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Case Report

Hypoparathyroidism Associated with Ossifications of Posterior Longitudinal Ligament of the Spine (OPLL) and Glucose Intolerance: Report of Two Cases

Fumito Akasu, Kazutaka Haraguchi, Shin-ichi Tsunoda, Zenji Shiozawa and Toshimasa Onaya

*The 3rd Department of Internal Medicine, Yamanashi Medical College**

Abstract: Two cases of idiopathic hypoparathyroidism (HP) associated with ossification of posterior longitudinal ligament (OPLL) and mild glucose intolerance are reported. A 67-year-old man had dysesthesia in both hands and some episodes of syncope for the last 10 years. Serum calcium was 6.6 mg/dl and inorganic phosphorus was 5.6 mg/dl. Serum PTH could not be detected and Ellsworth-Howard test was compatible with idiopathic HP. Segmental type of OPLL was found in the cervical spine by X-ray and extensive calcifications in cerebral cortex, basal ganglia and dentate nuclei were demonstrated by computed tomography. The other patient, a 71-year-old woman, had complained of headache and dysesthesia of distal extremities with a history of 33 years. Serum calcium was 5.3 mg/dl and serum inorganic phosphorus was 5.2 mg/dl. She also had segmental type of OPLL in the cervical spine and calcification of the basal ganglia. Both of them had mild glucose intolerance. We suggest that abnormal calcium and glucose metabolism plays an important role in the pathogensis of OPLL.

Key words: hypoparathyroidism, Ellsworth-Howard test, glucose intolerance, OPLL,

Although calcification of the soft tissue is known to be associated with hypoparathyroidism (HP), ligamentous ossification appears to be an unusual complication of HP. The ossification of the posterior longitudinal ligament of the spine (OPLL) has been reported to be occasionally associated with idiopathic and postoperative HP and often observed in patients with diabetes mellitus[1,8]. Therefore, in addition to abnormal glucose metabolism, the deterioration of calcium metabolism may provide a further background for OPLL. We report two cases of HP associated with OPLL and glucose intolerance.

* Tamaho, Nakakoma, Yamanashi, 409-38, Japan.
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Case Report

Case 1

A 67-year-old man was referred to our hospital with a 10-year history of dysesthesia in both hands and some episodes of syncope. One year prior to admission, he experienced a syncope attack and recovered spontaneously after 3–4 hours. There was neither overt nor latent tetany. Examination of the nervous system revealed rigidity in right extremities and slightly accentuated bilateral deep tendon reflexes. Babinski's sign was positive on the right side. Trousseau's sign and Chvostek's sign were negative.

Table 1. Laboratery data (Case 1)

CBC	
WBC	5200
RBC	439×14^4
Hb	12.5 g/dl
Plt	27.5×10^4
Urinalysis	
occult blood	(−)
protein	(−)
glucose	(−)
Stool	
occult blood	(−)
Chemistry	
T.P.	6.4 g/dl
Alb	4.1 g/dl
Creatinine	0.4 mg/dl
Ca	6.6 mg/dl
P	6.6 mg/dl
Na	143 mEq/l
K	3.9 mEq/l
Cl	105 mEq/l
Serum	
CRP	(±)
ESR	12 mm/hr

Anterior pituitary functions

TRH, LH-RH test

	0′	30′	60′	120′
TSH	4	19	18	13 μU/ml
LH	23	132	108	92 mIU/ml
FSH	18	34	29	29 mIU/ml

Thyroid functions

T_3 112 ng/dl

T_4 11.3 μg/dl

50 g OGTT

	0′	30′	60′	90′	120′
glucose	86	146	164	141	157 mg/dl
IRI	5	38	42	35	μU/ml

Ellsworth-Howard test

Urinary phosphate and cAMP: Response to intravenous administration of synthetic human parathyroid hormone (1-34) were tested.

