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Adrenal Insufficiency as a Cause of Loss of Consciousness: A Case Study

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Introduction: The current study introduces a case with adrenal insufficiency that was suspected to have congenital adrenal hypoplasia because of undescended testis and failure to thrive due to muscle involvement.
Case Presentation: The patient was a 34-month-old boy who had loss of consciousness, hypotension, hypoglycemia, hyponatremia and hyperkalemia with severe failure to thrive, hyper pigmentation of mucosa, hypotonia and no hypospadias. He was resistant to serum therapy and responded to hydrocortisone. Laboratory study elucidated elevated levels of adrenocorticotropin (ACTH) and muscle enzymes, decreased serum cortisol levels.
Discussion: Adrenal hypoplasia congenita is a differential diagnosis for adrenal insufficiency. Undescended testis, especially in absence of hypospadiasis, is a clue to diagnose and treat this lethal disease.

Keywords: Adrenal Insufficiency; Adrenal Hypoplasia, Congenital; Loss of Consciousness

1. Introduction

Adrenal cortex is a vital organ secreting three different types of hormones: aldosterone, hydrocortisone, and dehydroepiandrosterone. Clinical manifestations of adrenal insufficiency vary based on the type of hormone and are categorized into acute, chronic and acute on chronic. Increased level of adrenocorticotropin (ACTH) causes hyperpigmentation of skin and mucosa. Congenital adrenal hyperplasia (CAH) is the most common type of adrenal insufficiency. Patients with salt wasting forms of classic CAH have hypotension, hypoglycemia, hyponatremia, and hyperkalemia (1). Adrenal hypoplasia is a rare form of adrenal insufficiency and classically causes failure to thrive. Electrolyte imbalance is more prominent than hypoglycemia duo to dominance of aldosterone deficiency rather than cortisol deficiency (2). It is not distinguishable from CAH only based on clinical findings. Here a 34-month-old boy case with adrenal insufficiency is introduced who was suspected to have adrenal hypoplasia congenital (AHC) because of undescended testis and failure to thrive due to muscle involvement. Genetic study is not included in this report.

2. Case Presentation

The patient was a 34-month-old boy, presented to us with vomiting, diarrhea and loss of consciousness. He had not diarrhea and vomiting, for a week. There was no sign and symptom of urinary or respiratory infection and patient was not febrile. His medical history included failure to thrive since he was six months old and developmental delay; He had not started walking, could sit with help at the time of his referral and used bi-syllabled words. His delivery was an elective cesarean section after a non-complicated term pregnancy. His parents had two other children and their first child had died at the age of 30 months, because of a disease with seizure, probably expired by similar disease. His parents were not relatives. In emergency department, he was severely dehydrated and had a Glasgow consciousness score of 10. His blood pressure was 60 mmHg with a heart rate of 135 beat/min. His skin and mucosa were hyperpigmented. His Z-score curve values of weight and height were between -2 and -3(Z-score = -2.4). Complete physical examination after hydration showed generalized hypotonia and symmetric deep tendon reflexes. In examination of genital organs no hypospadias existed and both testes were touched. Left testis was touched in inguinal canal. Patient was resuscitated by rapid infusion of 20 mL/kg of normal saline besides dextrose serum. There was no response to serum therapy, repeated for three times; therefore, dopamine infusion was added. After blood sampling hydrocorti-

Implication for health policy/practice/research/medical education:
The current study aimed to report a case of adrenal insufficiency that the clinical findings suggested as Adrenal Hypoplasia diagnosis. It was a rare cause of adrenal insufficiency which was not much considered, since congenital adrenal hyperplasia most often has similar clinical findings but totally different pathology. Existence of ambiguous genitalia with adrenal insufficiency suggests Congenital Adrenal Hyperplasia (CAH). The patient did not have ambiguous genitalia. Here the exact ambiguous genitalia definition was used to emphasize that undescended testis is not always ambiguous genitalia. Adrenal hypoplasia was found simultaneously with undescended testes (UDT) without the mechanism of ambiguous genitalia.

sone infusion was added.

Laboratory data in Table 1, especially low serum sodium and elevated potassium and hypoglycemia guided the authors to adrenal insufficiency. According to differential diagnosis of adrenal insufficiency, hydrocortisone was continued and these factors were re-measured in blood sample (Table 2). According to decreased muscle force, in spite of adequate resuscitation, the serum test results listed in Table 3 were examined.

Elevated muscle enzymes were confirmed. Electromyography and conduction velocimetry revealed myopathic pattern with spontaneous opisthotonus in active phase. All of the above results guided the authors to a primary adrenal insufficiency and a myopathic process.

