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Case Report

Two cases of traumatic isolated ACTH deficiency

Abstract

Case 1: A 65- year-old man was accidentally injured by wooden hammer on his top of head on 34 years before. He was suffered from vomiting, diarrhea and hypotension, and the laboratory examination revealed increased CRP level, hyponatremia and decreased plasma cortisol and ACTH levels, suggesting isolated ACTH deficiency and Crohn disease diagnosed by colonoscopic biopsy, and finally transferred to University Hospital. LH-RH, TRH, CRH and GHRP stimulation tests showed normal response of plasma pituitary hormones except for no response of plasma ACTH and cortisol levels by CRH stimulation. ACTH stimulation test showed no response of plasma cortisol levels although hydrocotisone replacement therapy had already been started. MRI imaging showed bottom of anterior lobe was crushed and pituitary gland was atrophied, which suggested brain might be injured by any strong trauma.

Case 2: An 83-years old man was injured on brain contusion by staff's violence in nursing home, and introduce to our hospital to remove brain hematoma on 6 months before. He presented transient loss of consciousness because of hypoglycemia. Laboratory examinations revealed hyponatremia, and low levels of plasma ACTH and cortisol. Endocrinological examination showed normal LH-RH and TRH stimulations tests, basal GH and IGF-1 levels, and no response of plasma ACTH and cortisol levels by CRH stimulation, showing traumatic isolated ACTH deficiency. MRI imaging showed atrophic pituitary gland. These results suggest that traumatic isolated ACTH deficiency may be able to appear for short and long period after brain injury.

Introduction

Isolated ACTH deficiency is a rare disease characterized by secondary adrenal insufficiency with low or absent cortisol production and normal secretion of pituitary hormones other than ACTH [1]. Isolated ACTH deficiency has been caused by traumatic injury [2], lymphocytic hypophysitis due to autoimmune etiology [3,4], genetic origin in neonatal or childhood [1], and unknown origin. Previous reports have demonstrated that traumatic brain injury—mediated hypopituitarism could be more frequently occured [5-7]. High prevalence of neuroendoctine dysfunction in patients with traumatic brain injury has been reported [8].

In this study we have shown two cases of traumatic isolated ACTH deficiency.

Case Presentation

Case 1

A 65- year-old man was accidentally injured by wooden hammer on his top of head on 34 years before. He was suffered from vomiting, diarrhea and hypotension, and the laboratory examination revealed increased CRP (4.0 mg/dl) level, hyponatremia and decreased plasma cortisol (less than 1 μg/dl) and ACTH (less than 2.0 pg/ml) levels, suggesting isolated ACTH deficiency and Crohn disease diagnosed by colonoscopic biopsy, and finally transferred to University Hospital.

Laboratory examinations showed normal values exept for slightly hyponatremia and leukocytosis during hydrocortisone replacement therapy (Figures 1-a,b). Thyroid function was normal. Basal ACTH and cortisol levels were suppressed by hydrocortisone replacement therapy. LH-RH, TRH and CRH and GHRP stimulations tests showed normal response of plasma pituitary hormones except for no response of plasma ACTH and cortisol levels by CRH stimulation and hyperresponse of PRL by TRH stimulation with high level of PRL (Figures 2-a,b). ACTH stimulation test showed no response of plasma cortisol levels although hydrocotisone replacement therapy had already been started (Figure 2-b). MRI (T1 weighted image) imaging showed bottom of cerebral anterior lobe was crushed and anterior pituitary gland was atrophied, which suggested brain might be injured by any strong trauma (Figure 3).

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Case 2

An 83-years old man was injured on brain contusion by staff's violence in nursing home, and introduce to Gifu Municipal hospital to remove brain hematoma on 6 months before. He presented transient loss of consciousness because of hypoglycemia (37 mg/dl), and transferred to our hospital.

