Vitamin D deficiency in two young adults with biochemical findings resembling pseudohypoparathyroidism type I and type II

Toshiro Seki1), Michiko Yamamoto3), Hironari Kimura1,3), Mika Tsuiki1), Masami Ono1), Nobuhiro Miki1), Kazue Takano1) and Kanji Sato1,3)

1)Department of Medicine, Institute of Clinical Endocrinology, Tokyo Women's Medical University, Tokyo 162-8666, Japan
2)Faculty of Human Care, Teikyo Heisei University, Tokyo 170-8445, Japan
3)Field of Pathophysiology, Treatment of Thyroid and Parathyroid Disease, Graduate School of Medicine, Tokyo Women's Medical University, Tokyo 162-8666, Japan

Abstract. We report two patients with vitamin D deficiency due to unbalanced diet. The patients initially presented with severe hypocalcemia, normophosphatemia and markedly elevated serum PTH levels. Although nutritional vitamin D deficiency was suspected from their history of gastrointestinal problems and dietary restriction, we conducted Ellsworth-Howard test to exclude the possibility of pseudohypoparathyroidism (PHP). Both patients showed no incremental response of urinary phosphate excretion. However, the urinary cAMP response to exogenous PTH was different between the two. Case 1 showed a blunted response (5-fold and 1.54 µmol/h increase) and case 2 showed a normal response (39-fold and 3.04 µmol/h increase). According to the criteria of Ellsworth-Howard test, the data of case 1 was compatible with PHP type I, and of case 2 with PHP type II. The final diagnosis of vitamin D deficiency was established in both patients based on very low serum 25-hydroxyvitamin D levels (less than 5 ng/mL) and the effect of treatment. After calcium supplementation with or without vitamin D, their biochemical abnormalities disappeared. They maintained normocalcemia without medication after correction of their unbalanced diet. The present study indicated that patients with vitamin D deficiency occasionally showed biochemical findings suggestive of PHP and that such patients could exhibit not only PHP type II pattern of response to exogenous PTH but also of type I pattern. Thus our clinical observation suggests the complexity of PTH resistance in vitamin D deficiency and underscores the importance of diet to prevent the disorder.

Key words: Vitamin D deficiency, Pseudohypoparathyroidism, Parathyroid hormone, Hypocalcemia, Ellsworth-Howard test
activation or accelerate its clearance [1, 5, 6]. Severe form of vitamin D deficiency has been diagnosed by overt myopathy, osteomalacia in adults, and rickets in children [7]. However, mild form of less symptomat-
ic vitamin D deficiency could miss a proper diagnosis unless it is suspected and the serum concentration of 25-hydroxyvitamin D (25(OH)D), the best indicator of vitamin D status, is measured. Previous studies reported inadequate circulating 25(OH)D concentrations in various populations such as medical inpatients [8], postmenopausal women [9], free-living adults [10], adolescent girls [11], and the pediatric age groups. Thus, the prevalence of hypovitaminosis D has been estimated up to around 50 percent in high-risk populations in Western countries. It's prevalence in diverse populations including seemingly healthy people has not been well characterized in Japan.

Biochemical similarities and differences between vitamin D deficiency and PHP have been a matter of confusion. Typically, patients with vitamin D defi-
cency show normal or decreased serum phosphorus levels without or with mild hypocalcemia [1, 5, 6]. In some patients, however, marked hypocalcemia is accom-
panied by normo- or hyperphosphatemia [12-18]. When a patient presents with hypocalcemia and normo- or hyperphosphatemia, it is difficult to differenti-
ate between PHP and vitamin D deficiency based on routine biochemistry. Ellsworth-Howard test has been conducted on such occasion. As Rao et al. described that exclusion of vitamin D deficiency should be con-
sidered in the diagnosis of PHP type II [15], the re-

sults of Ellsworth-Howard test in vitamin D deficient pa-

tients were reported to be PHP type II pattern [12-15, 18, 19]. To the best of our knowledge, no previous study has reported that vitamin D deficiency mimics PHP type I in biochemical findings. Here we report two young adult patients with vitamin D deficiency, whose results of Ellsworth-Howard test were compat-
ible with PHP type I in one, and with PHP type II in another.

