Title
A Spectrum: Nephrocalcinosis-Nephrolithiasis

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Authors
Hsi, Ryan S
Stoller, Marshall L

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Nephrocalcinosis is a diagnosis frequently associated with referral to a urologist for treatment of stone disease. In the current era computerized tomography (CT) has enhanced our ability to detect renal calcifications with high resolution. Not surprisingly we are seeing more patients with nephrocalcinosis who are referred for management of urinary stone disease.

Strictly speaking the term nephrocalcinosis refers to calcifications in the kidney parenchyma. It has been most commonly used to describe the pattern of parenchymal calcifications in primary hyperparathyroidism, distal renal tubular acidosis and medullary sponge kidney.[1] This is distinct from nephrolithiasis, which identifies a mineralized calculus bathed and surrounded in urine in the collecting system. Nephrocalcinosis is a diagnosis made on a radiographic image.[2] Therefore, radiologists rather than urologists more frequently and routinely make this diagnosis.

If nephrocalcinosis also includes calcifications in the renal papillae, it is more prevalent than we think. Randall originally described calcified plaques on the papillae in 19.6% of human autopsies with gross examination and without the aid of CT.[3] He proposed that circumferential calcification of the basement membrane of the collecting ducts erodes with time through the papillary surface. We now know that these plaques are composed of interstitial deposits of hydroxyapatite and are integral to the process of stone formation for most calcium stone formers.[4] In a way the Randall plaque stands at the intersection between nephrocalcinosis and nephrolithiasis.

In this issue of The Journal Bhojani et al (page 1308) evaluated nephrocalcinosis in calcium stone formers who did not have a concurrent diagnosis of distal renal tubular acidosis, medullary sponge kidney or primary hyperparathyroidism.[5] The goal was to characterize the burden and prevalence of nephrocalcinosis in a population "without systemic disease."[5] A total of 54 patients (67 renal units with calcium oxalate or calcium apatite) underwent a rigorous protocol to determine whether renal calcifications were in the parenchyma (nephrocalcinosis) or the collecting system (nephrolithiasis). Noncontrast CT was performed after percutaneous nephrolithotomy. If there were residual calcifications, a second percutaneous nephroscopy was performed to determine whether the calcifications were truly in the parenchyma or were residual stones in the collecting system.

Bhojani et al report that the main finding of the study was that nephrocalcinosis was common in this cohort that did not have "systemic disease."[5] Nephrocalcinosis was present in 71%, 58% and 18% of hydroxyapatite, brushite and idiopathic calcium oxalate stone formers, respectively. The extent of nephrocalcinosis was highest in hydroxyapatite stone formers, followed by brushite and then idiopathic calcium oxalate stone formers. Comparison of 24-hour urine collections showed higher mean urinary calcium excretion and supersaturation of calcium phosphate but no differences in other urinary parameters.

This study raises several important issues. First, what is it that initiates nephrocalcinosis in the first place? If the etiology were systemic, we would expect it to develop symmetrically. However, quite often nephrocalcinosis occurs unilaterally and even focally.[6] One possible explanation lies in a potential mechanism involving differential renal and segmental perfusion combined with vascular injury to the renal papillary circulation.[7] The microvasculature of the papilla comprises the smallest vessels in a hypoxic and hyperosmolar environment, where turbulent tubular flow occurs at or near the tip of the papilla. Repair of the damage results in an atherosclerotic-like calcification process, which grows into the interstitium and eventually becomes detectable on imaging. Other theories implicate deposition of hydroxyapatite at the thin loops of Henle, overgrowth of deposits extending from the ducts of Bellini and interstitial fibrosis with crystal deposition in the inner medullary collecting ducts.[4] Because we frequently see the 2 conditions in combination, a better understanding of the etiology of nephrocalcinosis would help us understand the etiology of urinary stone disease.

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Second, overuse of CT to evaluate and routinely monitor stone disease is concerning. Beyond the risks of ionizing radiation exposure and the long-term risk of secondary malignancy, CT contributes to a higher cost of care for stone disease and leads to incidental diagnoses that lead to additional (and at times unnecessary) evaluation and treatment. A recent multicenter comparative effectiveness trial evaluating the use of CT or ultrasonography for suspected nephrolithiasis demonstrated that ultrasonography resulted in lower cumulative radiation exposure, no need for CT in most patients and no significant difference in adverse events.[8] Nephrocalcinosis is a prime example of an incidental diagnosis discovered on high resolution CT obtained by the primary care or emergency room physician as they are at the front lines of seeing patients with suspected acute renal colic. Patients and their referring physicians then fixate on the diagnosis of nephrocalcinosis as a diagnosis of kidney stones. Indeed, this is how the inbox of an endourologist can quickly fill up.

Third, we recognize nephrolithiasis as a systemic disease. Although Bhojani et al assumed that they were evaluating stone disease "without systemic disease,"[5] we believe the contrary. Epidemiological evidence links nephrolithiasis to cardiovascular disease and a cluster of systemic diseases that comprise metabolic syndrome.[9,10] In addition, stone disease is an inheritable disease and approximately half of patients have a family history of stones. Furthermore, when patients with nephrolithiasis are counseled about dietary and life-style modifications, we discuss the rationale for lowering salt and animal protein intake, moderating calcium intake, and increasing fluids and servings of fruit and vegetables (not to mention more exercise). These interventions are not dissimilar from a heart healthy program.

Therefore, we view nephrocalcinosis as a radiographic condition that exists on a spectrum. On one end is the asymptomatic patient with a small parenchymal stone for whom no intervention is ever needed. At the other end is the recurrent brushite stone former with diffuse parenchymal calcifications. Perhaps the only important clinical implication of nephrocalcinosis is that it signifies that a calcification process is occurring in the kidney.

Ryan S. Hsi and Marshall L. Stoller
Department of Urology
University of California-San Francisco
San Francisco, California

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