



Endourology

Recurrent Kidney Stone Episodes Leading to a Diagnosis of Occult Acromegaly



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ABSTRACT

The association between nephrolithiasis and acromegaly has been previously described. Although the mechanism has been established, the urological literature sparsely discusses clinically suspecting that patients with recurrent nephrolithiasis could have acromegaly and subsequently referring them for accurate diagnosis and treatment. We present a case of occult acromegaly secondary to a pituitary tumor discovered 20 years after the patient's first stone episode.

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Introduction

The association between acromegaly and nephrolithiasis has been previously described.^{1–4} Although the mechanism has been well studied, clinically suspecting patients with recurrent nephrolithiasis who could have acromegaly and referring them for accurate diagnosis and treatment has not been promulgated in urological literature. This is the first case to be reported in the United States of a Caucasian elderly man found to have acromegaly secondary to a pituitary adenoma, explaining his long-standing history of stones.

Case presentation

A 73-year-old Caucasian male with a history of nephrolithiasis since age 50 presented to our clinic with an episode of right renal colic. He described having undergone one lithotripsy procedure per year for the past 4 years (ESWL and ureteroscopic). His past medical history was significant for diet-controlled diabetes, chronic constipation, hypertension, and prior stone episodes dating back

23 years. He reported having developed a stooped posture and tilted gait over the past year.

On physical exam, the patient was noted to be obese with a height of 5'5" and weight of 200 lbs and to walk with a limp. Renal ultrasonography showed mild hydronephrosis of the right kidney without any intrarenal stones and a normal-sized left kidney with numerous scattered stones, including 2 clusters of stones that were 9 mm each. A non-contrast CT scan demonstrated an obstructing 1.2 cm mid-ureter stone on the right and confirmed the ultrasound findings on the left. The patient underwent right ureteroscopy followed by left retrograde intrarenal surgery 1 month later to achieve complete stone clearance. Stone analysis revealed a composition of calcium oxalate. A 24-h urine showed hypercalciuria (348 mg/day), hyperoxaluria (72 mg/day), and a normal citrate level at 933 mg/day. In reviewing his records from other providers, prior 24-h urine collections revealed similar findings. A parathyroid hormone (PTH) was ordered and was 82 pg/mL with serum calcium of 10.0 mg/dL, both within the normal range. Creatinine, potassium, and albumin were all normal at 0.74 mg/dL, 3.6 mEq/L, and 3.5 g/L, respectively (see Fig. 1).

The patient was started on chlorthalidone in addition to a low-oxalate diet and a magnesium oxide/vitamin B6 combination supplement. A follow-up 24-h urine collection continued to show elevated urine calcium and oxalate levels of 324 mg/day and 49 mg/day, respectively, while citrate levels remained within normal limits. Post-operative renal ultrasound showed resolved

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Figure 1. Renal ultrasonography of the right kidney.

hydronephrosis of the right kidney and no residual renal calculi. Given his persistent hypercalciuria, the patient was referred for endocrinology evaluation. Noting his coarse facial features, neurologic history of scoliosis and a sacralized L5 with several canal stenosis at L4/L5, and persistent hypercalciuria refractory to medical therapy, labs were ordered to evaluate his GH and IGF-1 levels. His GH was abnormally high at 48.30 ng/mL (normal <5 ng/mL) and IGF-1 was elevated at 894 ng/mL (normal 36–215 ng/mL). MRI of the brain with attention to the pituitary was then ordered and revealed a well-circumscribed mass characterized by decreased T2 signal and diminished enhancement within the left lateral pituitary gland measuring approximately 14 mm in maximal superior-inferior diameter \times 1 cm in the right-left diameter and 11 mm in anterior-posterior diameter consistent with a pituitary adenoma. Based on these findings, the patient was diagnosed with a pituitary tumor secreting GH that was the underlying cause of his acromegaly. He was subsequently referred to neurosurgery for transsphenoidal resection of his GH-secreting pituitary adenoma. Following removal of the adenoma, 24-h urine showed improvement in his calcium levels (down to 174 from 324) (see Fig. 2).

