excretion [9, 24]. The lower prevalence of renal lithiasis in patients with renal cyst found herein is striking and contradicts the obstructive theory for the genesis of simple renal cyst, in which a correlation between the presence of simple renal cysts and nephrolithiasis, ascribed to an obstructive factor caused by the lithiasis, has been proposed [5, 11]. Thus, we hypothesize that the observed lower incidence of nephrolithiasis in gout patients with renal cysts may be due to lower urinary excretion of uric acid in this subgroup of patients leading to higher deposit in renal parenchyma. In contrast, those who develop lithiasis would have a higher urinary excretion of uric acid in the luminal side of renal tubules. Although we have not specifically analyzed urinary pH, uricosuria, and citraturia in our patients, these parameters may also be involved, due to the fact that uric acid stones usually develop in acid urine [9, 24].

Alternatively, urate tubular injury may be the primary mechanism as demonstrated by the upregulation and increased urinary levels of *Kidney Injury Molecule-1* (KIM-1), a widely validated marker of proximal tubular injury [39], in gout patients [29]. The proximal tubule is known to play an important role in urine acidification, and injury in this segment of the nephron can increase the urinary pH [32, 40], resulting in higher urate solubility. Taken altogether, these mechanisms could be related to the lower prevalence of lithiasis in our gout patients with renal cysts.

In conclusion, gout patients have an increased prevalence of simple renal cysts. Further studies may provide some clues about the factors underlying this apparent protective effect of renal cysts in the development of nephrolithiasis in gout.

Conflict of interest None.

References

1. American Diabetes Association (2010) Diagnosis and classification of diabetes mellitus. *Diabetes Care* 33(Suppl 1):S62–S69
2. Al-Said J, Brumback MA, Moghazi S et al (2004) Reduced renal function in patients with simple renal cysts. *Kidney Int* 65:2303–2308
3. Avram Z, Krishnan E (2008) Hyperuricaemia—where nephrology meets rheumatology. *Rheumatology (Oxford)* 47:960–964
4. Babka JC, Cohen MS, Sode J (1974) Solitary intrarenal cyst causing hypertension. *N Engl J Med* 291:343–344
5. Baert L, Steg A (1977) On the pathogenesis of simple renal cysts in the adult. A microdissection study. *Urol Res* 5:103–108
6. Baert L, Steg A (1977) Is the diverticulum of the distal and collecting tubules a preliminary stage of the simple cyst in the adult? *J Urol* 118:707–710
7. Baker JF, Schumacher HR (2010) Update on gout and hyperuricemia. *Int J Clin Pract* 64:371–377
8. Cameron JS, Simmonds HA (2005) Hereditary hyperuricemia and renal disease. *Semin Nephrol* 25:9–18

