Progressively Increased Serum 1,25-Dihydroxyvitamin D<sub>2</sub> Concentration in a Hypoparathyroid Patient with Protracted Hypercalcemia due to Vitamin D<sub>2</sub> Intoxication

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Abstract. A 76-year-old female patient who had been taking vitamin D<sub>2</sub> 100,000 U/day for more than 14 years due to hypoparathyroidism following total thyroidectomy was admitted because of protracted hypercalcemia. On admission, the levels of serum vitamin D<sub>2</sub> (99.8 ng/ml) and 25-OHD<sub>2</sub> (356 ng/ml) were very high, and 1,25-(OH)<sub>2</sub>D<sub>2</sub> was low (4.0–18.7 pg/ml). Serum D<sub>3</sub>, 25-OHD<sub>3</sub> and 1,25-(OH)<sub>2</sub>D<sub>3</sub> were below the normal range. Despite intensive hydration with saline, intravenous hyperalimentation with phosphate-and calcium-free nutrients, and administration of glucocorticoid and calcitonin, the hypercalcemia persisted, accompanied by hypoproteinemia, edema, pleural effusion and congestive heart failure. The serum D<sub>2</sub> and 25-OHD<sub>2</sub> concentrations remained high and were accompanied by a gradual increase in 1,25-(OH)<sub>2</sub>D<sub>2</sub> (121 pg/ml), which further increased after the administration of bisphosphonate (pamidronate) to 183 pg/ml. Seventeen months later, serum calcium and 1,25-(OH)<sub>2</sub>D<sub>2</sub> were normalized but serum D<sub>2</sub> and 25-OHD<sub>2</sub> remained high. The serum 24,25-(OH)<sub>2</sub>D<sub>2</sub>/25-OHD<sub>2</sub> ratio was relatively constant throughout her clinical course, whereas the low serum 1,25-(OH)<sub>2</sub>D<sub>2</sub>/25-OHD<sub>2</sub> ratio at admission gradually increased during admission, suggesting that the increase in serum 1,25-(OH)<sub>2</sub>D<sub>2</sub> is due to increased production rather than decreased degradation. The administration of pamidronate further increased serum 1,25-(OH)<sub>2</sub>D<sub>2</sub>.

These features of the clinical course demonstrate that the 1,25-dihydroxyvitamin D concentration in hypercalcemic patients with protracted vitamin D intoxication may be decreased, normal or increased. Possible factors responsible for a protracted increase in serum 1,25-(OH)<sub>2</sub>D<sub>2</sub> are body weight loss, hypoproteinemia, and phosphate depletion. In addition, some bisphosphonates would certainly promote PTH-independent production of 1,25-(OH)<sub>2</sub>D<sub>2</sub>.

Key words: Hypercalcemia, Vitamin D intoxication, Bisphosphonate, 1,25-Dihydroxyvitamin D, Hypoparathyroidism

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generally believed to be the factor leading to suppression of PTH secretion and inhibition of renal 1α-hydroxylase [3]. Therefore, serum 1,25-(OH)2D is decreased, or at least not increased, in vitamin D2 intoxication [1-5].

In contrast, other investigators have reported that serum 1,25-(OH)2D levels are slightly or greatly increased [6-9], suggesting that 1,25-(OH)2D is the agent causing the toxicity [10]. Since previous assays for vitamin D metabolites were tedious and time-consuming [1], and required a large amount of serum, studies involving serial measurement of serum 1,25-(OH)2D levels have rarely been reported [8].

In Japan, the standard treatment for patients with idopathic or post-surgical hypoparathyroidism is administration of 1α-OHD3 [11]. Recently, however, we treated a 76-year-old patient with post-surgical hypoparathyroidism, who developed severe hypercalcemia after taking vitamin D2 for more than 14 years. On admission, the levels of serum vitamin D2 and 25-OHD2 were very high, and the serum 1,25-(OH)2D2 level was low. Interestingly, 1,25-(OH)2D2 gradually increased after admission, despite protracted hypercalcemia and an undetectable PTH level.

In the present report, we describe the measurement of vitamin D2 and D3 metabolites in this patient until normalization of the serum calcium concentration and our attempts to determine the factors responsible for the paradoxical activation of 25-hydroxyvitamin-D-1α-hydroxylase.