Laboratory examinations revealed hyponatremia (126 mEq/l), normal HbA1c (5.1 %) level (Figures 4-a,b, Figures 5-a), and low levels of plasma ACTH (6.8 pg/ml), cortisol (15.2 μg/dl) and suppression of PRA (less than 0.1 ng/ml/hr) and aldosterone (less than 10.0 pg/ml) levels during saline infusion (Figure 4-c, Figure 5-a).

Endocrinological examination showed normal LH-RH and TRH stimulation test, normal plasma basal GH (3.73 ng/ml) and IGF-1 (37 ng/ml) levels and no response of plasma ACTH and cortisol levels by CRH stimulation, showing traumatic isolated ACTH deficiency (Figures 5-a,b). ACTH stimulation test showed delayed low response of plasma cortisol levels (Figure 5-b). MRI imaging showed anterior lobe of atrophic pituitary gland (Figure 6).

Fig 1-a Laboratory Examinations

TP	7.0	g/dl	TG	104	mg/dl
Alb	3.9	g/dl	HDL-C	59	mg/dl
AST	24	IU/l	LDL-C	90	mg/dl
ALT	14	IU/l	T-Bil	0.8	mg/dl
LDH	211	IU/l			
ALP	199	IU/l	Na	134	mEq/l
γ-GT	15	IU/l	K	4.1	mEq/l
ChE	253	IU/l	Cl	103	mEq/l
AMY	148	IU/l	Ca	8.6	mg/dl
CRE	1.18	mg/dl	IP	2.6	mg/dl
UA	5.8	mg/dl	CRP	0.14	mg/dl
BUN	23.5	mg/dl	eGFR	>90	ml/min/1.73m^2

Fig 1-b Laboratory Examinations

WBC	7320	/μl	ANA	< x40	
Neut	67.8	%	Anti smooth muscle antibody		(-)
Mono	5.0	%	Anti mitochondrial antibody		(-)
Lymph	23.1	%	T-SPOT		(-)
Eosino	3.3	%	PR3-ANCA	<1.0	U/ml
Baso	0.8	%	MPO-ANCA	<1.0	U/ml
RBC	409	x10^4/μl	RF	<5	U/ml
Hb	12.4	g/dl	Anti SS-A antibody	<7.0	U/ml
Ht	38.4	%	Anti SS-B antibody	<7.0	U/ml
MCV	93.9	fl			
MCH	30.3	pg			
MCHC	35.2	%			
Plt	21.0	x10^4/μl			

Figure 1: Laboratory examinations in cae 1 during hydrocortisone replacement therapy. General laboratory (Fig.1-a) and immunological and blood examinations (Fig.1-b) were indcated, respectively.

Fig 2-a Endcrinological Examinations

TSH	4.36	μIU/ml	Plasma glucose level	91	mg/dl
FT3	2.87	pg/ml	HbA1c	5.1	%
FT4	1.17	ng/dl	Testosterone	4.37	ng/ml
ACTH	<2.0	pg/ml	ADH	1.7	pg/ml
Cortisol	<1.0	μg/dl			
PRA	0.7	ng/ml/hr			
Aldosterone	2.5	pg/ml			
GH	0.20	ng/ml			
IGF-1	70	ng/ml			
PRL	18.84	ng/ml			
LH	5.89	mIU/l			
FSH	4.15	mIU/l			

Fig 2-b Endcrinological Examinations

LH-RH, TRH and CRH stimulation test and GHRP stimulation test

	Before	30 min	60 min	120 min
ACTH(pg/ml)	<2.0	<2.0	<2.0	<2.0
Cortisol(μg/dl)	<1.0	<1.0	<1.0	<1.0
TSH(μU/ml)	4.10	13.12	14.68	13.27
PRL(ng/ml)	15.39	95.06	97.41	46.59
LH(mIU/ml)	7.56	11.84	13.61	13.39
FSH(mIU/ml)	4.36	4.74	4.83	5.04
GH(ng/ml)	0.08	18.00	16.70	5.82