Increment of phosphate; 41.8 mg/2 hr

Increment of cAMP; 7.7 mol/hr

c-PTH<0.10 ng/ml

%TRP 95%

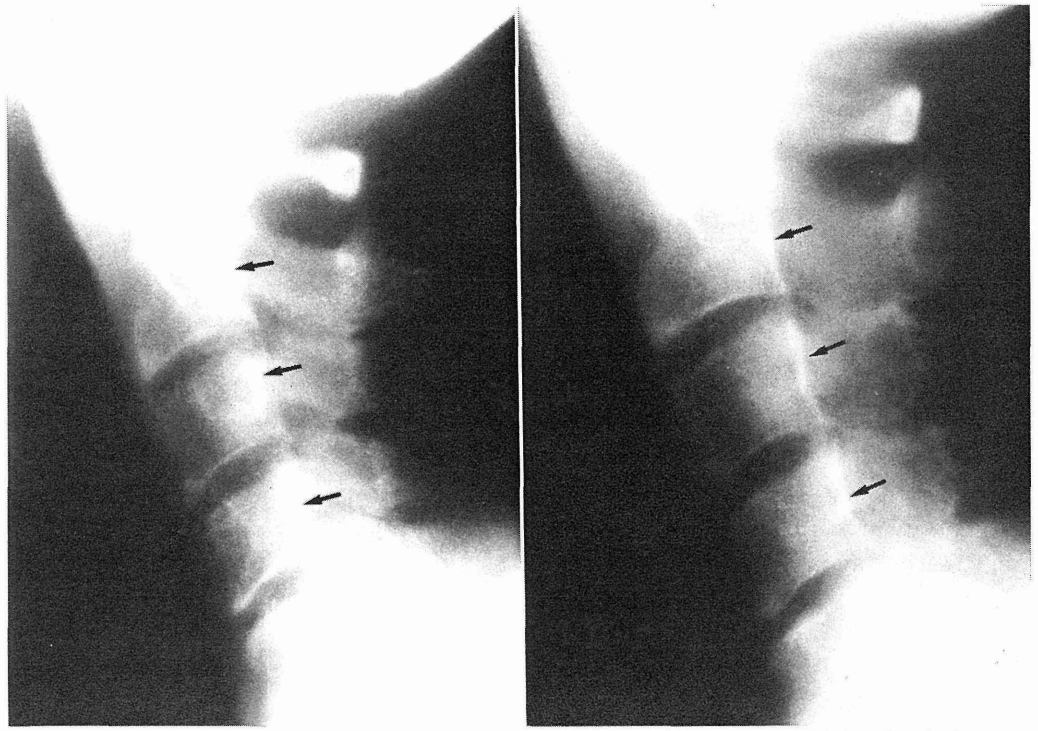

Fig. 1. Lateral tomography of the cervical spine. Case 1, (left); Case 2, (right). Cervical spine with ossification posterior to the vertebral bodies (arrows).

