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Hypervitaminosis D without toxicity

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ABSTRACT

Vitamin D deficiency is highly prevalent and there are an increasing number of reports of vitamin D toxicity, mostly related to the misuse of over-the-counter supplements. We report a case with marked hypervitaminosis D (25(OH)D 196 ng/mL) without clinical or biochemical toxicity and normal serum calcium, phosphorus, and 1,25(OH)2D levels. The decline and normalization of the patient's 25(OH)D and urine calcium after cessation of supplements indicated that these supplements were the likely etiology of her hypervitaminosis D. Over-the-counter medications would benefit from regulation by the Food and Drug Administration to prevent incidental toxicity, as seen in our patient.

KEYWORDS 1,25(OH)2D; 25(OH)D; hypervitaminosis D; over-the-counter supplements; vitamin D toxicity

Vitamin D deficiency is a common problem, with a prevalence of approximately 37% in US adults.[1] Reasons for this high prevalence may include inadequate sunlight exposure and poor dietary intake of vitamin D. Vitamin D status is best assessed by 25(OH)D levels. Physician-prescribed vitamin D is one source of replenishing 25(OH)D vitamin D levels. However, vitamin D can also be purchased over the counter (OTC). These OTC products are not regulated by the Food and Drug Administration (FDA), and wide variations in content may be seen. Excessive intake of vitamin D appears to be a growing risk and can result in toxicity.[2] This is only rarely a dispensing error.[3] Marked hypervitaminosis D without toxicity has rarely been reported. We describe marked hypervitaminosis D in a woman without clinical or biochemical manifestations of toxicity, which resolved with cessation of OTC supplements.

CASE DESCRIPTION

A 54-year-old woman was referred for a markedly elevated 25(OH)D level. Vitamin D was initially checked due to her history of osteopenia. She also had a prior lumbar compression fracture due to trauma. A dual-energy x-ray absorptiometry (DEXA) scan reported a femoral T-score of −1.9 and lumbar T score of −0.1. Her medications at presentation included coenzyme Q_{10} 300 mg, fish oil, a multivitamin including vitamin D (estimated to be 2000 IU of vitamin D), daily red yeast rice, vitamin C 100 mg, hydrocodone-acetaminophen 5 mg–325 mg twice daily, and tramadol 50 mg. She denied use of a solar tanning bed. Her thyroid function tests were normal. Her vitamin D value was high at 194 ng/mL (normal 30–100). The serum calcium, phosphorus, 1,25(OH)2 vitamin D levels, and intact parathyroid hormone levels were normal. Her 24-hour calcium was 503 mg/24 hour (normal <321). Ionized calcium was normal at 5.4 mg/dL (normal 4.8–5.6), as was her albumin. The patient was instructed to stop all supplements, and repeated tests confirmed marked elevation of 25(OH)D at 175 ng/mL (normal 30–100). Ionized calcium remained normal during her follow up. A month later, her vitamin D was at 159 ng/mL (normal 30–100); 1,25(OH)D, 70 pg/mL (normal 18–72); and urine calcium, 246 mg/24 hours (normal <321). At no time during observation did she show clinical or biochemical toxicity.

DISCUSSION

Despite marked elevation of vitamin D levels, our patient did not show any evidence of clinical or biochemical toxicity. To our knowledge, this is only the second such case reported.[4] Vitamin D toxicity is usually related to excessive

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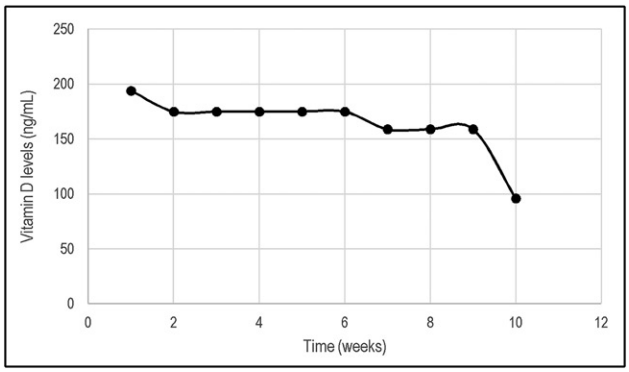

Figure 1. Sequential vitamin D levels following cessation of supplements.

ingestion and is rarely a result of physician prescriptions. Vitamin D toxicity is usually seen with a 25(OH)D level >150 ng/mL.[3] In vitamin D toxicity, common clinical manifestations include severe hypercalcemia, confusion, apathy, recurrent vomiting, abdominal pain, polyuria, polydipsia, and dehydration.[5]

Prior cases of hypervitaminosis D have presented with toxicity related to excessive consumption of vitamin D.[6] Vieth indicated that hypercalciuria occurs prior to hypercalcemia in vitamin D toxicity.[7] Our patient did indeed show such hypercalciuria, whereas the solo prior report indicated a normal urine calcium and parathyroid hormone level. This may relate to the patient's calcium ingestion.

Ketha et al described a case of hypervitaminosis D due to a dispensing error, where the contents of the supplement were found to be threefold the listed values.[6] This resulted in vitamin D toxicity and hypercalcemia in an infant.

The FDA does not regulate OTC supplements and as such we presume that our patient was consuming more vitamin D than was labeled. The gradual decline in her 25(OH)D over months is consistent with this explanation and is shown in *Figure 1*. We conclude that FDA regulation of OTC prescriptions may be needed since over 40% of US patients are taking OTC medications. Previous studies indicate that labeled and actual amounts of vitamin D supplements may differ.[8]

Free and total vitamin D levels in the body are regulated by vitamin D binding protein. Hypercalcemia may occur due to high free levels of vitamin D.[9] In this patient, free vitamin D levels were not measured since they were not readily available.[10] Future studies should measure both total and free levels of 25(OH)D and 1,25(OH)D. However, it appears that vitamin D may have a wider margin of safety than commonly recognized.

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