INTERNAL MEDICINE

□ CASE REPORT □

Treatable Bedridden Elderly—Recovery from Flexion Contracture after Cortisol Replacement in a Patient with Isolated Adrenocorticotropic Hormone Deficiency

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Abstract

Isolated adrenocorticotropic hormone deficiency (IAD) is a rare disorder with diverse clinical presentations. A 79-year-old man was bedridden for six months due to flexion contractures of the bilateral hips and knees, along with hyponatremia. He was diagnosed with IAD based on the results of endocrine tests. After one month of corticosteroid replacement, he recovered and was able to stand up by himself. Although flexion contracture is a rare symptom of IAD, steroid replacement therapy may be effective, even for seemingly irreversibly bedridden elderly patients. In bedridden elderly patients with flexion contractures, we should consider and look for any signs of adrenal insufficiency.

Key words: bedridden elderly, flexion contractures, isolated ACTH deficiency

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Introduction

Isolated adrenocorticotropic hormone (ACTH) deficiency (IAD) is very rare and difficult to diagnose. IAD was first described in 1954 and is a rare cause of secondary adrenocortical insufficiency (1). In Japan, the prevalence of IAD is 19.1 per one million and the incidence is 0.9 per year (2). It usually presents with weakness, hypotension, weight loss, anorexia, nausea, and vomiting; but musculoskeletal abnormalities are uncommon manifestations. Meanwhile, reports on flexion contracture in elderly patients with IAD are limited. We herein report an unusual reversible case of IAD in an elderly man with flexion contractures of the bilateral hips and knees.

Case Report

A 79-year-old man was admitted to our hospital with a six-month history of flexion contractures of the hips and knees, with accompanying anorexia, weight loss, malaise, and progressive weakness.

He had undergone left upper lobectomy and adjuvant chemotherapy for lung adenocarcinoma five years previously and remains in remission at the time of writing. He had never been treated with corticosteroids. About one year previously, he was admitted to another hospital due to a fracture of the sacral bone, which occurred due to a fall. During that admission, he developed severe hyponatremia (serum sodium, 110 mEq/L) of unknown etiology and recovered quickly after continuous oral salt supplementation. However, his bone fracture led to the gradual development of leg contraction and he became bedridden several months later.

On admission, body temperature was 37.3℃, his blood pressure was 85/50 mmHg, and his pulse was 70 beats/min. His body weight decreased from 56 kg to 43 kg over a period of one year. A physical examination revealed difficult passive movement of the bilateral hip and knee joints due to flexion contractures. The patient was unable to stand or walk. With the exception of his hips and knees, the patient's manual muscle test (MMT) results were almost normal; we could not assess perform the MMTs for the hips and knees due to the difficulties imposed by the flexion contractures. No muscle spasms, spontaneous joint and muscle pain, or neurologic abnormalities were observed and the patient's mental status was normal.

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Table 1. Plasma Hormone Level.

		Basal	30 min	60 min	120 min
TRH test (protireline 0.5 mg)	TSH (μU/mL)	3.6	16.3	10.7	9.6
	Free T4 (ng/dL)	1.5			
	Prolactin (ng/mL)	16.1	69.7	61.8	36.9
LH-RH stimuation test	LH (mIU/mL)	48.4	>200	>200	187
(gonadorelin acetate 0.1 mg)	FSH (mIU/mL)	55	86.5	91.1	94.5
GRH test	GH (ng/mL)	4.34	12.4	15.4	6.9
(somatorelin acetate 50 μg)					
CRH test (corticorelin 100 μg)	ACTH (pg/mL)	45.2	52.7	64.6	76.2
	Cortisol (μg/dL)	6.2	6.8	7.7	7.9

TRH:thyrotropin-releasing hormone, TSH: thyroid stimulating hormone, LH-RH: luteinizing hormone-releasing hormone, LH: luteinizing hormone, FSH: follicle stimulating hormone, GHRH: growth hormone releasing hormone, GH: growth hormone, CRH: corticotropin-releasing hormone, ACTH: adrenocorticotropic hormone

A laboratory evaluation results were as follows: white blood cell count of 6.8×10^9/L (neutrophils, 44.2%; eosinophils, 21.2%; basophils, 0.9%; lymphocytes, 25.6%; and monocytes 8.1%); hemoglobin, 9.2 g/dL; and platelet count, 120×10^9/L. The patient's serum levels of glucose, sodium, potassium and creatine kinase were 84 mg/dL, 121 mEq/L, 4.4 mEq/L, and 109 U/L, respectively.