Clinical Records

Case 1

A 31-yr-old woman, housekeeper at home, present-
ed to a local hospital with muscle cramp and low back pain in December 2007. Laboratory findings showed severe hypocalcemia (5.7 mg/dL [reference range 8.5-
10.0 mg/dL]), normophosphatemia (3.3 mg/dL [2.5-4.5 mg/dL]) and elevated serum alkaline phosphatase ac-
tivity (ALP) (516 U/L [115-359 U/L]). There was no family history of disorders of bone and mineral me-
tabolism. Past history revealed that she had been di-

gnosed as irritable bowel syndrome at age 24. Since then, she was withholding the intake of animal source foods. She was referred to us for detailed examination and admitted to our hospital in January 2008.

The patient was 156.7 cm tall and weighed 46.0 kg. Blood pressure was 90/60 mmHg. Trousseau sign was positive but Chvostek sign was negative. Physical ex-

amination and electrocardiogram were unremarkable.

The blood chemistry confirmed hypocalcemia, normo-

phosphatemia and elevated ALP (calcium 6.6 mg/dL, phosphorus 3.7 mg/dL and ALP 601 U/L). The se-

serum magnesium concentration was 1.6 mEq/L [1.2-2.0 mEq/L]. Her renal and liver functions were normal. There was no anemia or hypoalbuminemia. Serum intact PTH (iPTH) level was markedly elevated (529 pg/mL [10-65 pg/mL]). Both 25(OH)D and 1,25-
dihydroxyvitamin D (1,25(OH) 2D) levels were low (<5 ng/mL [10-40 ng/mL] and 13.4 pg/mL [20-60 pg/ mL], respectively). Urinary excretion of calcium and phosphate were <0.01 g/day and 0.48 g/day, respec-

tively. There were no radiological findings sugges-
tive of osteomalacia. Bone mineral density (BMD) in the lumbar region was low (0.728 g/cm 2, Z score -2.6 SD). Ellsworth-Howard test was performed accord-

ing to the standard method [4, 20] with iv injection of synthetic human PTH (1-34) (Asahi Kasei Co., Tokyo, Japan) at a dose of 100 U under conditions of hypocal-

cemia and elevated serum PTH concentration (before treatment). As shown in Fig. 1B, the incremental re-

sponse of urinary cAMP was blunted (5-fold and 1.54 µmol/h increase) and of urinary phosphate was absent (-2.89 mg/2h change).

While in hospital, the patient could eat a stan-
dard hospital diet without gastrointestinal symptoms. Treatment was started with 500 mg/day of calcium supplemen-
tation and 0.5 µg/day of 1α(OH)D3 (Chugai Pharmaceu-
tical Co., LTD., Tokyo, Japan,) in January 2008. The serum calcium levels became normal two months later (Fig. 2). The serum levels of iPTH de-

creased dramatically as serum calcium concentrations in-
creased. Serum ALP further increased initially and then decreased into the normal range six months later. The serum phosphorus levels remained normal throughout the treatment period. In June, 1α(OH) D3 therapy was stopped but calcium supplementation
was continued. Under treatment with calcium supplementation alone, the serum levels of iPTH began to increase again. In February 2009, vitamin D₃ supplementation (1000 IU/day) was started. Two months later, serum 25(OH)D concentration entered into the normal range (15 ng/mL) and iPTH decreased to near normal range. In April, both vitamin D₃ and calcium supplementation were discontinued. By that time, she had corrected her unbalanced vegetarian-like diet according to our advice. Thus without any medication, her serum calcium, phosphorus, and ALP were all within normal ranges (9.2 mg/dL, 2.8 mg/dL and 153 U/L, respectively) in June 2009. Serum levels of 25(OH)D, 1,25(OH)₂D and iPTH also normalized (23 ng/mL, 33.7 pg/mL and 31 pg/mL, respectively). BMD in the lumbar region increased markedly (0.924 g/cm²; Z score -0.9 SD in September 2008, and 0.965 g/cm²; Z score -0.5 SD in June 2009).

