

Isolated Adrenocorticotrophic Hormone Deficiency Accompanied by Impaired Cognitive Function: A Case Report

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Abstract

Background: Isolated adrenocorticotrophic hormone (ACTH) deficiency (IAD) is an adrenal insufficiency caused by a decrease in ACTH alone among the anterior pituitary hormones. IAD is often overlooked because it causes nonspecific symptoms. We report a case of IAD diagnosed after the appearance of mild cognitive impairment (MCI).

Case presentation: Our department was consulted on a case of a 46-year-old man for whom dementia was suspected because he was speaking incoherently, wiped his nose with his hands and showed mild brain atrophy on MRI. He was previously diagnosed with some psychiatric diseases, such as narcolepsy and adjustment disorder. He could not continue working due to somnolence, general fatigue and appetite loss. At the examination, he had difficulty concentrating and sustaining attention, exhibited restlessness, and scored 25 points on the Mini Mental State Examination-Japanese (MMSE-J); MCI was observed. Blood tests showed decreased ACTH, cortisol and free thyroxine and increased thyroid-stimulating hormone levels. He received further evaluation, and he was diagnosed with IAD and primary hypothyroidism. Hydrocortisone (15 mg) was started, after which his physical problems and his difficulty concentrating disappeared. His MMSE-J score also increased to 30. His cognitive functions completely recovered. He returned to work and continued to work stably.

Conclusion: This patient was diagnosed with IAD and treated with adrenocortical hormone replacement therapy. His cognitive functions recovered, his physical and mental disorders were alleviated, and he returned to society. It is important not to miss neurological and psychiatric symptoms that can be cured by physical treatment.

Introduction:

Isolated adrenocorticotrophic hormone (ACTH) deficiency (IAD) is a cause of adrenal insufficiency in which secretion of only ACTH is impaired, while secretion of other anterior pituitary hormones is maintained. Diagnosis is often delayed due to nonspecific symptoms such as general fatigue, appetite loss, weight loss, hypoglycemia, and hypotension. We herein report a case of a Japanese man with IAD complicated by primary hypothyroidism presenting with several neuropsychiatric symptoms, especially cognitive dysfunction, before diagnosis who showed complete improvement of cognitive function after administration of hydrocortisone.

Case Presentation:

A 46-year-old Japanese man who had cognitive impairment visited our department. He began working after finishing vocational school at the age of 20, but he changed jobs often beginning at the age of 25. He started to doze off and make careless mistakes during the daytime despite sleeping well at night. He visited the psychiatrist and was diagnosed with narcolepsy at the age of 38. He was administered modafinil, and his symptoms were relieved. Modafinil was discontinued. He was able to work at the age

of 40. He started to become fatigued easily, exhibited anorexia and weight loss and was diagnosed with eosinophilic gastroenteritis and hypereosinophilia at the Department of Internal Medicine, A Hospital, at the age of 44. Afterwards, the anorexia improved, but the fatigue was so severe that he took a leave of absence from work. He temporarily returned to work, but due to fatigue and somnolence, he was placed on leave again. He visited the psychiatrist, and he was diagnosed with adjustment disorder. He received rehabilitation and returned to work at the age of 45. He began to make incoherent remarks and wipe his nose with his hand, which were not appropriate behaviors for his age, at the age of 46. His Mini Mental State Examination-Japanese (MMSE-J) score was 25/30 points. The Wechsler Adult Intelligence Scale, Third Edition (WAIS-III) showed impairment (Full-Scale IQ 70, Verbal IQ 76, Performance IQ 69, Verbal Comprehension Index 78, Perceptual Organization Index 66, Working Memory Index 85, Processing Speed Index 81). His MRI showed mild cerebral atrophy, and he was suspected to have dementia. When he visited our department, his facial expression was anxious, his speech was polysyllabic and unorganized, he had difficulty sustaining attention, and he exhibited impulsiveness and restlessness. The scores of the MMSE-J and clock-drawing test (CDT) using the Freedman method were 25/30 and 14/15, respectively. The Japanese Adult Reading Test (JART) yielded a predicted total IQ of 110, a predicted verbal IQ of 111 and a predicted performance IQ of 106 at the time of examination. The patient showed mild cognitive impairment. Blood tests showed decreased ACTH, cortisol and free thyroxine (FT4) levels and increased thyroid-stimulating hormone (TSH) levels. He was diagnosed with hypopituitary secondary adrenal hypofunction based on the absence of cortisol in the rapid ACTH stress test, the response of urinary cortisol in the continuous ACTH stress test, and the absence of both ACTH and cortisol in the corticotropin-releasing hormone (CRH) stress test (Table 1). IAD was diagnosed because secretion of other anterior pituitary hormones was maintained. With regard to hypothyroidism, the FT4 level was low, the TSH level was high, and the thyrotropin-releasing hormone (TRH) stress test showed a positive response to TSH, leading to the diagnosis of primary hypothyroidism (Table 1). He was started on hydrocortisone (15 mg) as adrenal corticosteroid replacement therapy. By 1 month after starting hydrocortisone, his physical complaints, including anorexia, somnolence, and general fatigue, had disappeared, as had his forgetfulness and difficulty concentrating. His cognitive functions had recovered, and his MMSE-J score was 30/30. The WAIS-III scores improved (Full-Scale IQ 81, Verbal IQ 92, Performance IQ 72, Verbal Comprehension Index 92, Perceptual Organization Index 66, Working Memory Index 98, Processing Speed Index 81) after 3 months of hydrocortisone treatment. The hydrocortisone dose was decreased to 10 mg because his body weight increased during the same period. He returned to work after 5 months of hydrocortisone treatment and has been working stably since then with 10 mg of hydrocortisone. Hypothyroidism also recovered 7 months of hydrocortisone treatment.