Based on the above results, we considered the possibility of adrenal insufficiency and performed a further endocrine analysis. The basal plasma cortisol level was 4.8 μg/dL and the basal ACTH level was 37.1 pg/mL (normal, 7.2-63.3 pg/mL). A rapid ACTH test with tetracosactide acetate (0.25 mg) resulted in a low cortisol response, which was manifested as the following serial levels (μg/dL): 4.8 (before), 12.7 (at 30 min), and 10.4 (at 60 min). Furthermore, an assessment of the patient's pituitary function showed the following: 1) the basal ACTH level was inappropriately normal and the basal plasma cortisol was extremely low and non-responsive to stimulation by corticotropin releasing hormone; and 2) the thyroid stimulating hormone, prolactin, luteinizing hormone, follicle stimulating hormone, and growth hormone levels showed sufficient responses (Table 1). These results indicated a reduction of ACTH secretion, but the normal secretion of other pituitary hormones. Magnetic resonance imaging of the pituitary-hypothalamic region revealed normal findings. Computed tomography of the trunk revealed no remarkable findings. Anti-glutamic acid decarboxylase and anti-pituitary cell antibodies were not detected. Thus, we established a diagnosis of IAD. Electromyography (EMG), nerve conduction studies (NCS), and muscle biopsy were not performed.

We administered hydrocortisone (15 mg/day; 10 mg in the morning and 5 mg in the evening), which led to the immediate resolution of the patient's hyponatremia, eosinophilia, anorexia, and malaise. Furthermore, he eventually regained his ability to stand up and walk without assistance at one month after the administration of hydrocortisone. MMTs of the hips and knees showed a good recovery (4/5) after cortisol replacement. The clinical course of the patient is summarized in Figure.

Discussion

The present case suggested two clinically relevant points. First, cortisol replacement therapy may be effective for treating flexion contractures related to newly-diagnosed IAD, even in elderly bedridden patients. Second, it is important to rule out adrenal insufficiency in elderly individuals with no clear predisposition to being bedridden.

Although the age distribution of IAD is wide, to our knowledge, this case describes the oldest reported IAD patient with flexion contracture (3-9). Although the main causes of IAD are autoimmune, congenital/genetic, stroke, and head injury, the underlying cause of IAD is often undetectable in many cases, as was the case in our patient. Our patient was recognized to have hyponatremia several days after sustaining a fracture of the sacral bone. It has been reported that powerful stressors, such as external wounds, infections, surgery, or bleeding, can trigger acute adrenal insufficiency (10). However, the causal relationship between the fracture and the patient's IAD remains unclear.

The symptoms, clinical signs, and biochemical findings of adrenal insufficiency are varied and non-specific. Myalgia and joint pain are reported to occur in 6-13% of patients with adrenal insufficiency (11), but the data on IAD are insufficient. Flexion contractures are considered to be rare in IAD, and most reported cases are associated with Addison's disease or hypopituitarism (12).

In the past, flexion contractures with hypopituitarism has been reported as stiff-person syndrome—a chronic disorder that involves stiffness and painful spasms of the trunk (13). Although the pathogenesis of flexion contractures remains unknown, it is now considered that the flexion contractures associated with adrenal insufficiency differ from those of stiff-person syndrome. Approximately 60% of stiff-person syndrome cases show glutamic acid decarboxylase autoantibody positivity (14), without flexion contractures. Diazepam is an effective treatment for stiff-person syndrome, whereas glucocorticoid is a highly effective treatment for flexion contractures. On EMG, stiff-person syndrome manifests with continuous motor unit activity (15), whereas flexion contractures are associated with varying findings (9). For this pa-

