Successful Treatment for a Case of Near-Fatal Secondary Adrenal Insufficiency

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ABSTRACT

A thirty-six-year old female with shock was found to be unconsciousness a few days after developing a respiratory infection. Her past medical history included autoimmune hypothyroidism. Her state of shock was not controlled by massive fluid resuscitation with a vasopressor and antibiotics. However, an infusion of 250 mg methylprednisolone dramatically improved her shock state. Further examination indicated secondary acute adrenal insufficiency.

Adrenal insufficiency may complicate other endocrine disorders. Accordingly, a physician should consider hypoadrenocorticism, when patients are in a state of refractory shock in spite of massive infusion with a vasopressor, especially in patients with other endocrine disorders.

Key words: *Adrenocorticotropic hormone/hypothyroidism/shock/multiple organ failure.*

Tratamiento Exitoso de una Caso de Insuficiencia Adrenal Secundaria Casi Fatal

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RESUMEN

Una mujer de treinta y seis años en shock fue hallada inconsciente unos días después de desarrollar una infección respiratoria. Los antecedentes en su historia clínica incluían hipotiroidismo autoinmune. Su estado de shock no fue controlado por la reanimación con líquidos masiva con un vasopresor y antibióticos. Sin embargo, una infusión de 250 mg metilprednisolona había mejorado considerablemente su estado de shock. Un examen más detenido indicó insuficiencia adrenal aguda secundaria. La insuficiencia adrenal puede complicar otros trastornos endocrinos. En consecuencia, un médico debe considerar la posibilidad de hipoadrenocorticismo, cuando los pacientes se encuentran en estado de shock refractario a pesar de una infusión masiva con un vasopresor, especialmente en el caso pacientes con otros trastornos endocrinos.

Palabras claves: Hormona adrenocorticotrópica, hipotiroidismo, shock, fallo multiorgánico

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INTRODUCTION

Secondary adrenocortical insufficiency induced by adrenocorticotropic hormone (ACTH) can cause a myriad of clinical signs such as hypotension, hypoglycaemia, hyponatraemia, consciousness disturbance, psychosis or general fatigue (1). It is not difficult to diagnose adrenocortical insufficiency when a patient with chronic adrenocortical insufficiency no longer receives hormone replacement therapy, but acute adrenal insufficiency developing *de novo* is a challenging diagnosis in an emergency department. Patients can die in crisis within several hours without appropriate treatment (2, 3). This report presents a case of the successful treatment of near-fatal secondary acute adrenal failure with multiple organ failure.

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Case report

A thirty-six-year-old female was found to be unconsciousness a few days after developing a respiratory tract infection, and was transported to hospital in the middle of the night. Her past medical history included asthma, autoimmune hypothyroidism treated by levothyroxine, gestational diabetes mellitus and amenorrhoea after successful delivery of a pregnancy at the age of 32 years. She did not experience shock during the delivery or any postpartum haemorrhage, but developed a low-grade fever, amenorrhoea and

dysfunction of galactorrhoea after the delivery. She had no familial history of illness. Her vital signs on arrival were: blood pressure immeasurable, pulse 124 beats per minute, tympanic temperature 40.1°C and she was in a restless confusional state. She underwent sedative and transoral intubation. Her state of shock was not controlled by massive fluid resuscitation with a vasopressor and imipenem/cilastatin. Emergency laboratory tests (Table 1) disclosed leukocytosis without a shift to the left, dehydration, hyponatraemia, rhabdomyolysis, liver dysfunction, renal failure and coagulopathy. However, her cardiac function, as evaluated by sonography and electrocardiograms, and her respiratory function, as evaluated by an arterial blood gas analysis and chest computed tomography were within normal limits. Concomitant hypoadrenocorticism was strongly suspected because she had refractory shock against fluid resuscitation with a vasopressor, autoimmune hypothyroidism and hyponatraemia. An infusion of 250 mg methylprednisolone with continuous fluid resuscitation dramatically improved the shock state. Infusion of minocycline, acyclovir, immunoglobulin, glycyrrhizin (4) as additional antibiotics, and three days of treatment with 500 mg methylprednisolone per day resulted in amelioration of her multiple organ failure. She demonstrated transient hyperglycaemia requiring insulin treatment. Further examination indicated secondary acute adrenal insufficiency due to a pituitary malfunction including an adrenocorticotropic hormone (ACTH) deficiency, empty sella (Figure) and Chlamydia pneumoniae infection (Table 2). The results of tests of her pituitary function on the 17th hospital day showed the same tendency. Combined anterior pituitary function tests using corticotropin releasing hormone, growth hormone releasing hormone, thyrotropin-releasing hormone, and luteinizing hormone releasing hormone disclosed hyposecretaion of ACTH, cortisol, and gonadotropin, however, there was no elevation of growth hormone over the normal range. The