Case Report

A 52-year-old woman underwent total thyroidectomy because of a thyroid tumor in 1967. After the operation, hypoparathyroidism developed and vitamin D from an unknown source was given. From 1978, she was treated daily with vitamin D2 (ergocalciferol, Chokola-D), 100,000 units, and desiccated thyroid powder (Thyradin) 60 mg. In October, 1990 she was admitted for examination of cardiac arrythmia and syncope. Her body weight was 47 kg and height 150 cm. She was euthyroid and her serum calcium concentration was within the normal range (9.0 mg/dl). She had been doing well until February, 1991 when general malaise and anorexia developed. Hypercalcemia (11.8 mg/dl) was found and vitamin D2 was discontinued on April 10, 1991.

On April 22, the 76-year-old patient was admitted to our hospital because of protracted hypercalcemia. On admission, she was drowsy, and complained of general malaise, somnolence and anorexia. She weighed 38 kg. There was moderate anemia and slight pretibial edema. The lungs and abdomen were unremarkable. Serum total protein was 5.4 g/dl, and albumin 2.6 g/dl. Serum calcium was 15.3 mg/dl, phosphate 3.0 mg/dl, and Mg 0.7 mEq/l. A complete blood count revealed moderate anemia (Hb, 6.7 g/dl; RBC, 209 X 104/mm3, Ht, 19.5%). Liver function was normal. Renal function was slightly impaired (BUN 38.4 mg/dl, creatinine 1.0 mg/dl, creatinine clearance 30 ml/min). Proteinuria was not present. Twenty-four-hour urine calcium excretion had increased to 240 mg. Thyroid function was within the normal range. 201Tl and 99mTc scintigraphy revealed no parathyroid gland and was compatible with total thyroidectomy. Radiographic bone surveys and 99mTc-HMDP bone scintigraphy were normal. Gastro-intestinal and barium enema examinations gave normal results. Abdominal CT scans revealed small calcifications in the bilateral kidneys. The serum intact PTH concentration (Allegro PTH kit, Nichols Institute) was always undetectable (<5 pg/ml).

Under a diagnosis of vitamin D2 intoxication, saline was infused, and calcium-free, phosphate-free intravenous hyperalimentation was started. Upon administration of prednisolone (40 mg) and calcitonin (Elcitonin, 80 U/day), the corrected serum calcium level [12] decreased to 11 mg/dl (Fig. 1). Glucocorticoid gradually tapered off. To facilitate vitamin D excretion into feces, cholestyramine was prescribed on July 3 [13]. However, hypothyroidism developed [14], and the hypercalcemia worsened [15]. After increasing the dose of prednisolone and withdrawing cholestyramine, the hypercalcemia ameliorated. In June, hypoproteinemia worsened. Edema and bilateral pleural effusion developed, accompanied by congestive heart failure. Albumin was administered intensively and the symptoms improved slightly. In late August, a young physician inadvertently administered inorganic phosphate (10-38 mmol/day), which produced transient hypocalcemia, hyperphosphatemia, and azotemia.

In September, 3-amino-1-hydroxypropylidene-1,1-bisphosphonic acid (AHPrBP, pamidronate,
kindly supplied by Ciba-Geigy, Basel, Switzerland) 45 mg was administered iv, and this produced a slight decrease in the serum calcium concentration. AHPrBP (45 mg) was administered again at the end of admission. Prednisolone was tapered off to 20 mg, but infusion of 2 L saline was still necessary in order to keep the corrected serum calcium concentration below 12 mg/dl. In December 12, the patient was moved to Fuchu Hospital, where she was treated in the same way for an additional 6 months. Glucocorticoid was gradually tapered off, and then discontinued on May 18, 1992. After discharge, the patient did well. In August, 1992 the serum calcium concentration was 10.0 mg/dl, phosphate 2.9 mg/dl, albumin 3.6 g/dl, BUN 31.0 mg/dl, and creatinine 1.4 mg/dl. The bone mineral density in the lumbar spine (0.667 g/cm²) determined by dual X-ray absorptiometry (QDR-2000, Hologic) was within the normal range (Z score +0.05). In January, 1993 hypocalcemia (Ca, 7.0 mg/dl; P, 5.5 mg/dl; intact PTH, <5 pg/ml) developed, but the patient is now eucalcemic on 1α-OHD₃ at a dose of 1.5 µg/day.