Table 1. Endocrine examination results

Basal hormone values						
ACTH (pg/ml)	<1.5	ACTH: adrenocorticotrophic hormone				
cortisol (µg/dl)	0.1	TSH: thyroid-stimulating hormone				
TSH (mU/ml)	18.8	FT4: free thyroxine				
FT4 (ng/dl)	0.82	GH: growth hormone				
GH (µg/ml)	1.43	IGF-1: insulin-like growth factor				
IGF-1 (ng/ml)	49	LH: luteinizing hormone				
LH (mIU/ml)	6.7	FSH: follicle-stimulating hormone				
FSH (mIU/ml)	7.4	PRL: prolactin				
estradiol (pg/ml)	54.1	TG: thyroglobulin				
progesterone (ng/ml)	0.1	TPO: thyroid peroxydase				
testosterone (ng/ml)	6.44	CRH: corticotropin-releasing hormone				
PRL (ng/ml)	21.9	TRH: thyrotropin-releasing hormone				
		LHRH: luteinizing hormone-releasing hormone				
		GHRP2: growth hormone-releasing peptide 2				
Antibodies						
anti-TG antibody (U/ml)	27					
anti-TPO antibody (U/ml)	9					
Rapid ACTH stimulation test						
	0 Min	30 Min	60 Min			
cortisol (µg/dl)		0.1	2.7 3.3			
Continuous ACTH loading test						
	Day 1	Day 2	Day3			
urine cortisol		94.9	539 1630			
Hormone loading tests						
		0 Min	30 Min	60 Min	90 Min	
CRH test	ACTH (pg/ml)	<1.5	<1.5	<1.5		
	cotisol (µg/dl)	0.3		0.4	0.3	
TRH test	TSH (mU/ml)	16.5	77.7	60.7		
	PRL (ng/ml)	25	135	83.7		
LHRH test	LH (mIU/ml)	8.5	49.6	52.8		
	FSH (mIU/ml)	7.6	14.5	14.6		
		0 Min	15 Min	30 Min	45 Min	60 Min
GHRP2 test	GH (µg/ml)	0.52	10.2	10.9	7.17	4.86



Discussion:

IAD is a pituitary disorder characterized by decreased secretion of ACTH, which causes secondary adrenal insufficiency (AI). The main symptoms of IAD are caused by glucocorticoid deficiency. Steinberg reported the first case of IAD in 1954. Patients with IAD present with general fatigue, weight loss and hypoglycemia, which improve after ACTH administration [1]. The prevalence of IAD was found to be 1.91–7.3 per 100,000 persons in a Japanese cohort [2–3]. Individuals with IAD primarily present with symptoms of AI, such as general fatigue, loss of appetite, nausea, and vomiting. IAD is often misdiagnosed as a psychological disorder when patients have psychological symptoms, including apathy, depression, delusion and abnormal behavior [4]. In this case, the patient was diagnosed with some neuropsychiatric disorders, including narcolepsy, adjustment disorder, and mild cognitive impairment. Nagai reported that a 69-year-old man was admitted because of abdominal pain with IAD accompanying dementia [5]. Matsuo reported cognitive impairment and a depressive state caused by IAD in a 45-year-old Japanese man [6]. Goto reported an IAD case presenting with gait disturbance necessitating differential diagnosis from idiopathic normal pressure hydrocephalus [7]. Cognitive dysfunction is considered to be one of the symptoms of IAD. This case showed complete recovery of

cognitive function after the administration of hydrocortisone. The neuropsychiatric symptoms were also improved, such as difficulty in sustaining attention, impulsiveness and restlessness. The MMSE-J and WAIS-III scores increased. Since cognitive dysfunction resulting from IAD is treatable, clinicians should keep IAD in mind when assessing patients with impaired cognitive functions.

Conclusion:

Adrenocortical hormone replacement therapy is dramatically effective for the symptoms of IAD. This patient recovered from his cognitive dysfunction and physical and mental disorders and returned to society. The patient had IAD accompanied by impaired cognitive functions and dramatically improved after treatment with adrenocortical hormone replacement therapy. Clinicians must consider the possibility of IAD when assessing patients with impaired cognitive functions.

Declarations:

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Authors' contributions: AI, IS, NO, and YK were involved in the clinical investigations. AI wrote the first draft of the manuscript. RY and AI were involved in the literature review and corrections. All authors read and approved the final manuscript.

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