

[ CASE REPORT ]

## Cognitive Impairment Caused by Isolated Adrenocorticotrophic Hormone Deficiency without Other Hypo-adrenalism Signs - Autoimmune Encephalopathy Mimics

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### Abstract:

Isolated adrenocorticotrophic hormone deficiency (IAD) is a cause of adrenal insufficiency (AI), which shows impaired secretion of adrenocorticotrophic hormone (ACTH) with the preserved secretion of other anterior pituitary gland hormones. We herein report a case of IAD complicated by chronic thyroiditis presenting with neuropsychiatric symptoms without other signs indicative of AI that showed complete improvement of the cognitive function after the administration of corticosteroids. The clinical features of our case may be confused with autoimmune encephalopathies (AEs); however, IAD should be strictly differentiated from AEs, as it requires permanent hormone replacement without addition of immunosuppressive agents.

**Key words:** cognitive impairment, isolated adrenocorticotrophic hormone deficiency, anti-thyroid antibody, autoimmune encephalopathy

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### Introduction

Adrenal insufficiency (AI) is a cause of reversible dementia, and isolated adrenocorticotrophic hormone deficiency (IAD), a subtype of AI in which autoimmune mechanisms are hypothesized, is frequently associated with other autoimmune diseases (1). We herein report a case of IAD complicated by chronic thyroiditis presenting with neuropsychiatric symptoms without other signs indicative of AI that showed complete improvement of the cognitive function after the administration of corticosteroids. The clinical features of our case may be confused with autoimmune encephalopathies (AEs), such as Hashimoto's encephalopathy.

### Case Report

A 45-year-old Japanese man who had been in a depressive state and showed slowness to perform his routine tasks for 2 years was admitted to our hospital. Before admission, elevation of anti-thyroglobulin antibody [343.9 IU/mL (nor-

mal range: lower than 40 IU/mL)] with a low level of free triiodothyronine was highlighted. He was diagnosed with hypothyroidism because of chronic thyroiditis, and the oral intake of levothyroxine was prescribed. His depressive symptoms improved after hormone replacement; however, his difficulty sustaining attention did not change, resulting in his causing car accidents twice in a single year.

On admission, his blood pressure was normal with a normal pulse rate, and he was afebrile. There was no thyroid enlargement, lower leg edema, alopecia, weight loss, or hyperpigmentation. He was orientated but looked hazy, spoke slowly, and had a slightly ataxic gait. No other neurological abnormalities were noted. Laboratory data were not remarkable except for a low level of thyroid stimulating hormone and negative findings for anti-NH<sub>2</sub> terminal of  $\alpha$ -enolase antibodies. The results of a cerebrospinal fluid analysis and brain magnetic resonance imaging were normal, and an electroencephalogram showed only generalized slow waves (5 Hz). The mini-mental state examination (MMSE) score was 27/30 points (0/2 points on calculation and 5/6 points on recall), and the frontal assessment battery (FAB) score was 14/

18 points (1/3 points on lexical verbal fluency and 1/3 points on Go-No go). The Wechsler adult intelligence scale-third edition showed an impaired processing speed (full scale IQ=83, verbal comprehension IQ=80, perceptual reasoning IQ=97, working memory IQ=81, processing speed IQ=60). The times on a trail making test (TMT) were 51 seconds on part A and 219 seconds on part B. A further examination revealed that levels of plasma adrenocorticotrophic hormone (ACTH) [1.1 pg/mL (normal range: 7.2-63.3 pg/mL)], plasma cortisol [lower than 0.2 µg/dL (normal range: 7.07-19.60 µg/dL)] and urinary free cortisol in 24 hours [less than 31.3 nmol (normal range: 55.2-345 nmol)] were all decreased. Plasma levels of other pituitary hormones were within normal ranges. A pituitary stimulation test showed that only ACTH and cortisol responses were lacking, confirming the diagnosis of IAD. The oral administration of hydrocortisone 15 mg/day was initiated, and 2 months later, he achieved full points on the MMSE and FAB, and his times on the TMT improved to 48 seconds on part A and 100 seconds on part B. His ataxic gait was improved, slow waves on electroencephalography were diminished, and he returned to work as before.

## Discussion

IAD is a cause of AI, which shows impaired secretion of ACTH with preserved secretion of other anterior pituitary gland hormones. The clinical presentations of AI are non-specific, but signs such as low blood pressure, hyponatremia, hypoglycemia, and eosinophilia can be clues to the presence of this disease (2). Without the signs and symptoms of endocrine dysfunction, it would be challenging to suspect AI in the differential diagnosis of dementia with unknown origin. Our patient showed only loss of concentration and slowness in performing routine tasks. The mechanisms underlying cognitive dysfunction due to IAD remain unclear, but the findings on positron emission tomography (PET) of a decreased cerebral blood flow and metabolism, especially in the frontal lobe, improving after hormone replacement therapy suggest that metabolic or circulatory changes are associated with cognitive dysfunction as a consequence of IAD (3). AEs are also an important differential diagnosis in

reversible dementia and are characterized by rapid improvement following corticosteroid treatment, resembling cases of IAD. IAD is frequently complicated by other autoimmune diseases, and 11.6% of cases of IAD are reported to be accompanied by anti-thyroid antibodies (4). The common co-existence of autoantibodies and the efficacy of corticosteroids may obscure the diagnosis; however, IAD requires permanent hormone replacement. Conversely, the adrenal function should be added to the screening tests of cognitive impairment with some autoantibodies.

## Conclusion

Our case indicates that IAD should be considered in cases of steroid-responsive cognitive impairment, even when there are no other signs indicative of AI. Unlike AEs, dose reduction of corticosteroid leads to recurrence, and other immunosuppressive agents should not be added.

**The authors state that they have no Conflict of Interest (COI).**

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