![Fig. 1.](image-url)

The clinical course of the patient with vitamin D₂ intoxication. After admission on April 22, 1991, the patient was treated with saline, prednisolone, eel calcitonin (Elcitonin), salmon calcitonin (Salmotonin), cholestyramine (■, 18 g) and AHPrBP (arrows), as indicated in the figure. Serum calcium (□—□) and phosphate (●) concentrations are shown as mg/dl in the upper panel. Corrected serum calcium concentration is indicated above the serum calcium levels (cor Ca; □—□) [11]. Serum D₂ (□—□) and 1,25-(OH)₂D₃ (■—■) concentrations are indicated in the middle panel. Closed circles enclosed by a rectangle (■) indicate that samples were taken 2–3 days after AHPrBP (pamidronate) administration. Urinary excretion of calcium (□) and phosphate (●) is shown in the middle panel as mg/day. Urine volume (□, l/day) and urinary excretion of creatinine (●, mg/day) are shown in the lower panel. Dotted area indicates normal range of the corrected serum calcium concentration.
Materials and Methods

Blood was taken, and the serum was stored at -20°C until assay for vitamin D metabolites and cytokines. Vitamin D₂, 25-OHD₂, 24,25-(OH)₂D₂, 1,25-(OH)₂D₂, and vitamin D₃ metabolites were measured as described elsewhere [16, 17]. The sensitivity of the assay for 25-OHD₂, 24,25-(OH)₂D and 1,25-(OH)₂D was less than 1 ng/ml, 0.1 ng/ml, and 3.5 pg/ml, respectively. To avoid interassay variance, the samples obtained by November, 1991 (8 samples) and January, 1993 (6 samples) were simultaneously assayed after the patient was discharged. Serum free 25-OHD₂ was calculated according to the formula proposed by Bouillon et al. [18]. Vitamin D-binding protein (DBP) was determined by rocket immunoelectrophoresis [19]. DBP standard (Gc-globulin) was obtained from Calbiochem (La Jolla, CA).

Urinary excretion of C-terminal fragments of parathyroid hormone-related protein (PTHrP), which is increased in patients with malignancy-associated hypercalcemia [20], was determined as described previously [21].

Serum GH and prolactin, which may be involved in an increase in serum 1,25-(OH)₂D [4], were determined by radioimmunoassays. Tumor necrosis factor-alpha (TNF-α), which stimulates 1α-hydroxylase in keratinocytes and is known to be increased in patients with heart failure [22, 23], and interferon-γ, which is also capable of stimulating 1,25-(OH)₂D production in extrarenal tissues [24], were determined by two-site immunoradiometric assays.

Results

 Serum vitamin D₂, D₃, 25-OHD₂, 25-OHD₃, 24,25-(OH)₂D₂, 24,25-(OH)₂D₃, 1,25-(OH)₂D₂, and 1,25-(OH)₂D₃ concentrations are shown in Table 1. Although PTH was not detectable throughout her clinical course, the decreased serum 1,25-(OH)₂D₂ concentration which was on admission (4.0–18.7 pg/ml) gradually increased after admission (Fig. 1).

There was a significant correlation between the levels of serum D₂ and 1,25-(OH)₂D₂ (Fig. 2) and serum 25-OHD₂ and 24,25-(OH)₂D₂ (Fig. 3), whereas no significant correlation was found between the levels of serum 25-OHD₂ and 1,25-(OH)₂D₃ or between those of serum free 25-OHD₂ and 1,25-(OH)₂D₃.

The serum 1,25-(OH)₂D₂/25-OHD₂ ratio was low at the time of admission, and gradually increased

