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〔症例〕 A CASE OF HYPOTHYROIDISM WITH CEREBELLAR ATAXIA

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Summary

A case of a 65-old-male with cerebellar ataxia associated with hypothyroidism is described.

His recovery course was monitored by equilibrium function tests and with an electro-nystagmograph. It took about 2 months for the blood thyroxine level to return to normal. Although optokinetic nystagmus (OKN) could not be elicited before medication, the patient improved both in OKN and in the equilibrium function test in accordance with normalization of the blood thyroxine level.

In the thyrotropine releasing hormone (TRH) injection test, the square measure of sway of the center of gravity was approximately halved three minutes after injection, and this effect lasted about 70 minutes.

This is the first objective follow-up study for cerebellar ataxia with hypothyroidism, and the result of the TRH injection test suggests that TRH could participate in cerebellar ataxia associated with primary hypothyroidism.

Key words: Hypothyroidism, Cerebellar ataxia, TRH test, Optokinetic nystagmus, Case report

Introduction

Since White[1] described the first case of cerebellar ataxia associated with hypothyroidism in 1884, the association has been widely known with about 60 cases reported to date[2-9]. However, none of the reports has dealt with an objective evaluation of the clinical course by equilibrium function test and the eliciting test of optokinetic nystagmus (OKN).

The following case of hypothyroidism (Hashimoto disease) invoving cerebellar ataxia illustrates the recovery course after treatment with thyroxine by means of equibrium function tests performed with a gravicorder and eletro-nystagmograph. In addition, the effects of massive administration of thyrotropine relasing hormone (TRH) are described.

Case report

The patient was a 67-year-old male tailor, who noted onset of progressive giddiness on walking around 1975. His hearing became bilaterally worse in 1977. In 1978, the patient became fatigable, slow in movement, entangled in speech, and developed a low torelance for cold. In January 1982, the patient was admitted for a complete medical examination.

Family history was noncontributory. He had ingested about 250 ml of "sake" every day for the past 30 years and smoked about 15 cigarettes daily.

Physical examination revealed a height of 164 cm and a weight of 65 kg. The temperature was

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寺澤捷年，嶋田　豊，檜山幸孝，水越鉄理：小脳性運動失調を呈した甲状腺機能低下症の1例
* 富山医科薬科大学医学部・和漢診療部，** 同　耳鼻咽喉科学教室
昭和62年4月2日受付

36.1 °C, pulse 52/min and regular, and blood pressure 130/85 mmHg. The skin was pale and dry. The hair, eyebrows, and pubic hair were sparse with no axillary hair. The face was edematous and tongue was large. The thyroid measured 1.5×3.5 cm and of a gum-like consistency hardness. The heart sounds were attenuated without murmur. Cardiac dullness was enlarged two finger breadths to the left. The liver, spleen, and kindneys were not palpable. Remarkable pitting edema was noted in the legs.

The patient was clear and both memory and judgement were normal. The speech was slightly slurred and slow. Funduscopic examination revealed no abnormality. Visual acuity and field and light reflex were all within normal range. The ocular movements were not restricted but fixation nystagmus was noted in the right eye. The elicitation of OKN was unsatisfactory.

Hearing was markedly impaired bilaterally with total deafness in the left ear. No further abnormalities were noted in the rest of the lower cranial nerves.

There was no hypertrophy in the muscles, and the large muscles were normal in strength. The deep tendon reflexes were intact and knee jerks were slightly exaggerated. The ankle jerk was delayed. A slight mounding phenomenon was noted in the brachial biceps muscle. There was no pathological reflex such as extensor toe reflex.

He was incapable of standing with both feet together, and his gait had a wide base and atactic. When the patient was sitting on a chair with an erect posture, the trunk swayed. Dysdiadochokinesis was noted bilaterally in the upper extremities. A finger-nose test revealed hypermetria and decomposition. He could write letters, but clumsy. In the knee-heel test, the patient was awkward bilaterally and hypermetria was noted. The muscle tone was normal. No vesicorectal disorder was noted.

Laboratory data on admission: RBC 400×10^4/mm^3, Hb 11.2 g/dl, erythrocyte sedimentation 39 mm/h, LDH (250 IU), total cholesterol (330 mg/dl), and β-lipoprotein (927 mg/dl) all elevated, and CPK 838 IU and abnormal.