Case 2
A 34-yr-old woman, who had been followed up for chronic pancreatitis at the Gastroenterology Center of our hospital, was referred to us for evaluation of hypocalcemia (calcium 6.6 mg/dL) detected in December 1996. The patient developed chronic pancreatitis at age 29. Since then, she had restricted intake of fatty foods including meats, egg yolk, and oily fish such as salmon and sardine. She never drank much. With dietary restriction, she was free of gastrointestinal symptoms and continued to work at a department store. Family history was negative for bone and mineral metabolism disorders. On her first visit in April 1997, blood chemistries revealed mild hypocalcemia (calcium 8.1 mg/dL), normophosphatemia (phosphorus 3.5 mg/dL) and an increase in ALP (742 U/L). Serum iPTH was markedly elevated (518 pg/mL), 25(OH)D was low (4.8 ng/mL) and 1,25(OH)₂D was low normal.
and 0.46 g/day, respectively. Bone mineral density in the right forearm was 0.450 g/cm$^2$ (T score -2.2 SD).

Ellsworth-Howard test was performed when her serum calcium and iPTH concentrations were within normal ranges after 3 months of calcium supplementation. As shown in Fig. 1C, urinary cAMP excretion increased (39-fold and 3.04 µmol/h increase) after PTH injection. There was no increase in urinary phosphate excretion (-6.02 mg/2h change).

Since her serum calcium and iPTH levels remained normal and ALP decreased to normal range after six months of treatment, calcium supplementation was discontinued in December 1997 (Fig. 3). By that time, the patient had improved her unbalanced diet. At the end of April 1998, her serum levels of calcium, phosphorus and ALP were 9.2 mg/dL, 3.7 mg/dL and 203 U/L, respectively. The serum level of iPTH was 56 pg/mL.

Fig. 2  Clinical course of case 1. Upper panel: Open diamond (◇); serum levels of calcium (Ca) [reference range: 8.5-10.0 mg/dL], Open square (□); serum levels of phosphorus (P) [2.5-4.5 mg/dL], Filled triangle (▲); serum levels of alkaline phosphatase activity (ALP) [115-359 U/L]. Lower panel: Open diamond (◇); serum levels of intact PTH (iPTH) [10-65 pg/mL], Filled triangle (▲); serum levels of 25-hydroxyvitamin D (25(OH)D) [10-40 ng/mL], Open square (□); serum levels of 1,25-dihydroxyvitamin D (1,25(OH)$_{2}$D) [20-60 pg/mL]. Arrow indicates the time when Ellsworth-Howard test was performed.

(29.4 pg/mL). After initial evaluation, calcium supplementation (500 mg/day) was started.

In July 1997, she admitted to our hospital for further examinations. The patient was 149.2 cm tall and weighed 38.0 kg. Blood pressure was 114/68 mmHg. Trousseau and Chvostek signs were negative. Radiographs and electrocardiogram were unremarkable. The blood chemistry while on calcium supplementation revealed normocalcemia (8.9 mg/dL) and slightly elevated serum phosphorus concentration (4.6 mg/dL). ALP was still elevated (622 U/L), but serum iPTH level was decreased to 60 pg/mL. The serum magnesium was 1.9 mEq/L. Serum amylase and lipase levels were normal (151 IU/L and 53 IU/L, respectively). Her renal and liver functions were also normal. There was no anemia or hypoalbuminemia. Urinary excretion of calcium and phosphate were 0.02 g/day and 0.46 g/day, respectively. Bone mineral density in the right forearm was 0.450 g/cm$^2$ (T score -2.2 SD). Ellsworth-Howard test was performed when her serum calcium and iPTH concentrations were within normal ranges after 3 months of calcium supplementation. As shown in Fig. 1C, urinary cAMP excretion increased (39-fold and 3.04 µmol/h increase) after PTH injection. There was no increase in urinary phosphate excretion (-6.02 mg/2h change).
Discussion

The two patients reported here presented with chronic hypocalcemia, normophosphatemia and markedly elevated PTH levels with normal renal function. These findings suggested a diagnosis of some type of PHP or vitamin D related diseases. Although the presence of osteopenia and elevated serum ALP were compatible with vitamin D related diseases, there have been several studies showing elevated serum ALP levels and osteopenia in patients with PHP [21]. Thus, we measured serum levels of vitamin D metabolites to make a differential diagnosis. Based on very low serum 25(OH)D levels, we established the diagnosis of vitamin D deficiency.