<table>
<thead>
<tr>
<th>Sample No (date)</th>
<th>D₂ (ng/ml)</th>
<th>D₃</th>
<th>25-OHD₂ (ng/ml)</th>
<th>24,25-(OH)₂D₂ (ng/ml)</th>
<th>1,25-(OH)₂D₂ (pg/ml)</th>
<th>Ratio of 1,25-(OH)₂D₂/25-OHD₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 4/26, 91</td>
<td>99.8</td>
<td>ND</td>
<td>356.0</td>
<td>21.2</td>
<td>32.4</td>
<td>0.091</td>
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<td>2. 5/13, 91</td>
<td>132.5</td>
<td>ND</td>
<td>223.3</td>
<td>14.1</td>
<td>23.2</td>
<td>0.104</td>
</tr>
<tr>
<td>3. 6/10, 91</td>
<td>108.6</td>
<td>ND</td>
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<td>9.6</td>
<td>17.2</td>
<td>0.072</td>
</tr>
<tr>
<td>4. 7/22, 91</td>
<td>307.7</td>
<td>ND</td>
<td>282.4</td>
<td>11.1</td>
<td>22.9</td>
<td>0.081</td>
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<tr>
<td>5. 8/2, 91</td>
<td>282.3</td>
<td>ND</td>
<td>244.0</td>
<td>9.0</td>
<td>20.2</td>
<td>0.082</td>
</tr>
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<td>6. 8/22, 91</td>
<td>279.0</td>
<td>ND</td>
<td>254.0</td>
<td>9.7</td>
<td>21.9</td>
<td>0.086</td>
</tr>
<tr>
<td>7. 9/28, 91*</td>
<td>195.9</td>
<td>ND</td>
<td>186.8</td>
<td>7.4</td>
<td>13.0</td>
<td>0.069</td>
</tr>
<tr>
<td>8. 11/1, 91</td>
<td>170.1</td>
<td>ND</td>
<td>167.8</td>
<td>24.0</td>
<td>21.9</td>
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<td>188.6</td>
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<td>155.5</td>
<td>ND</td>
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<td>7.2</td>
<td>12.1</td>
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<td>4.5</td>
<td>11.8</td>
<td>0.070</td>
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<td>4.3</td>
<td>14.3</td>
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</tr>
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<td>131.4</td>
<td>ND</td>
<td>208.4</td>
<td>5.7</td>
<td>17.8</td>
<td>0.085</td>
</tr>
<tr>
<td>14. 1/22, 93</td>
<td>55.0</td>
<td>ND</td>
<td>80.0</td>
<td>3.9</td>
<td>3.3</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Normal range 1-5 10-40 1-4 20-70

* The sample was taken 2–3 days after AHPPrBP administration. ND, not detectable; less than 1 ng/ml for D and 25-OHD, 0.1 ng/ml for 24,25-(OH)₂D, and 3.5 pg/ml for 1,25-(OH)₂D. Date of sample; see Fig. 1.
in May–August, when the urinary excretion of phosphate was decreased (80–400 mg) (Fig. 4). In September, the urinary excretion of phosphate increased due to the infusion of phosphate, but serum 1,25-(OH)₂D₂ increased further after the administration of AHPrBP. In contrast, the serum 24,25-(OH)₂D₃/25-OHD₃ ratio was relatively constant throughout her clinical course (Fig. 4).

In keeping with the decreased serum albumin, the serum DBP level was also decreased on admission and increased after discharge (Table 2).

Serum GH and prolactin concentrations were within the normal range in most samples, and there was no significant correlation between the levels of these hormones and that of 1,25-(OH)₂D₂ (Table 2).

Serum IFN-γ was not detectable, but the serum TNF-α level was high in June, when pleural effusion developed. However, no significant correlation was seen between the levels of serum TNF-α and 1,25-(OH)₂D₂ (Table 2).

Discussion

There are a number of possible mechanisms by which serum 1,25-(OH)₂D₂ can increase in patients with post-surgical hypoparathyroidism receiving vitamin D₂ supplementation [1–4]. Although PTH
and PTHrP are very potent stimulators of 25-hydroxyvitamin D-1α-hydroxylase in the renal tubule, intact PTH was undetectable throughout the clinical course in the present patient. Furthermore, urinary excretion of the C-terminal fragments of PTHrP, which increased in patients with malignancy-associated hypercalemia, was in the normal range [21].

Recently, it was reported that the administration of calcitonin can increase the concentration of serum 1,25-(OH)2D in normal as well as X-linked hypophosphatemic rickets [25], by stimulating 1α-hydroxylase in the proximal straight tubule [26]. However, the reported increment was maximal within the first 24 h, and returned to baseline levels within a further 48 h. In the present patient, calcitonin was administered on two occasions, but there was no temporal relationship between calcitonin administration and the serum 1,25-(OH)2D2 concentration. Other possible factors such as GH, prolactin, interferon-γ, and TNF-α could not account for the gradually increased serum level of 1,25-(OH)2D2 [3, 4].