ACTH stimulation test

	Before	15 min	30 min	60 min	120 min
Cortisol(μg/dl)	<2.0	<2.0	<2.0	<2.0	<2.0

Figure 2: Endocrinological examinations in case 1
Basa thyroid function, pituitary hormones and endocrinological results (Fig.2-a), and LH-RH (100 μg), TRH (500 μg) and CRH (100 μg) simultaneously stimulations test, GHRP (100 μg) stimulation test and ACTH (250 μg) stimulation test (Fig.2-b) were shown, respectively.

Fig 3 MRI imaging in case 1

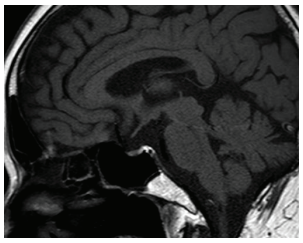

Figure 3: MRI (T1 weighted image) imaging in case 1
Arrows indicated crushed anterior lobe and atrophic pituitary gland, respectively.

Fig 4-a Laboratory Examinations

TP	4.4	g/dl	TG	34	mg/dl
Alb	1.4	g/dl	HDL-C	36	mg/dl
AST	19	IU/l	LDL-C	48	mg/dl
ALT	23	IU/l	T-Bil	0.4	mg/dl
LDH	166	IU/l			
ALP	451	IU/l	Na	126	mEq/l
γ-GT	61	IU/l	K	3.7	mEq/l
ChE	85	IU/l	Cl	106	mEq/l
AMY	72	IU/l	Ca	7.1	mg/dl
CRE	0.42	mg/dl		(Corrected Ca 9.7mg/dl)	
UA	4.8	mg/dl	IP	2.1	mg/dl
BUN	9.6	mg/dl	CRP	5.54	mg/dl
			eGFR	>90	ml/min/1.73m^2

Fig 4-b Laboratory Examinations

WBC	9520	/μl	IgG	1432	mg/dl
Neut	84.2	%	IgA	529	mg/dl
Mono	0.0	%	IgM	145	mg/dl
Lymph	2.1	%	ANA	< x40	
Eosino	0.0	%	Anti smooth muscle antibody		(-)
Baso	0.0	%	Anti mitochondrial antibody		(-)
RBC	395	x10^4/μl	T-SPOT		(-)
Hb	12.0	g/dl	PR3-ANCA	<1.0	U/ml
Ht	34.1	%	MPO-ANCA	<1.0	U/ml
MCV	86.3	fl	RF	<5	U/ml
MCH	30.4	pg	Anti SS-A antibody	<7.0	U/ml
MCHC	35.2	%	Anti SS-B antibody	<7.0	U/ml
Plt	15.9	x10^4/μl			

Figure 4: Laboratory examinations in case 2
General laboratory (Fig.2-a) and immunological and blood examinations (Fig.2-b) were indcated, respectively. Basal endocrinological data were shown in Fig-c.

Discussion

It has been reported that the percentage of probability in the appearance of endocrinological abnormality was 15-68%, especially in hypopituitarism of anterior lobe was 27.5% and that hypofunction in hypophysico–pituitary axis occurs within half year after brain trauma. Gonadal hypofunction and insufficiency of growth hormone secretion occurred in highest rate, and in the next rate hypoadrenocortism and

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Fig 5-a Endcrinological Examinations

TSH	2.86	μIU/ml	Plasma glucose level	37	mg/dl
FT3	<1.0	pg/ml	HbA1c	5.1	%
FT4	1.06	ng/dl	Insulin	0.5	μU/ml
ACTH	6.8	pg/ml	C-peptide	0.32	ng/ml
Cortisol	15.2	μg/dl	Insulin antibody	<0.4	U/ml
PRA	<0.1	ng/ml/hr			
Aldosterone	<10.0	pg/ml	GAD antibody	(-)	
IGF-1	37	ng/ml	Testosterone	2.55	ng/ml
PRL	16.42	ng/ml	ADH	1.7	pg/ml
LH	3.65	mIU/l			
FSH	10.63	mIU/l			