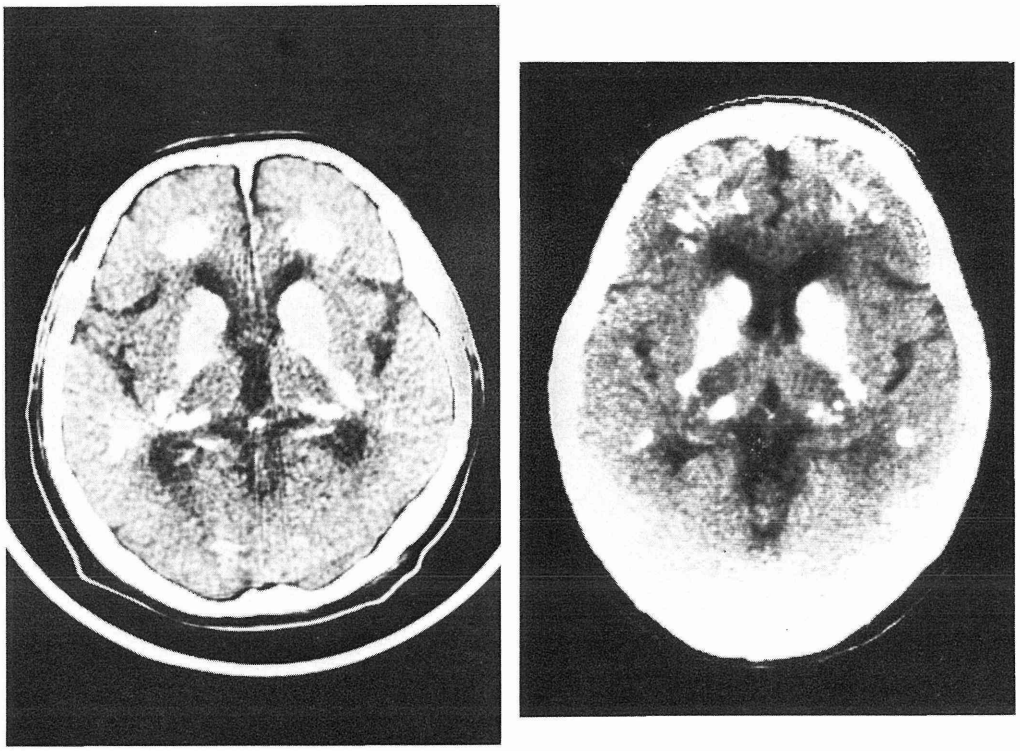

Fig. 2. CT scan. Case 1 (left) and Case 2 (right). Dense, extensive calcification of the basal ganglia, the dentate nuclei, and the cerebral cortex.

Laboratory data (Table 1): Serum calcium was 6.6 mg/dl and inorganic phosphorus was 5.6 mg/dl. No immunoreactive parathyroid hormone (PTH) was detected in the serum. Ellsworth-Howard test was compatible with idiopathic HP.

Radiology: Segmental type of OPLL was found in the cervical spine (Fig. 1; A). Very mild calcification was present in the capsules of both hip joints. Skull X-ray also showed calcifications in the basal ganglia. Computed tomography (CT) demonstrated extensive calcifications in the cerebral cortex, basal ganglia and dentate nuclei (Fig. 2; A).

The diagnosis was idiopathic HP, Parkinson's syndrome and OPLL. la(OH)-D_3 (2.0 μg/day) and L-DOPA (0.6 g/day) were prescribed. Restorations of serum levels of calmium and phosphorus were achieved in two weeks and no further syncopal attacks occurred.

Case 2

A 71-year-old woman visited our hospital with the chief complaints of headache and dysesthesia of the distal extremities. Her dysesthesia had a 33-year history although it was not progressive. When she was 60 years of old, she first experienced an episode of mild tetany, which occurred 1–2 times a month. At the age of 63, she underwent an operation for cataract in the right eye at a hospital, where she was noted to have hypocalcemia. She was not followed thereafter since she had neither severe tetany attacks nor other intolerable symptoms. Six months prior to the first visit to our hospital, she began to suffer from headache and noticed the development of her dysesthesia.

Table 2. Laboratery data (Case 2)

CBC

WBC	3400
RBC	408×10^4
Hb	13.1 g/dl
Plt	19.2

Urinalysis

occult bloop	(−)
protein	(−)
glucose	(−)

Stool

occult blood	(−)

Chemistry

T.P.	6.9 g/dl
Ald	4.6 g/dl
Creatinine	0.5 mg/dl
Ca	5.3 mg/dl
P	5.2 mg/dl
Na	141 mEq/l
K	3.7 mEq/l
Cl	107 mEq/l
Mg	1.8 mg/dl

CRP	(−)
ESR	13 mm/hr
RA	(−)

Anterior pituitary functions

TRH, LH-RH test

	0′	30′	60′	90′	120′
GH	2	2	2	1	1 ng/ml
PRL	9	113	94	72	50μU/ml
TSH	3.4	14.6	14.6	12.9	10.3 μU/ml

LH-RH test

	0′	30′	60′	90′	120′
LH	122	138	202	212	193 mIU/ml
FSH	138	141	179	180	162 mIU/ml

Thyoid functions

T_3	128.2 ng/dl
T_4	9.8 μg/dl
FT_4	1.2 ng/dl
TBG	22.0 μg/ml

75 g OGTT

	0′	30′	60′	90′	120′
glucose	84	179	192	185	118 mg/dl
IRI	6	14	27	30	21 μU/ml

Ellsworth-Howard test

Method: same as in Table 1.
Increment of phosphate; 43.7 mg/2 hr
Increment of cAMP; 5.8 μmol/hr

c-PTH	<0.10 ng/ml
%TRP	98.2%

Physical examination revealed the presence of latent tetany by positive Trousseau's sign. Cataract was observed in the left eye. Deep tendon reflexes in the lower legs were slightly accentuated bilaterally. No pathological reflexes were observed.