Compared to the serum 25(OH)D levels, serum 1,25(OH)₂D levels are less useful for the diagnosis of vitamin D deficiency. 1,25(OH)₂D levels are either very low or very high in rare disorders of vitamin D metabolism or vitamin D receptor abnormalities [1]. They are low or low-normal in hypoparathyroid disorders including PHP, and can be low, normal or even high in vitamin D deficiency [5]. Thus, after obtaining low to low-normal serum 1,25(OH)₂D levels we could not rule out a possibility of coexistence of PHP and vitamin D deficiency in our patients.

It would be of help if there is a difference in the degree of secondary hyperparathyroidism between PHP and vitamin D deficiency. Allgrove et al. investigated this issue and found that the concentrations of bioactive PTH were similarly high in patients with untreated PHP and those with untreated vitamin D deficiency compared to normal subjects [22]. Dambacher et al. also found no significant differences in circulating im-
munoreactive PTH levels between patients with PHP and vitamin D deficiency [23]. It seemed impossible therefore to separate PHP and vitamin D deficiency depending on the degree of elevation in serum PTH concentrations.

The best way to exclude the possibility of coexistence of PHP and vitamin D deficiency in our patients was the follow-up of their clinical courses after treatment, as suggested previously [16, 18]. Vitamin D deficiency can be treated easily with vitamin D (ergocalciferol or cholecalciferol) with or without calcium supplementation [1, 18]. On the other hand, administration of active vitamin D preparations, either 1α(OH)D₃ or 1,25(OH)₂D₃, is a standard treatment regimen for PHP [1]. Unfortunately, both cholecalciferol and ergocalciferol are currently unavailable as prescription drugs in Japan. Therefore, our case 1 was initially treated with 1α(OH)D₃, and later with cholecalciferol, available as an OTC (over the counter) drug. Case 2 was treated with calcium supplementation alone. After they discontinued their restricted diets, our patients could maintain normocalcemia and normal serum iPTH levels. Thus, coexistence of PHP was excluded in both patients.

Ellsworth-Howard test was conducted in each patient before the final diagnosis being made based on the clinical course. The test has been considered to be the most reliable test for the diagnosis of PHP and the classification of the variant forms of PHP [1, 3, 4]. After the synthetic human PTH (1-34) peptide became available for human use, several protocols [24] including the Japanese standard method [4, 20] have been developed. The patients with PHP type I do not show an appropriate increase in urinary excretion of either cAMP or phosphate, whereas type II patients show a normal or even enhanced increase in urinary cAMP excretion with an impaired phosphaturic response [25, 26]. Theoretically, therefore, PHP type I and type II can be distinguished easily. But from a practical viewpoint, the distinction between normal and impaired response is not clear-cut. There have been no worldwide-unified diagnostic criteria to interpret the results of PTH infusion test.

In Japan, standard procedures of the Ellsworth-Howard test and the diagnostic criteria for cAMP and phosphaturic responses were proposed in 1984 [20], and being used thereafter nationwide. In spite of some differences in the protocols of PTH infusion test, it is a common finding that normal subjects and patients with hypoparathyroidism usually display a 10-fold or more increase in urinary cAMP excretion [20, 27]. Thus in Japanese criteria, normal cAMP response was defined as a more than 10-fold increase in urinary cAMP excretion [9, 20, 27]. On the other hand, it is sometimes difficult to classify a phosphaturic response as normal or subnormal regardless of the criteria used. Interpretation of the phosphaturic response to PTH is often complicated by random or diurnal variations in phosphate excretion [27]. Taking these into consideration, normal phosphaturic response in Japanese criteria was defined as a more than 35 mg/2h increase in phosphate excretion [9, 20, 27]. According to these criteria, our case 1 showed a response of PHP type I pattern. Our case 2 showed a response of PHP type II pattern, although the test was not conducted under hypocalcemic condition.

It is generally accepted that patients with vitamin D deficiency occasionally show biochemical findings resembling PHP type II [12-19]. We conducted extensive literature survey and found several case studies written in English and reporting both the data of serum 25(OH)D levels and the results of PTH infusion test (Table 1) [12-15, 18, 19]. The number of case collected was smaller than we expected probably because PTH infusion test was not usually conducted on patients with proven vitamin D deficiency and because serum 25(OH)D levels were not measured in hypocalcemic patients without hypophosphatemia unless vitamin D deficiency was strongly suspected. As shown in Table 1, it was reported that PTH infusion elicited normal incremental responses in urinary cAMP excretion in all patients tested before treatment (n=6) and after treatment (n=3). Only our case 1 showed a blunted response in urinary cAMP excretion. Phosphaturic responses were variable in the earlier reports, but they were unequivocally absent in our 2 patients.

