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Hypercalcemia, Hypercalciuria, Nephrolithiasis, Elevated Serum 1, 25-(OH) 2 Vitamin D Levels in a Patient with Mutation in CYP24A1 Gene

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Introduction: Hypercalcemia with nephrolithiasis due to a mutation in the CYP24A1 enzyme has rarely been described. Failure to recognize the diagnosis can lead to recurrent nephrolithiasis and eventually renal failure. Herein, we describe a patient with nephrolithiasis and CYP24A1 mutation.

Case Presentation: A 21 year-old male was evaluated for recurrent nephrolithiasis. Physical examination was normal. Laboratory: serum calcium 11.1 mg/dL (ref 8.6-10.2), serum calcium (ionized) 5.7 mg/dL (ref 4.5 – 5.6), 24 hour urine calcium 416 mg (ref 100 – 300), vitamin D 25-OH 53 ng/mL (ref 30 – 100), PTH 8.6 pg/mL (ref 15-65), 1,25-(OH)2 Vitamin D 74 pg/mL (ref 18 – 72), 24 hrs urine: uric acid 797 mg (ref <750), citrate 467 mg (ref 320 – 1240). CT of abdomen: multiple renal stones and nephrocalcinosis. Renal biopsy showed chronic tubulointerstitial changes. Serum 24, 25- (OH) 2 vitamin D 0.31 ng/mL (ref 3.5 ± 1.6) when 25(OH) D levels are 15-50 ng/mL. Genetic analysis of CYP24A1: a homozygous mutation E143del. Although ketoconazole is effective in this disorder, our patient refused to take this drug. Patient was placed on a low calcium diet (<400 mg per day), low purine diet, and high fluid intake.

Discussion: CYP24A1 encodes the 24-hydroxylase enzyme which regulates 1, 25-dihydroxyvitamin D3. A mutation can result in elevated serum calcium levels due to increased renal and GI calcium absorption. A mutation in CYP24A1 should be considered in the context of unexplained hypercalcemia associated with elevated 1,25-(OH) 2 Vitamin D level and nephrolithiasis.