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A Case of Idiopathic Hypoparathyroidism Associated with Psoriasis Vulgaris

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ABSTRACT

A 31-year-old Japanese male had been hospitalized for idiopathic hypoparathyroidism associated with psoriasis vulgaris. Just after hospitalization, he had experienced severe hypocalcemia resulting in dyspnea. Despite hypocalcemia, the level of PTH stayed within the lower limit of the normal range. The results of the Ellsworth-Howard test revealed a normal renal response to PTH. Taking the above results into account, we diagnosed his condition as idiopathic hypoparathyroidism. Treatment with oral 1α-(OH)-D_3 and calcium lactate maintained the serum calcium and phosphorus levels in the normal range. He also had sensorineural hearing impairment and renal abnormality, suspecting the HDR syndrome.

Key words: Hypoparathyroidism, Psoriasis vulgaris, Hypocalcemia, HDR syndrome

INTRODUCTION

It is well-known that hypoparathyroidism is accompanied by hypocalcemia, which may

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result in tetany. In addition, it has been reported that hypocalcemia exacerbates psoriasis vulgaris (1). However, it is rare for both hypoparathyroidism and psoriasis vulgaris to occur together. Here, we report a case of hypoparathyroidism that was diagnosed during an admission for psoriasis vulgaris.

CASE REPORT

A 31-year-old Japanese male with psoriasis vulgaris was admitted to the Department of Dermatology at Nagoya City University Hospital in mid-February 2006. He had a history of hearing impairment since infancy and psoriasis vulgaris since junior high school. With respect to family history, his father had myasthenia gravis and his mother had hypertension. He had a healthy sister. There was no positive family history for psoriasis, congenital malformation, convulsion and mental retardation.

Three and a half months prior to admission, the patient had an exacerbation of his psoriasis vulgaris. There were also symptoms of diarrhea and appetite loss. One and a half months after the onset of the exacerbation, he was treated at a different hospital by using methotrexate, but there was no improvement in his skin condition. He was admitted to the Department of Dermatology of our hospital for further management. Just after hospitalization, he experienced dyspnea and a decrease in his consciousness level (Japan Coma Scale II, 30). Both were attributed to severe hypocalcemia, which was noted to be 5. 6 mg/dL. Immediate intravenous injection of calcium gluconate improved his dyspnea and level of consciousness. Subsequently, he was transferred to our department for further investigation of his hypocalcemia.

On examination in our department, his height was 171. 9cm, weight 75. 6kg, BMI25. 6kg/m^2, temperature 37. 4℃, pulse 86/min, and blood pressure 112/45 mmHg. No goiter was palpable. Heart sounds were dual without gallops or murmur, and breath sounds were clear. No abdominal or pelvic masses were palpable. There is no particular facial feature. Numbness of his forearms and myospasm of his fingers were observed. Erythema and scaling were present all over his body (Fig 1). We administered a continuous drip infusion of calcium gluconate, which gradually resolved the hypocalcemia-related symptoms.

Table 1 shows the laboratory data on admission. Although the serum level of calcium and phosphorus were 5. 6 mg/dL and 9. 0 mg/dL, respectively, intact PTH remained at the lower limits of the normal range. These data strongly suggested that the patient had hypoparathyroidism. The fact that %TRP was 95. 8% supported this. 25-OH-D_3 and Mg values were within the normal range. Antinucler antibody was less than 40 times. Both anti-TPO antibody and antithyroglobulin were less than 0. 3 μM/IU. High sensitive IgE was 86. 9 IU/ml. Although low levels of ACTH and cortisol were seen on admission, they recovered to