The chest roentgenogram revealed a cardiothoratic ratio of 68 %, suggesting cardiac enlargement. Echocardiography demonstrated a slight pericardial effusion. The electrocardiogram gave a normal tracing except for sinus bradycardia.

Serum levels of T_3 (40 ng/dl RIA) and T_4 (0.7 μg/dl RIA) were low, T_3 resin uptake was 25.7 % (just above the lower limit of normal) and TSH level (150 μl/ml) was high. Thyroid test and microsome test were positive, 1 : 640[2] and 1 : 320[2], respectivelly. The TRH stimulation test revealed a high baseline level of serum TSH (143 μl/ml) and an excessive reaction (15 min-169, 30 min-257, 60 min-248, 90 min-245 and 120 min-223 μU/ml). The results were compatible with primary hypothyroidism. The thyroid uptake of ^{123}I was markedly decreased.

Thyroid biopsy showed atrophic thyroid follicles with a remarkable infiltration of small round cells (Fig. 1). Partial fibrosis was noted. These findings indicate chronic thyroiditis.

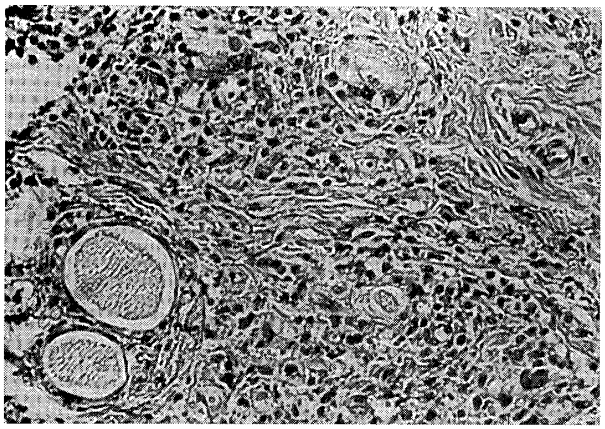

Fig. 1. Photomicrograph of the thyroid gland showing atrophic follicles, remarkable infiltration of small round cells and fibrosis. (HE stain×100)

Cerebrospinal fluid demonstrated increased pro tein (132 mg/dl), and a positive Pandy test.

Maximal conduction velocities measured in the motor nerves were all within normal limits in the four extremities. Electroencepharosgram were normal.

Equilibrium function tests such as based on OKN (Fig. 2) and eye tracking suggested impairment in the cerebellum and brain stem. A calorie test

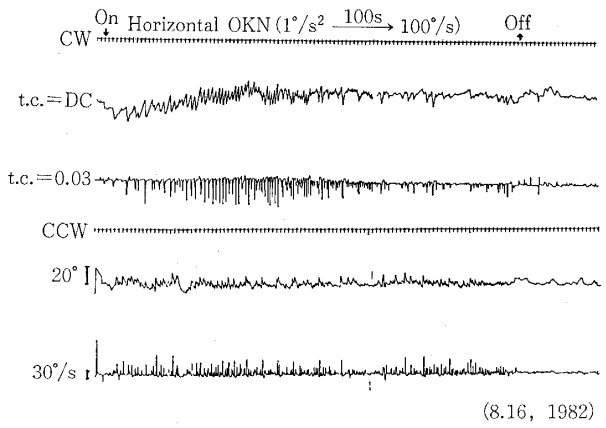

Fig. 2. Horizontal optokinetic nystagmogram obtained on August 6, 1982, before thyroxine administration. Essentially no optokinetic nystagmus was induced in either direction. CW, clockwise: CCW, counter-clockwise: t. c. time constant

demonstrated slight abnormality in both ears. An audiometry showed total deafness in the right ear, and marked impairment (40 db) in the left ear.

Roentogenogram of the cranium disclosed no enlargement of the sella turcica and computed tomography of the brain revealed pictures compatible with his age without abnormalities such as cerebellar atrophy.

