The authors respond to "Misconception about the cause of vitamin D toxicity"

We thank Charoenngam and colleagues for their prompt feedback[1] on the conclusions from our case study.[2] In light of their comments, it is important to provide further clarity.

First, the observational studies and opinion pieces referenced by Charoenngam and colleagues examined acute vitamin D toxicity. Patients received relatively high doses for short periods (usually < 6 mo).[3,4] Our case study highlights a patient who took vitamin D that exceeded the recommended daily dose for at least 30 months.[2,5]

Charoenngam and colleagues failed to highlight a key statement from the Institute of Medicine: "serum [25-hydroxyvitamin D] levels above 50 ng/mL (125 nmol/L) should raise concerns among clinicians about potential adverse effects."[5] Furthermore, the population studies cited by Charoenngam and colleagues did not include patients exposed to large (> 10 000 IU) daily doses of vitamin D for 30 consecutive months.

One randomized controlled trial (RCT) highlighted in one of the cited reviews[4] gave 100 000 IU boluses once every 4 months for 5 years.[6] In a 5-year period, these patients would have received the equivalent of 1.5 million IU of vitamin D. Our patient's cumulative dose of vitamin D over a 4-month interval ranged from 960 000 to 1.44 million IU. In a 30-month period, this would equate to 10.8 million IU. Evidently, our patient received nearly 10 times the dose in half the duration of time in comparison to that RCT, in which serum calcium levels were not measured.[6]

Additionally, it has been reported that chronic vitamin D toxicity should be considered when values exceed 200 nmoL/L.[7,8] Further to this point, other published case reports and case series have shown vitamin D toxicity associated with hypercalcemia in patients exposed to smaller doses and over a shorter duration than in our case study.[9,10]

Second, Charoenngam and colleagues cite a case report of a patient with a large upper urinary tract carcinoma, specifically metastatic clear cell renal carcinoma.[11] Our patient had a lower urinary tract urothelial noninvasive carcinoma of the bladder with no metastatic disease. Furthermore, nonmetastatic bladder cancer associated with humoral hypercalcemia is exceedingly rare, normally requiring excision of the carcinoma to treat elevated 1,25-dihydroxyvitamin D levels and hypercalcemia, as this condition is usually refractory to medical treatment.[12,13]

In our case study, the patient's 1,25-dihydroxyvitamin D levels started to decrease with medical treatment and before the resection of his noninvasive carcinoma, which suggests it was not the driver for his vitamin D toxicity. Our patient also had evidence of chronic calcium deposition, as reinforced by the renal biopsy findings, supporting that the toxicity was long standing. It is difficult to accept that a locally noninvasive bladder carcinoma resulted in the burden of hypercalcemia that our patient experienced, which left him with permanent kidney damage.

Finally, Charoenngam and colleagues contend that 25-hydroxyvitamin D cannot result in elevated 1,25-dihydroxyvitamin D levels. However, it has been reported that chronically elevated 25-hydroxyvitamin D levels can lead to oversaturation of the vitamin D binding protein, increasing the levels of free active 1,25-dihydroxyvitamin D.[8,14,15]

Charoenngam and colleagues propose esoteric differential diagnoses for our patient's hypercalcemia, failing to acknowledge the potential risks of vitamin D toxicity associated with chronic misuse. The purpose of our case study was not to minimize the importance of vitamin D, but rather to raise awareness that chronic misuse can result in permanent renal damage.

Bourne L. Auguste MD
Staff nephrologist, Sunnybrook Health Sciences Centre; Department of Medicine, University of Toronto, Toronto, Ont.

Joanne Bargman MD
Staff nephrologist, Toronto General Hospital, University Health Network; professor of medicine, Department of Medicine, University of Toronto, Toronto, Ont.

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