Since there is no similar previous case report, we cannot make a detailed discussion about the mechanisms of PHP type I pattern (blunted cAMP) response to exogenous PTH in our case 1. It is established that PTH resistance in PHP type I is caused by a defect in the hormone-sensitive signal transduction pathway that activates adenylate cyclase in renal tubular cells [28]. It is also elucidated that the molecular defects responsible for PHP type I reside in GNAS, the gene encoding the α-subunit of the stimulatory GTP binding protein [29]. It is evident that the defects in patients with PHP type I are irreversible, while the ab-
normalities seen in patients with vitamin D deficiency are reversible. Lewin et al. reported that the incremental responses of urinary cAMP to exogenous PTH were subnormal in most patients with vitamin D deficiency and the magnitude of responses became much greater after vitamin D repletion [19]. Kruse et al. by measuring baseline urinary cAMP also suggested that the renal cAMP production in response to endogenous PTH was decreased in vitamin D deficient states [30]. Taken these together, it is possible that urinary cAMP response to exogenous PTH could diminish to the extent of PHP type I in some patients with severe vitamin D deficiency with markedly elevated endogenous PTH levels, as in our case 1. As suggested by others, chronic elevation in plasma PTH might induce desensitization of PTH receptors and lead to the development of hormone resistance [19, 31-33].

An important question left is whether vitamin D deficiency of such severity as seen in our patients is a rare occurrence or not in Japan, where vitamin D deficiency has been considered less prevalent than in other countries [34]. Our patients are young adults in their thirties and living a seemingly normal life. One patient has been suffering from irritable bowel syndrome, a relatively common functional disease in young females, and the other asymptomatic chronic pancreatitis. Although the prevalence of vitamin D deficiency in diverse populations has not been well characterized in Japan, it is emphasized that vitamin D deficiency remains an under-recognized problem in the general population worldwide. According to the recent study by Nakamura [34], vitamin D nutrition in young women was poorer than people in middle and advanced age groups. He speculated that low fish

### Table 1

Summaries of previous studies showing the results of PTH infusion test in patients with vitamin D deficiency.

<table>
<thead>
<tr>
<th>Reference No</th>
<th>Study</th>
<th>Time of evaluation</th>
<th>Age</th>
<th>Gender</th>
<th>Ca (mg/dL)</th>
<th>P (mg/dL)</th>
<th>25(OH)D (ng/mL)</th>
<th>Response to exogenous PTH</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Kanis et al. (1976)</td>
<td>A 12 yrs F</td>
<td>9.0 (9.0-10.0)</td>
<td>4.9 (2.7-4.5)</td>
<td>25 (4-23)</td>
<td>11 fold</td>
<td>Osteomalacia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 Matsuda et al. (1979)</td>
<td>B and A</td>
<td>14 yrs M</td>
<td>B: 5.5-7.1 A: 4.3 (9-10)</td>
<td>B: &lt;5 A: 47.5 (8-50)</td>
<td>40 fold A: 50 fold</td>
<td>Anticonvulsant rickets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Lewin et al. (1982)</td>
<td>B 26 yrs F</td>
<td>8.6 (8.8-10.2)</td>
<td>2.2 (3-30)</td>
<td>50 nmol/min increase</td>
<td>Osteomalacia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 Dandona et al. (1983)</td>
<td>B 19 yrs M</td>
<td>4.9 (8.4-10.4)</td>
<td>5.1 (2.2-4.0)</td>
<td>3 (6-18)</td>
<td>60 fold A: 5 fold</td>
<td>Rickets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>B 19 yrs F</td>
<td>5.2 (8.4-10.4)</td>
<td>5.0 (2.2-4.0)</td>
<td>3 (6-18)</td>
<td>50 fold A: 8 fold</td>
<td>Rickets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 Rao et al. (1985)</td>
<td>B 59 yrs F</td>
<td>5.98 (8.6-10.2)</td>
<td>3.90 (2.4-4.0)</td>
<td>&lt;10</td>
<td>peak cAMP 233 nmol/mgCr (41-1589) Fall in P 0.03 mg/dLCr (0.32-1.52)</td>
<td>Celiac sprue/ Osteomalacia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>B 51 yrs M</td>
<td>5.98 (8.6-10.2)</td>
<td>3.90 (2.4-4.0)</td>
<td>&lt;10</td>
<td>peak cAMP 423 nmol/mgCr (41-1589) Fall in P reabsorption 0.39 mg/dLCr (0.32-1.52)</td>
<td>Total gastrectomy/ Osteomalacia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Inamo (2005)</td>
<td>A 1.1yrs F</td>
<td>9.4 (8.8-10.6)</td>
<td>4.3 (4.0-7.0)</td>
<td>6 (10-55)</td>
<td>15 fold (&gt;10 fold)</td>
<td>4.24 mg/2h (&gt;25 mg/2h)</td>
<td>Rickets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seki et al. (2010)</td>
<td>B 31 yrs F</td>
<td>6.6 (8.5-10.0)</td>
<td>3.7 (2.5-4.5)</td>
<td>&lt;5 (10-40)</td>
<td>5 fold (&gt;10 fold)</td>
<td>-2.89 mg/2h (&gt;35 mg/2h)</td>
<td>Irritable bowel syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A 34 yrs F</td>
<td>8.9 (8.5-10.0)</td>
<td>4.6 (2.5-4.5)</td>
<td>4.8 (10-40)</td>
<td>39 fold (&gt;10 fold)</td>
<td>-6.02 mg/2h (&gt;35 mg/2h)</td>
<td>Chronic pancreatitis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: A; after treatment, B; before treatment, Ca; serum levels of calcium, P; serum levels of phosphorus, 25(OH)D; serum levels of 25-hydroxyvitamin D, U-cAMP; urinary cAMP excretion, U-P; urinary phosphate excretion. The numbers in parentheses indicate reference ranges.
consumption and low activity in the daytime might have contributed to the relatively low mean serum 25(OH)D concentrations in young women. This observation may have some relevance to the findings of our patients.