Table 1 Laboratory date on admission

CBC		FE_{Na}	0.35 %
WBC	12300 /μL	$\%C_{UA}/Ccr$	9.2 %
Neutro.	56.0 %	**Endocrinology**	
Lympho.	17.0 %	TSH	1.351 μIU/mL
Mono.	8.0 %	FT_4	1.06 ng/dL
Eosino.	19.0 %	FT_3	2.81 pg/mL
Baso.	0.0 %	ACTH	6.8 pg/mL
RBC	$390x10^4$ /μL	Cortisol	1.9 μg/dL
Hb	12.4 g/dl	u-Cortisol	10.2 μg/day
PLT	$31.6x10^3$ /μL	17-OHCS	1.6 mg/day
Biochemistry		17-KS	3.2 mg/day
TP	7.3 g/dL	GH	0.28 ng/mL
Alb	3.5 g/dL	IGF-1	169 ng/mL
AST	28 U/L	ADH	1.3 pg/mL
ALT	12 U/L	LH	11.1 mIU/mL
ALP	269 U/L	FSH	15.9 mIU/mL
LDH	522 U/L	PRL	17.7 ng/mL
CPK	719 U/L	PRA	0.1 ng/ml/hr
T-Bil	0.4 mg/dL	PAC	25.0 pg/mL
Glu	96 mg/dL	Intact-PTH	17 pg/mL
BUN	22.0 mg/dL	$1,25\text{-}(OH)_2\text{-}D_3$	36.6 pg/mL
Cre	3.2 mg/dL	IRI	7.9 μU/mL
UA	19.2 mg/dL	**Urinalysis**	
Na	143 mEq/L	Ketone	(−)
K	5.2 mEq/L	Glucose	(−)
Cl	100 mEq/L	Protein	(−)
Ca	5.6 mg/dL	Ca	0.3 mg/dL
P	9.0 mg/dL	**Blood Gas Analysis**	
Mg	1.9 mg/dL	pH	7.382
CRP	0.03 mg/dL	$PaCO_2$	40.1 Torr
Ccr	37 ml/min	PaO_2	84.1 Torr
%TRP	95.8 %	HCO_3	23.8 mEq/L

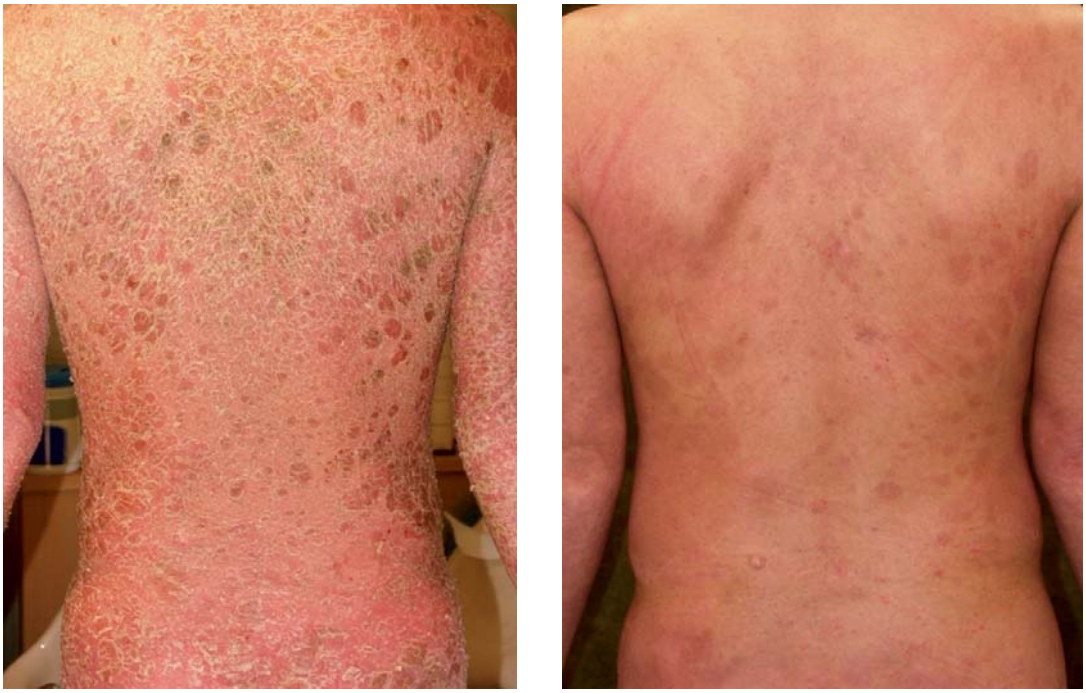

Fig 1 Skin appearances before and after treatment for hypoparathyroidism and psoriasis vulgaris. Erythema and scaling were significantly reduced after 29 days of treatment.