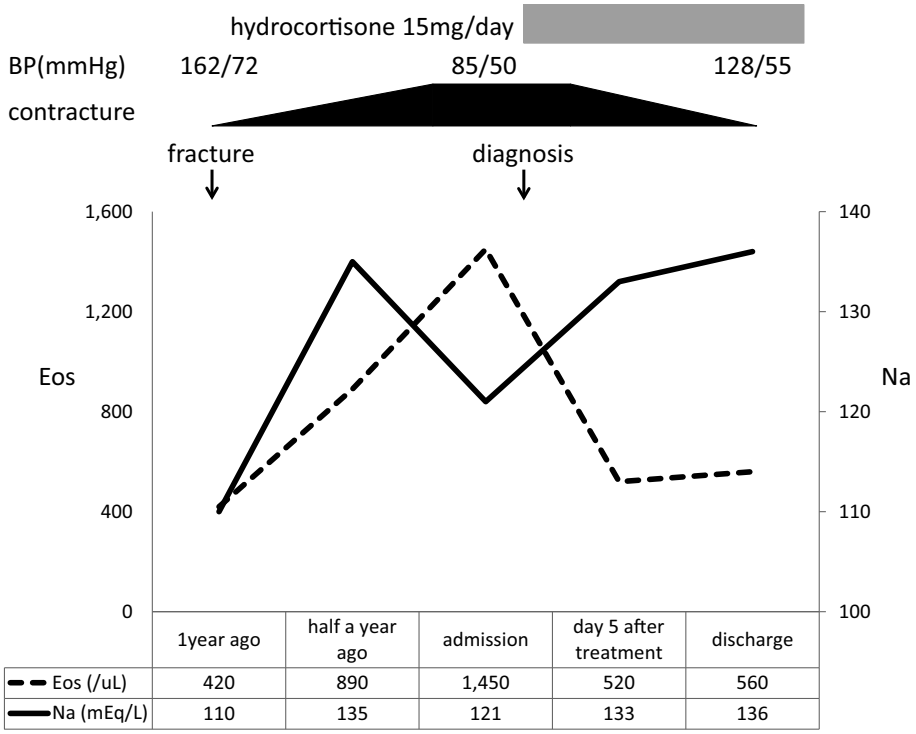

Figure. **Clinical course. BP: blood pressure, Eos: eosinophil, Na: sodium**

Table 2. **Lists of the Patients with Flexion Contractures Related to Isolated Adrenocorticotropic Hormone Deficiency.**

No	Sex/Age	NCS	EMG	Muscle biopsy	Reference
1	M/56	-	normal	normal	3
2	F/55	CMAP, SMAP amp ↓ MCV, SCV ↓	normal	atrophy of type2 fiber	4
3	F/51	-	neurogenic myogenic	-	5
4	M/73	-	silent	-	6
5	M/58	-	-	-	7
6	M/55	-	-	-	8
7	M/61	normal	normal	number of type1 fiber↓	9
8	M/79	-	-	-	our case

NCS: nerve conduction study, EMG: electromyography, CMAP: compound muscle action potential, SMAP: sensory nerve action potential, amp: amplitude, MCV: motor nerve conduction velocity, SCV: sensory nerve conduction velocity

tient, we did not perform NCS, EMG, or muscle biopsy; nevertheless, the significance of such investigations remains inconclusive (9), and the tests have variable results (Table 2). The response to glucocorticoids, however, may be a diagnostic finding in cases of flexion contracture.

Our patient regained his ambulatory ability with glucocorticoid therapy. We underscore the importance of the prompt initiation of glucocorticoid therapy after the early recognition of contracture and IAD. If the period between the diagnosis of IAD and the initiation of treatment is prolonged, the recovery period from contracture will be delayed (7, 8). Various hypotheses on the development of musculoskeletal symptoms in patients with adrenocortical insufficiency have been proposed. Electrolyte abnormalities and muscle membrane excitability were previously thought to be associated with the development of musculoskeletal symptoms in patients with adrenal insufficiency, however, the underlying mechanism has not been conclusively identified (9). Recently, polymorphisms of the glucocorticoid receptor gene and the relevant affected pathways have been presumed to determine inter-individual differences in the relationship between glucocorticoids and the neuromuscular system (9, 16).

Our patient did not belong to any of the three major causes (stroke, dementia, and senile decay) of being bedridden. Furthermore, there were some key physical and laboratory findings regarding the adrenal insufficiency in our patient. The unexplainable bedridden status in elderly patients should therefore be evaluated more carefully to detect any potential signs of adrenal insufficiency so that treatable disorders, such as IAD, are not overlooked.

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

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