Discussion

The mechanism in which acromegaly underlies kidney stone formation involves intestinal hyperabsorption of calcium via the increased promotion of vitamin D activation in the kidneys by excess growth hormone (GH).^{1,4} Increased serum calcium is then excreted into the urine and binds with oxalate to form calcium oxalate stones.^{1,3} Although previous reports have elucidated the causative factors of the relationship between a pituitary tumor secreting excess GH and chronic development of primarily calcium oxalate stones in the urinary tract, these reports have not delineated the process by which accurate and timely diagnosis is reached. The patient was refractory to both medical and surgical therapy for his kidney stones over 2 decades of his life. Multiple follow-up 24-hour urine collections revealing persistent hypercalciuria raised the index of suspicion for an endocrinopathy, warranting further work-up.

While most cases of idiopathic hypercalciuria in the setting of kidney stones are attributable to primary hyperparathyroidism, this patient's PTH and serum calcium were both found to be within

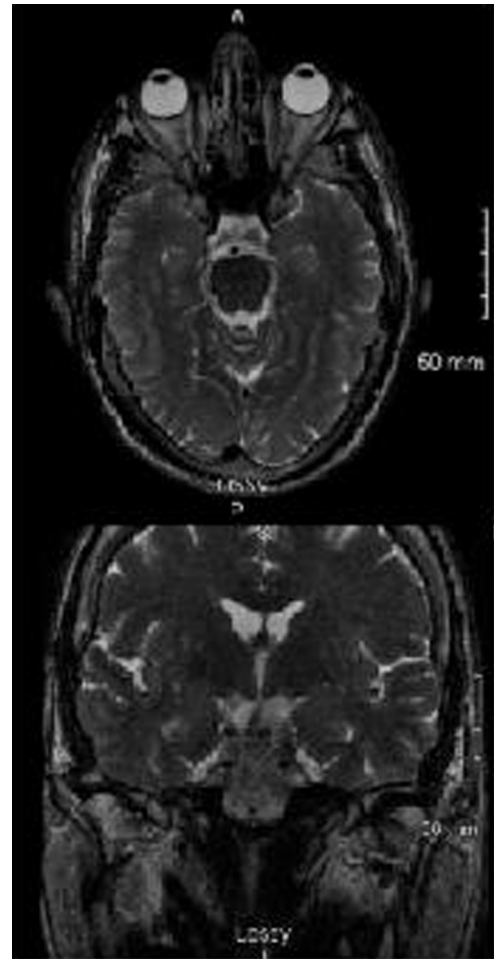


Figure 2. MRI of the brain with attention to the pituitary.

normal limits. Moreover, the patient did not exhibit symptoms of bone pain, depression, or tiredness and fatigue that are strongly associated with overactive parathyroid glands. Once eliminating primary hyperparathyroidism, we focused on kidney failure as a cause for the patient's hypercalciuria. However, a comprehensive metabolic panel returned normal creatinine and potassium. His glomerular filtration rate and albumin were also appropriate for his age and health status.

Another point of interest is that although he had a past medical history of diabetes mellitus and hypertension, both of which are consistent with a picture of acromegaly, as well as coarse facial features and skeletal deformities, these clinical correlations were not established early on.

As acromegaly is rare and has an insidious onset, the patient's diagnosis was delayed, as his presentation was atypical and consisted of several seemingly disparate pieces of clinical information. These clinical pieces eventually prompted a referral to an endocrinologist, which was crucial to make a definitive diagnosis of a pituitary tumor secreting excessive growth hormone. Eventually, this diagnosis led to surgical resection of the tumor and thus improving the patient's urologic symptoms and condition.

Since urologists are primarily involved in the diagnosis and treatment of kidney stones and would be in most cases the first to diagnose hypercalciuria, this case highlights the importance of referring patients for endocrine evaluation if hypercalciuria is severe or does not respond appropriately to thiazide therapy, even if serum calcium is normal.

Conclusion

An elderly man with chronic kidney stones was found to have a growth hormone secretory pituitary tumor more than 20 years after his first episode of stones. A good physical exam, careful attention to metabolic findings, and strong index of suspicion are keys to making a diagnosis of acromegaly in a patient with recurrent kidney stones and persistent hypercalciuria and can result in successful resolution of stone disease as well as prolonged life expectancy and avoidance of skeletal complications.

Consent

The Institutional Review Board at the Icahn School of Medicine at Mount Sinai reviewed and approved this study.

Conflict of interest statement

None of the contributing authors have conflicts of interest, including specific financial interests or relationships and

affiliations relevant to the subject matter or materials discussed in this article.

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