Clinical course

Bed rest and a low salt diet were indicated, because cardiac decompensation was evident on admission. To improve cardiac decompensation, the traditional Chinese prescription of medicinal plants "Juzen-Daiho-To"[10] was administered. This prescription consists of ginseng 3.0 g, hoelen 3.0 g, astragalus 3.0 g, tang-kuei 3.0 g, paeonia 3.0 g, rehmania 3.0 g, cnidium 3.0 g, cinnamon 3.0 g and licorice 1.0 g.

After attenuation of symptoms of cardiac insufficiency, treatment with increasing doses of sodium levothyroxine was initiated with a 12.5 mg/day dose. As shown in Fig. 3, the serum levels of T_3, T_4, and TSH were normalized about 2 months after the start of thyroid hormone administration. The patient also recovered normal levels of serum CPK, LDH, and total cholesterol.

Parallel to the improvement shown by various examinations, the cerebellar ataxic symptoms including slow motion, ataxic gait, slurred speech, and the incapability of standing with his feet together, improved. The clinical improvement was quantified by equilibrium function tests, in which body sway measured with a Gravicorder G 1803 (ANIMA Co., Ltd., Tokyo,) and expressed in terms of area within which the center of gravity of the body travelled while the patient was standing with feet together for 30 seconds with both eyes opened and closed (Fig. 3).

Improvement in equilibrium function, as determined by standing with open eyes, was attained about 1 month after TSH, and about 2 months after the serum levels of T_3 and T_4, had become normal.

At first, the patient could not stand with feet together when with closed eyes. This function improved about six months after normalization of T_3 and T_4. It is notable that this improvement was about 4 months behind that with open eyes.

Fig. 4 presents changes in OKN measured with an electro-nystagmograph, model 124 A, (Sanei Sokuki Co., Ltd., Tokyo,). While manifestation of OKN was markedly suppressed at both low and high rates before instituting the treatment (Fig. 2), improvement became apparent about 2 month after its start (Fig. 4 A). The pattern became normal essentially in acordance with normalization in T_3 and T_4. OKN was seen to have further recovered 8 months after the beginning of the therapy (Fig. 4 B). However, abnormality of carolic test and impairment of hearing persisted even after about one year of the treatment.

TRH injection test

The effects of massive administration of TRH were evaluated by the equilibrium function test depending on body sway. The test was performed in May 1983 when the patient became capable of standing with feet together with both open and closed eyes.

Prior to giving TRH, the area was measured with open eyes repeatedly at 10-minute intervals until the value became constant, and the value was taken as the base line value. For the TSH sti-