Table 1: Results of emergency examinations

Arterial blood gas under ten liters of a naso-oral oxygen mask					
pH	7.326	PCO_2	28.2 mmHg	PO_2	561.2 mmHg
HCO_3^-	14.9 mmol/L	base excess	-11.4 mmol/L		
A complete blood count					
white blood cells		12000/mm^3 (neurtrocyte 55.2%, lymphocyte 35.8%)			
red blood cells		442 x 10^4/mm^3			
platelets		13.6 x 10^4/mm^3			
Serum biochemistries					
total bilirubin		1.7 mg/dl			
aspartate aminotransferase		551 international unit (IU)/L			
alanine aminotransferase		235 IU/L			
alkaline phosphatase		763 IU/L			
total protein		6.3 g/dl			
albumin		3.5 g/dl			
amylase		110 IU/L			
blood urea nitrogen		23 mg/dl			
creatinine		2.05 mg/dl			
creatine phosphokinase		1895 IU/L			
sodium		132 mEq/L			
potassium		3.3 mEq/L			
chloride		98 mEq/L			
blood sugar		77 mg/dl			
c-reactive protein		14.0 mg/dl			
ammonia		124 ug/dl			
prothrombin time		15.6 (10.8) second			
activated partial thromboplastin time		56.1 (30.1) second			
fibrinogen		350 mg/dl			
fibrinogen degradation products		14 ug/ml			
surface antigen of the hepatitis B Virus		(-)			
antibody of the hepatitis C virus		(-)			
antibody of the human immunodeficiency virus		(-)			
Urinary biochemistry findings					
pH 6	protein (3+)		sugar (-)	occult blood (3+).	
A rapid antigen detection for the diagnosis					
streptococcus pyogenes pharyngitis		(-)			
Legionella		(-)			
Streptococcus pneumoniae		(-)			
A test using an enzyme immunoassay for the rapid detection					
Influenza A		(-)			
Influneza B viruses		(-)			

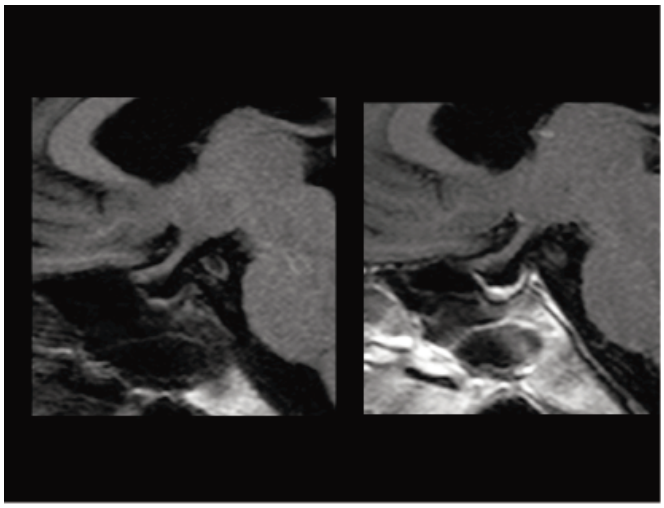

Figure: The patient's head magnetic resonance image (MRI). The head MRI shows an empty sella (left: plain, right: enhanced).

She began to menstruate after beginning these treatments without oestrogen.

DISCUSSION

This is the first case of successful treatment for near-fatal secondary acute adrenal failure with multiple organ failure.

Adrenocorticotropic hormone deficiency frequently occurs among patients with pituitary hormone deficiency (1). Adrenocorticotropic hormone deficiency complicating autoimmune endocrine disorders and thyroiditis is the most common condition associated with isolated ACTH deficiency (5, 6). Adrenocorticotropic hormone deficiency may be associated with anti-pituitary antibody (7, 8) and the co-existence of autoimmune disorders with secondary adrenal insufficiency suggests an autoimmune aetiology for the ACTH deficiency, in other words, lymphocytic hypophysitis (9). As she had never experienced shock during her first delivery or postpartum haemorrhage, but had developed a low-grade fever, amenorrhoea and dysfunction of galactorrhoea after the delivery, and because an empty sella may be the final outcome of lymphocytic hypophysitis (10), it was concluded that she most likely had lymphocytic hypophysitis rather than Sheehan syndrome (9). Since she had autoimmune hypo-