normal range on the 16th day (ACTH: 16. 5 pg/ml; cortisol: 9. 5 μg/dl). Acute renal failure due to diarrhea and vomiting was obserbed on his admission, however it was recovered to normal range on the 8 th day of his hospitalization. Ellsworth-Howard test was perfomed on the 12th day of his hospitalization. The increase of urinary phosphoric acid indicated a normal renal response (254. 9 mg/dl), but the increase of cAMP was not sufficient (difference: 0. 27 μmol/H; ration: 3. 1). Hypomagnesemia was observed from the 3rd day (1. 3 mg/dl) to the 8th day (1. 6mg/dl). We diagnosed the patient with idiopathic hypoparathyroidism due to sufficient increase of urinary phosphoric acid. The clinical course is shown in figure 2. The serum level of PTH were 13 pg/ml on the first day, 17 pg/ml on the second day and 6 pg/ml on the 17th day. Head and abdominal CT revealed slight calcification of the globus pallidus and significant enlargement of the right kidney (Fig 3). Electrocardiogram showed QT prolongation. Sensorineural bilateral hearing loss (46 dB on the left and -50 dB on the right) was confirmed by the otolaryngologist in our hospital. Hearing impairment was more severe at the higher end of the frequency range. The triad of hypoparathyroidism, hearing impairment and renal abnormality suggested that this patient had HDR (hypoparathyroidism, deafness,

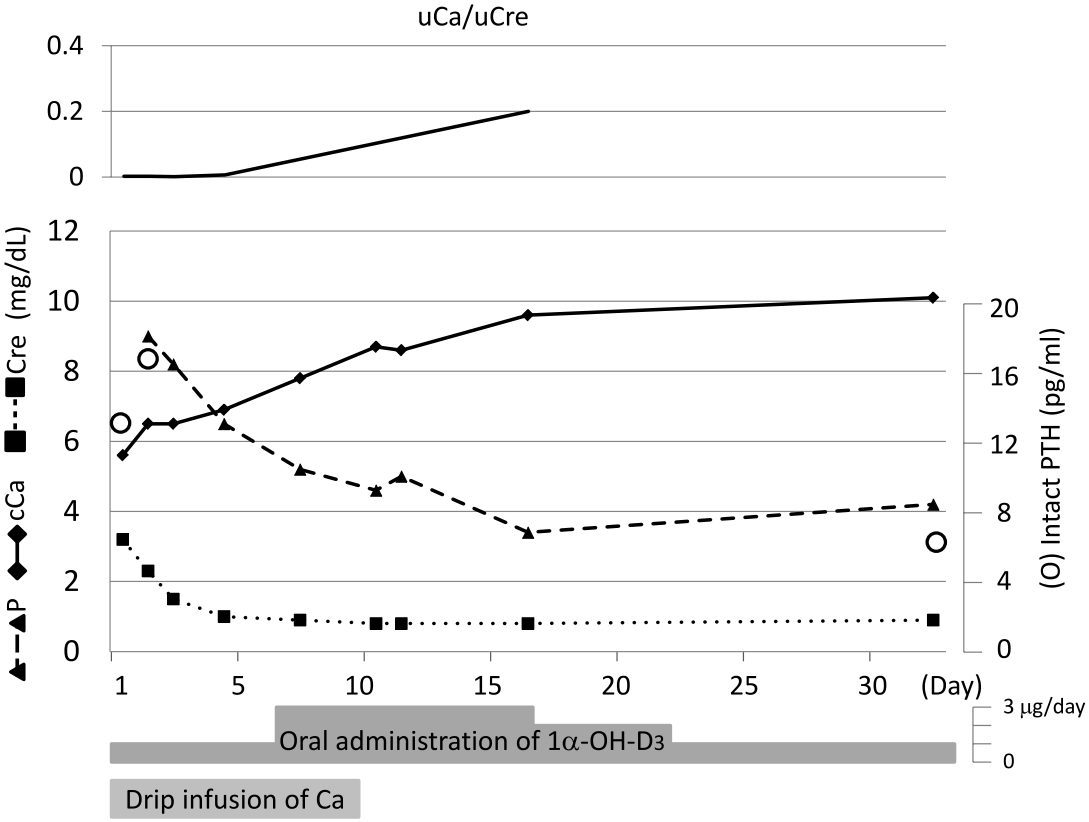

Fig 2 Chronological changes in corected Ca (cCa), P, PTH, Cre and uCa/uCre in the clinical course.

