Bilateral Medullary Nephrocalcinosis Secondary to Vitamin D Toxicity: A 14-year Follow-up Report

Sir,

Vitamin D deficiency (VDD) is widely prevalent in Asian-Indians despite the presence of adequate sunshine.[1] Vitamin D toxicity (VDT) is being increasingly reported from our country because of overzealous correction of VDD with mega-doses of vitamin D by the general healthcare providers.[2-4] Nephrocalcinosis (NC) is a well-known but rare complication of VDT, which is usually irreversible.

We previously reported an infant with acute VDT and NC.[5] Briefly, the child presented to a local physician at the age of 8 months with symptoms of hypocalcemia and was prescribed one dose of intramuscular vitamin D containing cholecalciferol 600,000 units and oral calcium carbonate 500 mg daily. However, the parents continued the intramuscular injection for 3 consecutive weeks, and a week following the final injection, the child was brought to us with features of hypercalcemia. The child was diagnosed to have parathyroid hormone (PTH)–independent hypercalcemia due to VDT (serum total calcium 11.5 mg/dL, 25-hydroxyvitamin D >100 ng/mL, and undetectable intact PTH) and was treated with intravenous normal saline and subcutaneous calcitonin injections, with improvement in hypercalcemic state. During the initial presentation, he was also found to have hypercalciuria (24-h urine calcium >4 mg/kg and elevated urine calcium: creatinine ratio of 0.83) and bilateral medullary NC. In this report, we present the long-term follow-up data of this child.

The child was followed up annually with serum total calcium value, urine calcium: creatinine ratio, and ultrasonography of bilateral kidneys. On serial follow-up visits, serum calcium level, urine calcium: creatinine ratio, and estimated glomerular filtration rate (eGFR) remained normal, and there was no reduction in NC. On a recent follow-up visit (14 years after the initial presentation), the child was growing normally with good scholastic performance. His total serum calcium value, urine calcium: creatinine ratio, and eGFR were normal at 9.4 mg/dL, 0.015, and 138 mL/min/1.73 m^2, respectively. Ultrasonography and computerized tomography of kidneys revealed persistent medullary NC with minimal reduction in size [Figure 1].

NC is defined as generalized deposition of calcium salts (calcium oxalate or phosphate) in the kidney, predominantly in the interstitium. It usually involves the renal medulla (>97% cases), and less commonly the cortex.[6] The common causes of medullary NC include primary hyperparathyroidism (PHPT), distal renal tubular acidosis (dRTA), primary hyperoxaluria, Barter's syndrome, hereditary hypophosphatemic rickets with hypercalciuria, Dent's disease, idiopathic hypercalciuria, medullary sponge kidney, Williams–Beuren syndrome, VDT, and treatment with active vitamin D for hereditary hypophosphatemic rickets.

In a pediatric series of 40 patients from North India with NC (median age at presentation 72 months), dRTA (50%), idiopathic hypercalciuria (7.5%), primary hyperoxaluria (7.5%), and VDT (5%) were reported as the most common causes.[7] At a median follow-up of 35 months, no patient showed resolution of NC while GFR declined significantly from 82 to 73 mL/min/1.73 m^2. In another study from the Netherlands, NC in preterm neonates was found to be associated with long-term adverse effects on glomerular and tubular function.[8] In a series of 41 patients from Italy (median age at presentation 15 months), renal tubulopathies (41%) and VDT (10%) were reported as the most common causes of NC.[9] The authors also reported the follow-up data (median 53 months) for 26 patients with NC. The degree of NC worsened in 16 (62%), remained stable in 8 (31%), and improved in 2 (8%) patients. The two children with improvement in NC on follow-up had VDT and unknown cause, respectively. The authors also concluded that progression of NC was not related to glomerular function, because GFR remained stable in 14 of 16 patients showing worsening of NC. Similarly, Lin *et al.* reported data of 16 children with NC from Taiwan [VDT (31%), dRTA (19%), and

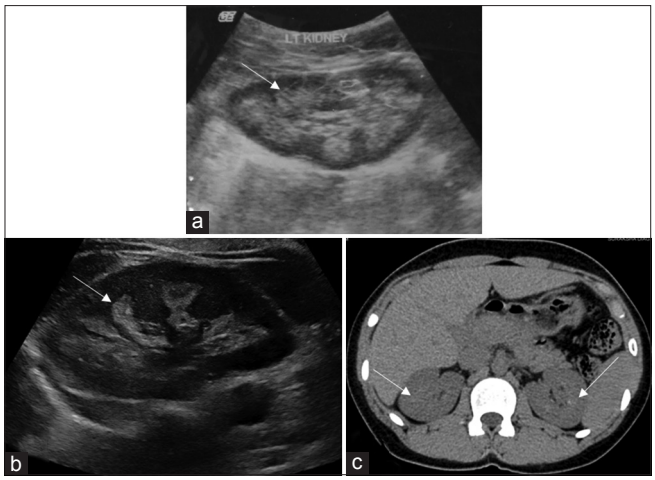

Figure 1: Serial ultrasonography (USG) (a- baseline, b- recent follow-up) and non-contrast computerized tomography (NCCT) images (c-recent follow-up) showing medullary nephrocalcinosis (arrow). It may be noted that the findings are better seen on USG (b) than on NCCT (c) which highlights the importance of high resolution USG in the diagnosis of medullary nephrocalcinosis

furosemide-induced (12%)], none of whom showed resolution on follow-up.[10]

Our patient presented in infancy with VDT, hypercalciuria, and NC. NC persisted even after 14 years of the initial presentation despite correction in hypercalcemic and hypercalciuric state. However, in contrast to some of the existing literature, the child continues to maintain stable GFR. We hypothesize that deterioration of renal function is more likely in patients exposed to hypercalciuria for prolonged periods (such as PHPT, dRTA) or those with repeated, intermittent exposures (treatment with active vitamin D for hereditary hypophosphatemic rickets), compared with brief one-off exposure, as seen in our patient.

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Conflicts of interest

There are no conflicts of interest.

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