Laboratory data (Table 2): Serum calcium was 5.3 mg/dl and inorgaic phosphorus was 5.2 mg/dl. PTH was not detected in the serum. Ellsworth-Howard test was compatible with idiopathic HP. Seventy-five g OGTT revealed mild glucose intolerance.

Radiology: Segmental type of OPLL was also found in the cervical spine in this patient (Fig. 1; B). Calcification of the basal ganglia was clearly visible on CT (Fig. 2; B).

The patient was diagnosed as having idiopathic HP and OPLL. She was given 1.0 μg of la(OH)-D_3 daily. In a few weeks, both serum calcium and phosphorus were normalized and Trousseau's sign also became negative.

Discussion

Soft tissue calcification is known to be frequently associated with HP. Recently, ligamentous ossification was also reported to be associated with HP. Adams *et al.*[1] reported a patient with idiopathic HP and extensive paravertebral and ligamentous ossification. In their report, they discussed

four other reported cases with features resembling those in their case. Shimizu *et al.*[6] described a 40-year-old woman who presented HP associated with a bamboo like spine after thyroid surgery. Okazaki *et al.*[3,4] also described a 66-year-old man who had idiopathic HP associated with extensive ossification of the ligament of the spine. They investigated 17 cases of HP and found that 53% of them had ligamentous ossifications.

A high incidence of glucose intolerance among the patients having OPLL was reported[8]. Among the patients with OPLL, 76.8% had glucose intolerance, and among the diabetic patients, OPLL was noted in 22%. Combination of glucose intolerance with OPLL was also pointed out by other investigators[5]. On the other hand, the combination of HP with glucose intolerance has not thoroughly been discussed and the etiology of OPLL is still obscure. Several studies were performed to clarify the general and local factors relevant to OPLL. Osazaki *et al.*[4] suggested that the responsible mechanism is related as much to chronicity of the disorder as to the severity of hypocalcemia and hyperphosphatemia. Tomita *et al.*[7] noted that the levels of Ca^{2+} pool in OPLL tended to be higher than in normal controls. Our case 1 had HP for more than 10 years, and case 2 for more than 30 years. As these cases have had long histories of HP, they may provide a background for OPLL, and perhaps there may be some relationships between glucose intolerance and OPLL, although the exact mechanism is still unknown. It is impossible to observe prospectively a patient with HP without therapy. Deeper understanding of the developmental course of OPLL, including the possibility of relationships among OPLL, HP and glucose intolerance, is a matter of importance to be explored in the the future.

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後縦靱帯骨化症と耐糖能異常を伴った副甲状腺機能低下症の2例

赤須　文人，原口　和貴，角田　伸一，塩沢　全司，女屋　敏正
山梨医科大学第三内科学教室

抄　録：副甲状腺機能低下症（HP）に異所性石灰化が高頻度にみられることはよく知られているが，後縦靱帯骨化症（OPLL）をはじめとする，脊椎靱帯骨化症をも合併することが注目されている。一方，OPLL になぜか耐糖能異常の合併率が高い事実もすでに報告されている。今回われわれは，特発性 HP に，OPLL，耐糖能異常を合併した二症例を報告した。症例1は67歳，男性。意識喪失発作と両手のしびれ感を主訴に受診，血清カルシウム 6.6 mg/dl，血清無機リン 5.6 mg/dl，血清 PTH-C 感度以下の低値。症例2は71歳，女性。頭痛と四肢のしびれ感を主訴に受診。血清カルシウム 5.3 mg/dl，血清無機リン 5.2 mg/dl，血清 PTH-C 感度以下。両症例とも，Ellsworth-Howard 試験にて特発性 HP と診断。経口糖負荷試験で耐糖能異常と頸椎の分節型 OPLL をみとめた。糖代謝異常と OPLL の合併については多くの報告，検討がなされているが，因果関係については定説をみていない。また，HP に OPLL をはじめとする脊椎靱帯骨化症が約60%に合併し，HP の罹病期間が長い程，骨化病変の頻度も高いと報告されている。2症例においては HP と，併発した耐糖能異常により，OPLL の発見がさらに促進された可能性が示唆された。

キーワード　副甲状腺機能低下症，エリスワースハワード試験，耐糖能異常，OPLL，靱帯骨化症