Table 2: Results of further examinations

Factor	value	Normal range	Unit	Hospital day
Thyroid stimulating hormone	17.5	(0.6 – 4.6)	uIU/ml	day 1
FT3	2.9	(2.4 – 4.1)	pg/ml	day 1
FT4	0.6	(0.7 – 1.6)	ng/dl	day 1
Adrenocorticotropic hormone	2.1	(7.2 – 63.3)	pg/ml	day 1
Cortisol	< 1.0	(3.7 – 19.4)	ug/dl	day 1
HbA_1C	5.0		%	day 1
Results of culture of blood	–			day 1
Sputum	–			day 1
Urine	–			day 1
Rheumatoid factor	–		IU/ml	day 3
Anti-nucleotide antibody	< 20			day 3
Endotoxin –				day 3
β-D glucan –				day 3
Chlamydia pneumoniae	+			day 3
C-peptide	5.59	(0.6 – 2.4)	ng/ml	day 3
Anti-thyroid peroxidase antibody	> 50	(< 0.3)		day 3
Anti-pituitary antibody	–			day 6
Growth hormone	0.18	(0.28-1.64)	ng/ml	day 6
Follicle stimulating hormone	7.9	(9.2 – 124.7)	mIU/ml	day 6
Lutenizing Hormone	5.0	(14.6 – 56.4)	mIU/ml	day 6
Progestogen	< 0.1		ng/ml	day 6
Estradiol	11		pg/ml	day 6
Prolactin	22.3	(1.4 – 14.6)	ng/ml	day 6
Antidiuretic hormone	1.0	(0.3 – 3.59	pg/ml	day 6
Adrenocorticotropic hormone	< 2.0	(7.2 – 63.3)	pg/ml	day 6
Cortisol	<1.0	(3.7 – 19.4)	ug/dl	day 6
Thyroid stimulating hormone	5.5	(0.6 – 4.6)	uIU/ml	day 6
FT3	1.3	(2.4 – 4.1)	pg/ml	day 6
FT4	0.5	(0.7 – 1.6)	ng/dl	day 6
Aldosterone	30.2	(29.9 – 159.0)	pg/ml	day 6

ACTH stimulation test failed to increase the cortisol level. She was diagnosed to have acute secondary adrenal crisis induced by Chlamydia pneumoniae infection with multiple organ disturbance. She was discharged from hospital on hormone replacement therapy with 50 micrograms of levothyroxine sodium and 15 mg of hydrocortisone per day.

thyroidism, glucose intolerance and malfunction of the pituitary gland, this case might be classified as polyglandular autoimmune syndrome type 3 or 4 (11). The presence of autoimmune thyroid disease with subclinical adrenal insufficiency can lead to adrenal crisis when thyroxine is initially prescribed (12). However, thyroxine is started four years prior, so sepsis was the more likely causative factor of the adrenal crisis.

The American College of Critical Care Medicine recommends the use of hydrocortisone at a dose of 200 mg/day in four divided doses or as a continuous infusion at a dose of 240 mg/day (10 mg/hr) for at least 7 days in patients with adrenal insufficiency and septic shock (13). Methylprednisolone at a dose of 1 mg/kg/day for at least 14 days is recommended for patients with adrenal insufficiency and severe early acute respiratory distress syndrome (13). In contrast, we used 250 mg of methylprednisone, which was equivalent to 1000 mg of hydrocortisone, even though the present case did not have combined acute respiratory distress syndrome. Because the present case was transported at midnight, and because of a lack of adequate information about her past medical history, we were concerned about triggering autoimmune encephalopathy or nephritis (15, 16) as a result of a polyglandular autoimmune syndrome type 3 or 4, so we decided to use a high dose of steroid. Retrospectively, this case did not need such a high dose.

An acute adrenal insufficiency developing *de novo* is a most challenging diagnosis in an emergency department (17). However, adrenal insufficiency is a more common disease and it is classified into two categories, elderly patients undergoing major surgery and a subgroup of patients with septic shock (18). Although the present patient was neither elderly nor had sepsis, patients with this condition should have a favourable outcome when treated appropriately (19). Accordingly, a physician should consider hypoadrenocorticism, when patients are in a state of refractory shock in spite of massive infusion of a vasopressor, especially in patients with other endocrine disorders (20).

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