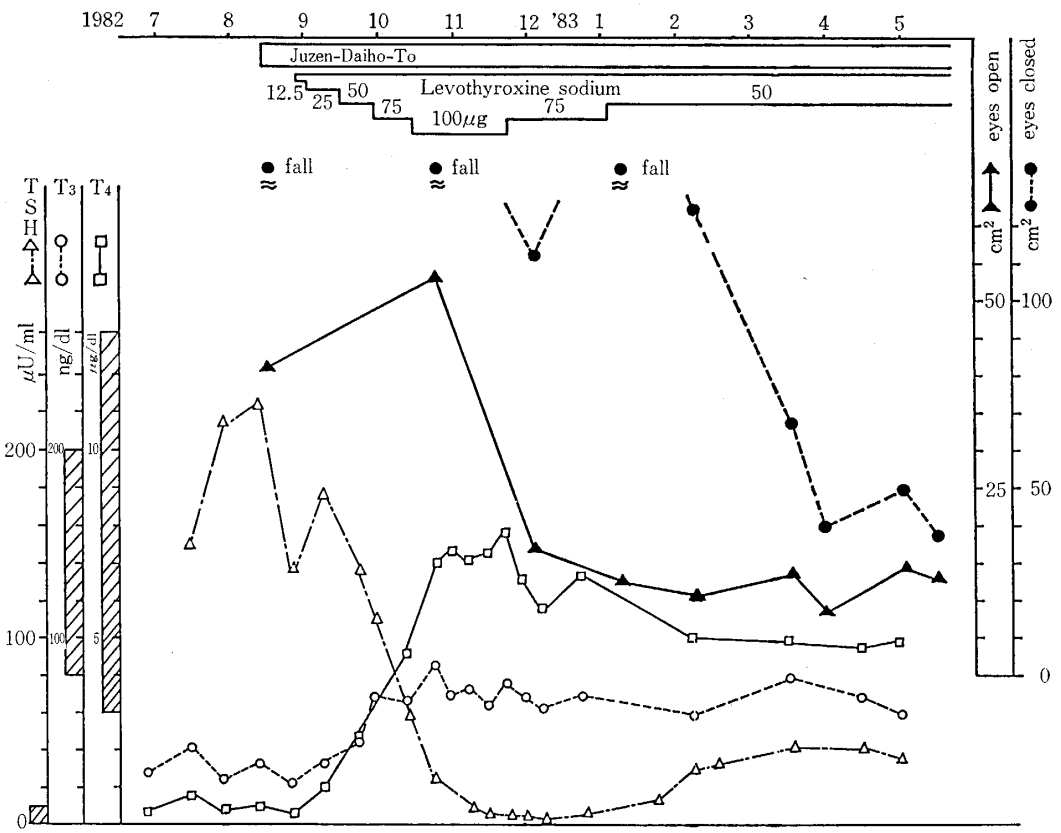

Fig. 3. Graph showing the course of medication, thyroid hormone levels and equilibrium function. The lined areas along the scale for TSH, T_3, and T_4 represent their normal ranges.

mulation test, a 1000 μg intravenous bolus of TRH was used, and 2 ml physiological saline solution was injected intravenously for control. The area was measured twice and the smaller value was recorded. The results are shown in Fig. 5. When the patient opened his eyes, the area was reduced to about 50 % of the base line value about 3 minutes after TRH administration. The effect seemed to last about 70 minutes.

As shown in the middle column of Fig. 5. the blood levels of T_3 and T_4 were essentially unchanged even when TRH was injected, suggesting that its effect on body sway depended on neither level.

Discussion

In the present case, the serological and histological findings led to the diagnosis of hypothyriodism due to Hashimoto disease.

The presence of impairment in the vestibulum, spinal cord, peripheral nerves and muscles need to be excluded, however, before the whole ataxia associated with hypothyroidism is described as cerebellar ataxia. The ataxia seen here was thought to result mainly from impaired cerebellar function for the following reasons:

1) Ataxia was remarkable in the trunk and lower extremities, without abnormalities in large muscle strength, articular sense of position and velocity of nerve conduction in the lower extremities. Consequently, this ataxia could not be attributed to impairment of the spinal posterior funiclus, peripheral nerves, or muscle strength.

2) Neuro-otological examination revelaled that the patient was slightly abnormal in a calorie test and his hearing was markedly impaired, possibly suggesting concomitant vestibular impairment. It was, however, difficult to consider that the impairment in vestibular and spinal system was mainly responsible for the ataxia in the present case, because the abnormalities persisted without change in degree even when the ataxia had become to be improved by thyroxine administration.

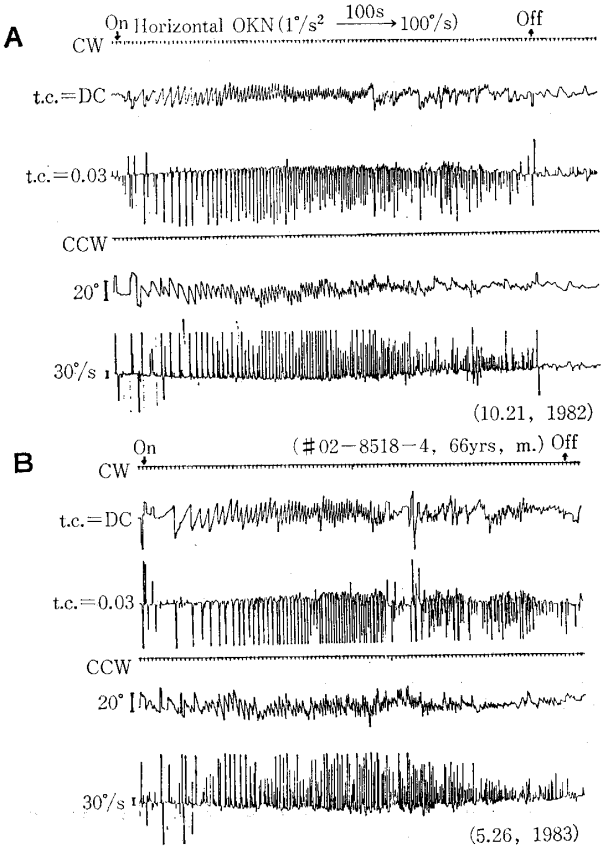

Fig. 4. Horizontal optokinetic nystagmogram revealing evident improvement after thyroxine administration. A; Electro-nystagmogram obtained in October, 1982. B; Electro-nystagmogram obtained in may, 1983. Abbreviations are the same as in Fig. 2.