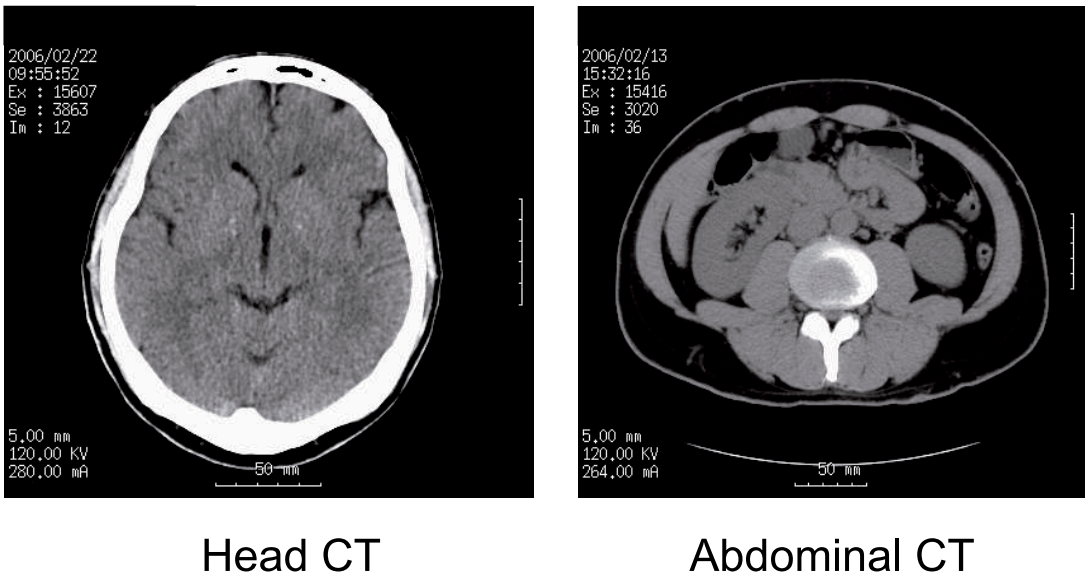

Fig 3 Head and abdominal computed tomography (CT). Head CT revealed slight calcification of the globus pallidus. Abdominal CT revealed enlargement of the right kidney.

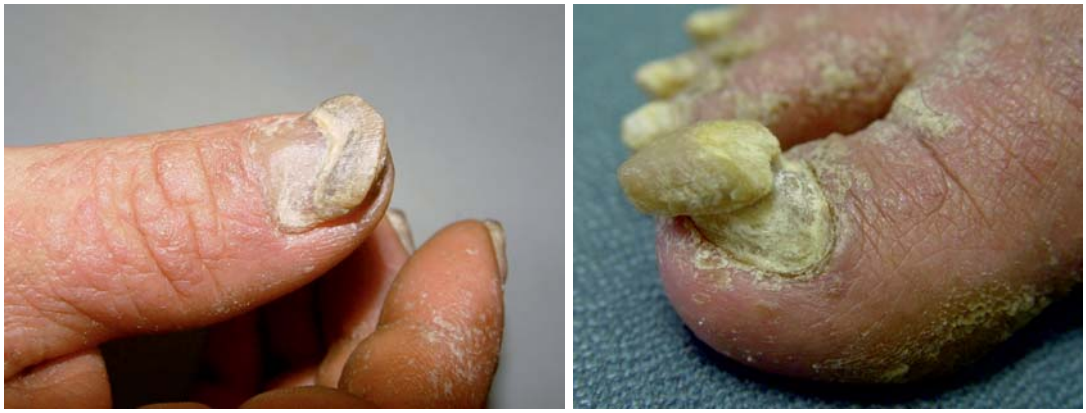

Fig 4 The picture of the fingernails and toenails. The change in thickness of his nails indicated the start of treatment for hypocalcemia.

renal dysplasia) syndrome. Regrettably, he did not consent to an analysis of GATA3 abnormalities for the diagnosis of the HDR syndrome.

Oral administration of 1α-(OH)-D_3 increased the serum calcium level gradually, and it returned to the normal range on the 16th day of his admission. As the serum level of calcium increased, his psoriasis improved with PUVA-bath therapy and steroid ointments (Fig 1). He was discharged on the 40th day of his admission. Figure 4 shows a picture of his fingernails and toenails in May 2006. The distal portion of the nail plate was thickened and fragile. The proximal part of the nails was thin and hard. The border of these two parts of the nail indicates the start of the treatment for hypocalcemia (Fig 4).

DISCUSSION

In the present case, the exacerbation of psoriasis vulgaris and the symptoms of dyspnea were likely due to severe hypocalcemia in the setting of idiopathic hypoparathyroidism. Furthermore, sensorineural hearing impairment and renal dysplasia were present.