9. Cameron MA, Sakhaee K (2007) Uric acid nephrolithiasis. *Urol Clin North Am* 34:335–346
10. Capasso G, Jaeger P, Robertson WG et al (2005) Uric acid and the kidney: urate transport, stone disease and progressive renal failure. *Curr Pharm Des* 11:4153–4159
11. Chang CC, Kuo JY, Chan WL et al (2007) Prevalence and clinical characteristics of simple renal cyst. *J Chin Med Assoc* 70:486–491
12. Chin HJ, Ro H, Lee HJ et al (2006) The clinical significances of simple renal cyst: Is it related to hypertension or renal dysfunction? *Kidney Int* 70:1468–1473
13. Chobanian AV, Bakris GL, Black HR et al (2003) The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 289:2560–2572
14. Choi HK, Ford ES, Li C et al (2007) Prevalence of the metabolic syndrome in patients with gout: the Third National Health and Nutrition Examination Survey. *Arthritis Rheum* 57:109–115
15. Curry NS, Bissada NK (1997) Radiologic evaluation of small and indeterminate renal masses. *Urol Clin North Am* 24:493–505
16. Gascue C, Katsanis N, Badano JL (2011) Cystic diseases of the kidney: ciliary dysfunction and cystogenic mechanisms. *Pediatr Nephrol* 26(8):1181–1195
17. Grantham JJ (1994) Pathogenesis of renal cyst expansion: opportunities for therapy. *Am J Kidney Dis* 23:210–218
18. Grundy SM, Cleeman JI, Merz CN et al (2004) Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 110:227–239
19. Keller DL (2011) Gout and chronic kidney disease. *Cleve Clin J Med* 78:81 (author reply-2)
20. Kramer HM, Curhan G (2002) The association between gout and nephrolithiasis: the National Health and Nutrition Examination Survey III, 1988–1994. *Am J Kidney Dis* 40:37–42
21. Liu JS, Ishikawa I, Horiguchi T (2000) Incidence of acquired renal cysts in biopsy specimens. *Nephron* 84:142–147
22. Marangella M (2005) Uric acid elimination in the urine. Pathophysiological implications. *Contrib Nephrol* 147:132–148
23. Mejias E, Navas J, Llubes R et al (1989) Hyperuricemia, gout, and autosomal dominant polycystic kidney disease. *Am J Med Sci* 297:145–148
24. Moe OW, Abate N, Sakhaee K (2002) Pathophysiology of uric acid nephrolithiasis. *Endocrinol Metab Clin North Am* 31:895–914
25. Mosharafa AA (2008) Prevalence of renal cysts in a middle-eastern population: an evaluation of characteristics and risk factors. *BJU Int* 101:736–738
26. Murshidi MM, Suwan ZA (1997) Simple renal cysts. *Arch Esp Urol* 50:928–931
27. Nahm AM, Ritz E (2000) The simple renal cyst. *Nephrol Dial Transpl* 15:1702–1704
28. Neogi T (2011) Clinical practice. Gout. *N Engl J Med* 364:443–452
29. Nepal M, Bock GH, Sehic AM et al (2008) Kidney injury molecule-1 expression identifies proximal tubular injury in urate nephropathy. *Ann Clin Lab Sci* 38:210–214
30. Pascual E, Perdiguero M (2006) Gout, diuretics and the kidney. *Ann Rheum Dis* 65:981–982
31. Pedersen JF, Emamian SA, Nielsen MB (1997) Significant association between simple renal cysts and arterial blood pressure. *Br J Urol* 79:688–691
32. Quigley R (2006) Proximal renal tubular acidosis. *J Nephrol* 19(Suppl 9):S41–S45
33. Shimizu T, Hori H (2009) The prevalence of nephrolithiasis in patients with primary gout: a cross-sectional study using helical computed tomography. *J Rheumatol* 36:1958–1962
34. Suher M, Koc E, Bayrak G (2006) Simple renal cyst prevalence in internal medicine department and concomitant diseases. *Ren Fail* 28:149–152
35. Terada N, Arai Y, Kinukawa N et al (2008) The 10-year natural history of simple renal cysts. *Urology* 71:7–11 (discussion-2)
36. Terada N, Arai Y, Kinukawa N et al (2004) Risk factors for renal cysts. *BJU Int* 93:1300–1302
37. Terada N, Ichioka K, Matsuta Y et al (2002) The natural history of simple renal cysts. *J Urol* 167:21–23
38. Thompson GR, Weiss JJ, Goldman RT et al (1978) Familial occurrence of hyperuricemia, gout, and medullary cystic disease. *Arch Intern Med* 138:1614–1617
39. van Timmeren MM, van den Heuvel MC, Bailly V et al (2007) Tubular kidney injury molecule-1 (KIM-1) in human renal disease. *J Pathol* 212:209–217
40. Waanders F, van Timmeren MM, Stegeman CA et al (2010) Kidney injury molecule-1 in renal disease. *J Pathol* 220:7–16
41. Wallace SL, Robinson H, Masi AT et al (1977) Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum* 20:895–900
42. Yamagishi F, Kitahara N, Mogi W et al (1988) Age-related occurrence of simple renal cysts studied by ultrasonography. *Klin Wochenschr* 66:385–387
43. Zerem E, Imamovic G, Omerovic S (2009) Simple renal cysts and arterial hypertension: does their evacuation decrease the blood pressure? *J Hypertens* 27:2074–2078