From June to September, when the serum 1,25-(OH)2D2 concentration increased, the patient developed severe pleural effusion. Some macrophages in the pleural effusion may have been activated and produced the 1,25-(OH)2D2, as demonstrated in tuberculous patients with pleural effusion [27]. However, no granulomatous disease was found, and the 1α-hydroxylase activity in the patient was resistant to glucocorticoid treatment, a feature inconsistent with macrophage 1α-hydroxylase [28].

We think that the most likely factor responsible for the increase in 1,25-(OH)2D2 is phosphate depletion [29]. The patient was anorectic and could not take phosphate solution (Joliv solution) per os. In addition, she received calcium- and phosphate-free intravenous hyperalimentation. Although hypophosphatemia was not remarkable because of vitamin D intoxication and slightly decreased renal function, hypophosphaturia was evident in May-August, 1991, when serum 1,25-(OH)2D2 was steadily increasing (Fig. 1). Therefore, as demonstrated in thyroparathyroidectomized rats maintained on a low-phosphate diet [1, 30], phosphate depletion was at least partly responsible for a PTH-independent stimulation of the conversion of 25-OHD2 to 1,25-(OH)2D2. The increased serum level of 1,25-(OH)2D2 in the present patient probably reflects increased production rather than decreased degradation of 1,25-(OH)2D2, as reported in healthy subjects on a phosphate-restricted diet [29]. Indeed, the serum 1,25-(OH)2D2/25-OHD2 ratio, an indicator of 1α-hydroxylase activity, was progressively increased, whereas the serum 24,25-(OH)2D2/25-OHD2 ratio, an indicator of 24-hydroxylase activity and catabolism of 1,25-(OH)2D2 [1], was relatively constant (Fig. 4). It should be pointed out that the Km values of renal 24-hydroxylase for 1,25-(OH)2D3 and 25-OHD3 are

### Table 2. Serum concentrations of calcium, DBP, hormones and cytokines

<table>
<thead>
<tr>
<th>Sample No</th>
<th>Ca (mg/dl)</th>
<th>Albumin (g/dl)</th>
<th>DBP (µg/ml)</th>
<th>GH (ng/ml)</th>
<th>Prolactin (ng/ml)</th>
<th>IFN-γ (U/ml)</th>
<th>TNF-α (pg/ml)</th>
</tr>
</thead>
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<td>1. 4/26, 91</td>
<td>15.5</td>
<td>2.9</td>
<td>225</td>
<td>0.79</td>
<td>3.0</td>
<td>0.15</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>2. 5/13, 91</td>
<td>9.5</td>
<td>2.2</td>
<td>197</td>
<td>4.82</td>
<td>19.9</td>
<td>0.27</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>3. 6/10, 91</td>
<td>9.1</td>
<td>2.2</td>
<td>225</td>
<td>5.38</td>
<td>20.8</td>
<td>0.50</td>
<td>309</td>
</tr>
<tr>
<td>4. 7/22, 91</td>
<td>10.0</td>
<td>2.4</td>
<td>225</td>
<td>0.67</td>
<td>11.7</td>
<td>&lt;0.10</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>5. 8/2, 91</td>
<td>10.6</td>
<td>2.5</td>
<td>204</td>
<td>1.95</td>
<td>12.6</td>
<td>0.55</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>6. 8/22, 91</td>
<td>11.4</td>
<td>2.6</td>
<td>204</td>
<td>3.07</td>
<td>5.6</td>
<td>0.21</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>7. 9/28, 91</td>
<td>9.4</td>
<td>2.6</td>
<td>211</td>
<td>1.07</td>
<td>7.9</td>
<td>0.33</td>
<td>&lt;7.0</td>
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<tr>
<td>8. 11/1, 91</td>
<td>9.6</td>
<td>2.5</td>
<td>231</td>
<td>0.99</td>
<td>13.2</td>
<td>&lt;0.10</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>9. 12/7, 91</td>
<td>10.9</td>
<td>2.4</td>
<td>296</td>
<td>1.81</td>
<td>10.1</td>
<td>0.40</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>10. 3/2, 92</td>
<td>10.1</td>
<td>2.6</td>
<td>310</td>
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<td>7.8</td>
<td>&lt;0.10</td>
<td>&lt;7.0</td>
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<tr>
<td>11. 4/8, 92</td>
<td>9.9</td>
<td>2.7</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>13. 8/17, 92</td>
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<td>3.6</td>
<td>324</td>
<td>8.45</td>
<td>10.9</td>
<td>0.18</td>
<td>&lt;7.0</td>
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<td>3.8</td>
<td>324</td>
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Normal range: 8.8–10.5 3.5–5.1 300–500 <5 1.4–1.6 0.40 <7.0