Vitamin D deficiency results from inadequate dietary intake, reduced exposure to sunlight, malabsorption, chronic liver diseases and drugs such as anticonvulsants [1, 5, 6]. The cause of vitamin D deficiency in our patients seemed to be of dietary origin. Both patients had put themselves on restricted unbalanced diets for a long time on their own decision. It is unlikely that their sunlight exposure had been extremely insufficient because their daily activities were not much different from those of contemporary Japanese women. They did not have liver diseases and were not taking any drugs. There was no evidence of malabsorption in either patient though both had problems in their digestive organs. They did not show diarrhea, anemia and hypoalbuminemia. The observation that they could maintain normal calcium metabolism without medication after they stopped unnecessary dietary restriction indicated that their underlying diseases were not serious as to cause malabsorption of vitamin D and calcium.

The major contributing factor to vitamin D deficiency in our patients was obviously their unbalanced diet. The low-fat diet taken by our patients might be similar to vegetarian (or lactovegetarian) diet eliminating animal products from the meal. There are several reports on vitamin D status and bone metabolism of vegetarians [35-37]. It was shown that dietary intake of vitamin D, serum 25(OH)D concentrations and bone mineral density in the lumbar region of the spine were significantly lower and serum iPTH concentrations were higher in strict vegetarians compared with controls [36]. Thus, anybody on strict vegetarian-like diets for any reason could develop severe vitamin D deficiency.

As mentioned above, clinical course of our patients suggested that their underlying diseases themselves had little, if any, influence on their vitamin D status. However, it is well known that gastrointestinal disorders affect vitamin D status. Many investigators reported high prevalence of vitamin D deficiency in patients with inflammatory bowel diseases [38, 39], chronic pancreatitis [40, 41] and malabsorption from various causes [42]. Generally, the severity of vitamin D deficiency in patients with gastrointestinal disorders depends on the duration and the severity of underlying diseases. It appeared difficult though to separate between direct effects of the diseases and the influences of dietary components relating to the diseases.

In summary, in the differential diagnosis of hypocalcemia, measurement of serum 25(OH)D level along with PTH is very helpful. Unfortunately, however, the cost for the measurement of serum 25(OH)D level is currently not covered by the national health insurance. In order not to overlook vitamin D deficiency, it is important to take a detailed history, especially seeking for evidence of dietary deficiency. PTH infusion test has only limited value in the differential diagnosis between vitamin D deficiency and PHP.

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