3) The slurred speech, decomposition and disdiadochokinesis of the upper extremities, and the suppression of OKN are all symptomatic of cerebellar ataxia.

4) This case and some described previously[2,5,6] were in agreement on the point that cerebellar ataxia was remarkable in the trunk and lower extremities. Accordingly, the diagnosis of cerbellar ataxia associated with hypothyroidism was made.

None of the the previous reports has dealt with objective evaluation of thyroid hormone therapy in patient with cerebellar ataxia. In starting the treatment, however, it appeares to be of great significance to be able to make a forecast of the clinical course, because it will allay apprehensions of such patients and their families.

In the case described here, when the serum T_3 and T_4 levels were normalized, 1) the suppression of OKN became diminished simultaneously, 2) the equilibrium function of standing with open eyes became normal about 2 months, and 3) the closed eyes one recovered after about 6 months.

Also it was characteristic that the ataxic symptoms became suddenly improved certain periods after normalization of T_3 and T_4, just as if the motor control system had been switched "on" from "off". The fact that the cerebellar ataxia became to be improved, OKN first followed by standing with open and then closed eyes in this order, suggests that if the most foci were located in the cerebellum, improvement in the visuo-oculomotor system preceded, whereas improvement of the sensory-motor control system by way of the spinal cord was delayed considerably. Whether the time lags seen in such improvement depending on the in-put system could be attributed to localization of cerebellar lesions or to specificity of the controlling system remains to be elucidated.

According to Sobue[10] and his co-workers[11,12], TRH improved cerebellar ataxia in patient with spino-cerebellar degeneration and pathological model animals. These authors described that, in the brain or especially in the brain stem, TRH is involved in noradrenaline metabolism in cells from which noradrenergic neurons originate, increasing the activity of cerebellar Purkinje cells.

The usefulness of TRH in the treatment of patients with cerebellar ataxia associated with hypothyroidism was, as far as we know, first demonstrated in the present case. The following are the possible mechanisms of the involvement of TRH in cerebellar ataxia, although still somewhat conjectural because the behavior of TRH in the brain is as yet not fully understood. In the case of primary hypothyroidism as seen in this case, increased levels of TSH persist, probably resulting in relatively low levels of TRH produced by a negative feed back. The low levels of TRH in cooperation with low levels of T_3 and T_4 will likely augument cerebellar ataxia. However, this is only one case report, so that further publication of such case reports is called for.