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32 and 331 nM, respectively [31], suggesting that the substrate of 24-hydroxylase in vivo is 1,25-(OH)2D2 rather than 25-OHD. Therefore, two to three fold fluctuations in serum 25-OHD levels would not affect the catabolic rate of 1,25-(OH)2D2.

In addition to phosphate depletion, a decrease in serum DBP would have increased serum free 25-OHD2 [32], and may have been at least partly responsible for increased synthesis of 1,25-(OH)2D2 [10]. However, since DBP is abundant in serum, and less than 5% of DBP is saturated with 25-OHD in normal subjects [1], a slight decrease in DBP to 35% would not substantially increase serum free 25-OHD2. Whatever the mechanism, 1,25-(OH)2D2 produced in excess by residual 1α-hydroxylase in the kidney or in extrarenal tissues through a mass action effect [10] would have exceeded its degradation rate, particularly when the patient was losing body weight.

Another likely factor responsible for the transient increase in 1,25-(OH)2D2 is bisphosphonate. In contrast to early bisphosphonates (ethane-hydroxy-1-bisphosphonate and EHBP), which markedly decrease serum 1,25-(OH)2D [33], recently developed bisphosphonates, such as 1-hydroxypentane-1,1-bisphosphonate (HPeBP) and (cycloheptylamine) methylene-1,1-bisphosphonic acid, YM-175) increase serum 1,25-(OH)2D and stimulate intestinal Ca transport in normal as well as parathyroidectomized rats [34, 35, 36]. Similar findings have been reported in patients with Paget’s disease treated with AHPrBP [37]. Therefore, although AHPrBP decreases bone resorption, its stimulatory effect on renal and/or extrarenal 1α-hydroxylase and the subsequent increase in intestinal Ca absorption may have overcome the inhibitory effect on bone resorption, resulting in attenuation of the decrease in serum calcium. Therefore, EHBP seems preferable to AHPrBP for the treatment of patients with vitamin D2 intoxication.

Finally, it should be pointed out that the patient’s body weight loss and cachetic state contributed to a marked prolongation of the hypercalcemia. She had lost 9 kg prior to admission. In addition, hypoproteinemia, anemia, muscle weakness, edema, pleural effusion and cardiac failure developed in August–September, 1991, when 1,25-(OH)2D2 was generally high. It is highly likely that vitamin D2, which had accumulated in body fat and muscle for more than 14 years to a level as high as that in cod liver oil [2, 38], would be released slowly into the circulation, increasing the serum D2 and 25-OHD2 concentrations. The significant correlation between serum D2 and 1,25-(OH)2D2 also supports this possibility.

In summary, by serially measuring the serum levels of vitamin D metabolites in a patient with chronic vitamin D2 intoxication, we have clearly demonstrated that serum 1,25-(OH)2D2 may be decreased, normal, or increased, depending upon the 25-hydroxyvitamin D-1α-hydroxylase activity of the patient. These data may help to explain the inconsistent levels of serum 1,25-(OH)2D thus far reported in patients with vitamin D intoxication [1–9]. Possible factors responsible for a prolonged and paradoxical increase in serum 1,25-(OH)2D2 are body weight loss, hypoproteinemia, and phosphate depletion. In addition, some bisphosphonates would certainly promote PTH-independent production of 1,25-(OH)2D2.

Addendum: The patient was eucalcemic and doing well in April, 1994, on a daily dose of 1.5–2.0 µg 1α-OHD3. The serum calcium concentration was 9.2 mg/dl, P; 4.8 mg/dl, albumin; 4.1 g/dl, BUN; 33.4 mg/dl, creatinine; 1.4 mg/dl. The serum 25-OHD2 level was gradually decreased to 20.7 mg/ml (25-OHD2; 5.3 mg/ml). Serum 1,25-(OH)2D2 was not detectable while serum 1,25-(OH)2D3 level was in the normal range (33.4 pg/ml).

References