Interestingly, hypoparathyroidism had not been diagnosed prior to the current admission, although insufficient secretion of intact PTH was observed. It is generaly accepted that renal failure cused dismetabolism of vitamin D, resulting in hypocalcemia. However, in the present case, 25-(OH)-D_3 remained with in normal range. Hypocalcemia led to the diagnosis of hypoparathyroidism. A similar case has been reported (2). It may be possible that the partial production of PTH was sufficient to prevent a significant decrease in the calcium level, thus avoiding symptomatic hypocalcemia. In this case, the PTH level stayed at the lower limit of the normal range in spite of significant hypocalcemia. PTH secretion is regulated by extracellular calcium, and it has been reported that PTH secretion is only 25% of the maximum at a normal calcium concentration (3). Therefore, we diagnosed this case as hy-

poparathyroidism. However, it was necessary to differentiate whether this case was idiopathic or pseudohypoparathyroidism. The Ellsworth-Howard test demonstrated a normal response of phosphaturia, resulting in the diagnosis of idiopathic hypoparathyroidism. It remains unknown why the response of urinary cAMP was insufficient. We hypothesize that insuffient formation of cAMP by PTH was due to the lack of Mg. Mg deficiency causes the resistance of PTH actions on terget organs (4). In the present case, hypomagnesemia was observed after admission.

Transient eosinophilia was observed on admission in the present case. Some allergic reaction was suspected, however high sensitive IgE was not elevated. We were unable to detect the obvious evidence for the participation of allegic mechanism in this phenomenon. Low levels of ACTH and cortisol were also observed on the 3rd day. Idiopathic hypoparathyroidism is often accompanied with Addion disease, namely autoimmune polyendocrine syndrome type 1 which is cused by the mutaion of autoimmune regulator gene (AIRE). However, the elevation of autoimmune antibodies were not seen in the present case, and the lowering of ACTH and cortisol were recoverd on the16th day. On admission, large amount of steroid ointments were administered immedeately for the treatment of psoriasis. It is speculated that external administration of steroids suppressed both ACTH and cortisol transiently.

Hypocalcemia is an exacerbating factor of psoriasis vulgaris, and severe psoriasis often accompanies hypocalcemia. There have been case reports of hypoparathyroidism-induced hypocalcemia leading to the worsening of skin symptoms in psoriatic patients (2, 5-7). The similar situation is also reported in HDR syndrome. In that case, it is suggested that generalized psoriasis might have been induced by hypocalcemia due to hypoparathyroidism associated with HDR syndrome (8). We suppose that functional disorder of cadherin played an important role in this situation. Cadherin is a calcium-dependent adhesion molecule (9). Cadherins are subdivided into several subclasses, and E-cadherin is involved in the adhesion of keratinocytes (10). Furthermore, it has been reported that a decrease in the concentration of extracellular calcium reduced cell-to-cell contact and the expression of E-cadherin in human keratinocytes (11). We suggest that hypocalcemia induced dysfunction of Ca^{2+} dependent adhesion molecules, resulting in epidermal abrasion and squama, in addition to the thickened and fragile nails. Interestingly, 3 months after his hospitalization, the peculiar appearance of the fingernails and toenails indicated the time of the commencement of therapy (Fig 4). The distal part of the nails were thick and fragile, and the proximal part of the nails were thin and hard. We speculate that the difference in the thickness and hardness of the nails are due to the changes in cell adhesion due to hypocalcemia.

In the present case, hypoparathyroidism, sensorineural hearing impairment and right renal hypertrophy and were observed. Ordinarily, the renal abnormalities of HDR syndrome

were revealed hypoplasia (8) or aplasia (12). In some cases with GATA3 gene abnormalities, renal anomalies are absent (12). Thus, the combination of hypoparathyroidism and sensorineural hearing impairment suggested the possibility of HDR syndrome in the present case. HDR syndrome is an autosomal dominant disorder, caused by the mutation of the zinc finger transcription factor, GATA3 (13), that is expressed in developing parathyroid glands, inner ears and kidneys (14). However, we were unable to perform the mutation analysis to achieve a genetic diagnosis on the patient. Thus, other possibilities should be considered. APS type 1 was one of the candidates. Furthermore, the production of autoantibody for calcium-sensing receptor (CaSR) (15, 16) and the gain-of-function mutations in CaSR (17) were suggested for differential diagnosis. Especially, Canaff *et al.* reported that proinflammatory cytokine (IL-6) increased CaSR expression in the parathyroid gland and kidney, and decreased secretion of PTH (16). In the present case, CRP was positive on admission. Thus, such a mechanism was also partly involved in the hypocalcemia.

In summary, we report a rare case of idiopathic hypoparathyroidism which was diagnosed during hospitalization for psoriasis vulgaris. In addition, his hypoparthyroidism was noted to be associated with sensorineural hearing impairment and renal abnormality. This instructive case reminds us to consider the relationship between hypoparathyroidism and psoriasis vulgaris.

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