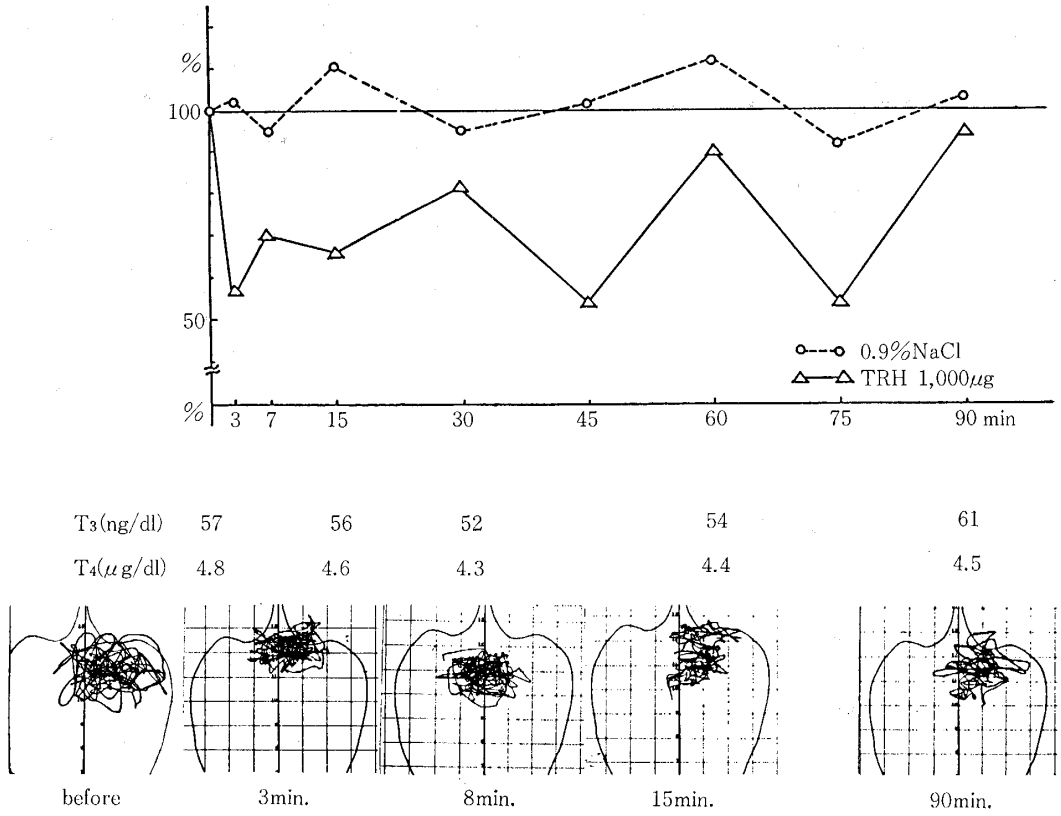

Fig. 5. Changes in levels of T_3, T_4 and TSH, and areas of equilibrium test after intravenous injection of TRH.

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References

1) White, E. W.: A case of myxoedema associated with insanity. Lancet **1**, 974-976, 1884.
2) Jellinek, E. H. and Kelly, R. E.: Cerebellar syndrome in myxoedema. Lancet **7114**, 225-227, 1960.
3) Nickel, S. N., Frame, B., et al.: Myxedema neuropathy and myopathy. A clinical and pathological study. Neurology **11**, 125-137, 1961.
4) Price, T. R. and Netsky, M. G.: Myxoedema and ataxia. Neurology **16**, 957-962, 1966.
5) Cremer, G.: Myxedema and ataxia. Neurology **19**, 37-46, 1969.
6) Wakata, N. and Okazaki, T., et al.: Case of myxedema associated with cerebellr ataxia and enlarged sella turica. Clin. Neurol. (Tokyo) **12**, 259-265, 1972. (in Japanese)
7) Saku, A. and Wakata, Y., et al.: Ataxia in hypothyroidism. Naika (Tokyo) **41**, 155-158, 1978. (in Japanese)
8) Takayanagi, K. and Satoh, A., et al.: A case of myxoedema associated with cerebellar ataxia and various neurological findings. Nippon Naika Gakkai Zasshi (Tokyo) **71**, 995-998, 1982. (in Japanese)
9) Hammer, G. H. and Regli, F.: Zerebellare Ataxie infolge Hypothyreose beim Erwachsenen. Dtsch. Med. Wschr. **100**, 1504-1506, 1975.
10) Hsu, H-Y. and Douglas, H. E.: A practical introduction to major Chinese herbal formulas. Oriental Healing Art Institute, Long Beach, CA., 1980, p 63.
11) Sobue I: New correlation between hypothalamic hormone and the function of central nervous system. Clin. Neurol. (Tokyo) 17, 791-799, 1977. (in Japanese)
12) Konagaya, M. and Takayanagi, T., et al.: Noradrenaline metabolism in the brain of rolling mouse Nagoya and the influence of thyrotropin releasing hormone. Clin. Neurol. (Tokyo) **20**, 181-187, 1980 (in Japanese)
13) Yamamoto, H. and Sobue, I.: Analysis of the abnormal ocular movements in spinocerebellar degenerations and the influence of the thyrotropin releasing hormone. Clin. Neurol. (Tokyo) **20**, 637-645, 1980. (in Japanese)