Fig 5-b Endcrinological Examinations

LH-RH, TRH and CRH stimulation test

	Before	30 min	60 min	120 min
ACTH(pg/ml)	9.9	10.8	11.7	11.4
Cortisol(μg/dl)	15.5	15.5	14.8	15.0
TSH(μU/ml)	4.62	10.75	9.92	8.87
PRL(ng/ml)	15.49	65.87	53.25	40.72
LH(mIU/ml)	4.16	9.78	14.86	18.16
FSH(mIU/ml)	11.86	13.70	14.83	18.20

Rapid ACTH stimulation test

	Before	30 min	60 min
Cortisol(μg/dl)	21.8	18.4	32.0

Figure 5: Endocrinological examinations in case 1
LH-RH(100 μg), TRH (500 μg) and CRH (100 μg) stimualtions test and rapid ACTH (250 μg) stimulation test were shown for before, 30, 60 and 90 min and before, 30, and 60 min, respectively.

Fig 6 MRI imaging in case 2

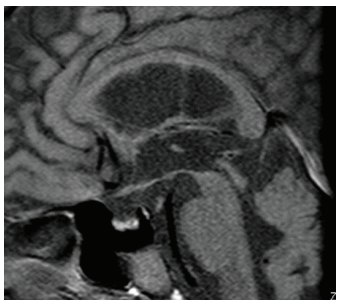

Figure 6: MRI (T1 weighted image) imaging in case 2
Arrow indicated atrophic anterior lobe and high intensity of posterior lobe of pituitary gland.

hypothyroidism occurred. Schneider et al. [2] also reported that grade of brain damage evaluated in Glasgow Coma Scale (GCS) was correlated with occurrence rate in hypothalamo-pituitary hypofuction as follows: Severe damage (GCS 9-12 points), moderate damage (9-12 points) and slight damage (13-15 poins) was 35.3%, 10.9% and 16.8%, respectively. However, even if in the case of slight brain damage, occurrences of endocrinological abnormality should be taken care. They conclude that hypopituitarism is a common complication of both traumatic brain injury and aneurysmal subarachnoid hemorrhage. This systematic review showed ACTH deficiency was occurred in 0-19.2% after traumatic brain injury. Tanriverdi et al. [9], also reported that some 5.8% of the traumatic brain injury patients had TSH deficiency, 41.6% had gonadotropin deficiency, 9.8% had ACTH deficiency, and 20.4% had GH deficiency, and that pituitary function may improve or worsen in a considerable number of patients over 12 months. A patient presented in case 1 occurred clinical symptoms of hypopituitarism for 34 years after severe traumatic injury. Recent report indicated 3cases of isolated ACTH or TSH deficiency following mild traumatic brain injury with long-term follow (10 days- 20 years) [10], which was similar to our case 1. Sixty-five years-old man occurred both isolated ACTH deficiency and Crhon's disease at the same time in case 1. Kalambokis et al. [11], had been reported that isolated ACTH deficiency associated with Croh's disease without traumatic brain injury which might be associated with immune reactions. Therefore, etiology of our case 1 might be a little relevance for complication of Crhon's disease. Recently, old men and women received violent brain traumas in old people's home have been happened. Clinical symptoms and results of laboratory examinations such as nausea vomiting, hyponatremia and increased CRP levels should be paid attention.

Conclusion

Two cases of these disorders were treated with 15-20 mg of hydrocortisone and continued to live in good health. These results suggest that traumatic isolated ACTH deficiency may be able to appear for short and long period after brain injury.

Disclosure

None of the authors have any potential conflict of interest associated with this research.

The ethical committee in the Gifu Municipal Hospital have been approved in this study.

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