Table 1. Lab Date: Hypoglycemia, Hyponatremia and Hyperkalemia Are Noted [a]

Laboratory Test	Value/Unit
Blood sugar	45 mg/dL
Na	120 meq/L
K	5.8 meq/L
AST	132 U/L
ALT	104 U/L
Alb	4.5 g/dL
ESR	36 mm/h
Hemoglobin	9.6 g/dL
Platelets	311 10^9/L
WBC	7.5 10^9/L
Triglyceride	141 mg/dL
Cholesterol	173 mg/dL
pH	7.34
PCO_2	32.7 mmHg
HCO_3	17 mM
PaO_2	104 mmHg
O_2sat	94%

[a] Abbreviations: Alb: albumin; ALT: alanine amino transferase; AST: aspartate amino transferase; ESR: erythrocyte sedimentation rate; sat: saturation; WBC: white blood cell.

Table 2. Elevated ACTH and Suppressed Serum Cortisol Recommended Adrenal Insufficiency Besides Clinical Findings

Laboratory Test	Value/Unit
ACTH level	> 2000 pmol/L
Serum cortisol	4.4 ng/dL

Table 3. Elevated Muscle Enzymes After Stabilization

Laboratory Test	Value/Unit
Creatinine phosphokinase	5400 mg/dL
Lactate dehydrogenase	1330 mg/dL

Patient was treated with dextrose saline and stress dose of hydrocortisone; the treatment was continued by administration of increasing dose of drug in diseases and stressful conditions and the patient was discharged after tapering to 12 mg/m^2/day hydrocortisone. After four months, he was able to walk and the growth parameters, weight and height, improved to z-scores between -1 and 0 (height Z-score = -0.5, weight Z score = -0.8). Hyper pigmentations subsided after six months. Now the patient is six years old and is able to walk and talk and has no crisis under treatment.

3. Discussion

Hypotension, hypoglycemia, hyponatremia, and hyperkalemia and mucosa hyperpigmentation guided the authors to a primary adrenal insufficiency. High level of serum ACTH and low level of serum cortisol confirmed the diagnosis. As a differential diagnosis to CAH, adrenal hypoplasia could be considered for this patient. Improvement in growth and developmental delay after corticosteroid replacement, demonstrated that the developmental delay was secondary to adrenal insufficiency. The only clue to differentiate this complication from CAH is that DAX-1 gene has an antitestis activity against sex determining region (3). Its deletion leads to bilateral or unilateral cryptorchidism. Undescended testes were prevalent in reported cases of congenital adrenal hypoplasia as the current case (4). It should be considered that ambiguous genitalia are definite signs, as well as hypospadias, besides undescended testis or bilateral undescended testes (5). Therefore the patient's genitalia could not be considered ambiguous. He only had a unilateral undescended testis touched in inguinal canal. X-linked form of adrenal hypoplasia is caused by a deletion in DAX-1 gene within X chromosome and is associated with hypogonadotropic hypogonadism (6). Due to contiguous chromosome deletion, Duchene dystrophy and glycerol kinase deficiency may coexist. DAX-1 is a nuclear hormone receptor family without known ligand. It has an unknown role in adrenal cortex development. Autosomal recessive forms had been also reported, involving other genes (7). Some studies have reported occasional cases of AHC presenting dominantly with hyperpigmentation and failure to thrive. (8) Some have also reported late diagnosed cases of AHC at adulthood with lack of puberty and skeletal immaturity. (9) It is clinically vital to diagnose AHC, a rare syndrome, from the more prevalent syndrome CAH, when the signs and symptoms are not specific for AHC, as in the current case. To confirm the diagnosis and exclude CAH, it is necessary to analyze cortical steroids and evaluate DAX-1 gene deletion with karyotyping, fluorescent in situ hybridization or microarray analysis. Abdominal sonography in infants and computerized tomography scan in older children may also be helpful. A review on 16 cases of AHC has reported bone age acceleration by 60 months of life after corticosteroid therapy and has

suggested close observation on these patients for exact follow-up of the treatment and comorbidities (8). In adrenal insufficiency, whether hyperplasia or hypoplasia, the critical point is early diagnosis and emergent replacement of hormones as the 2002 consensus statement has approved (10). Since clinical manifestations vary widely based on the genetic syndrome, confirming the net diagnosis through genetic consultation is vital in order to protect other kids of the family from the same disease and prevent lethal adrenal insufficiency crises. Yet, this question remains unanswered: How can his myopathy be explained? Can cortical hormones deficiency be responsible for that? Documentation of AHC or CAH diagnosis by genetic study, which was not possible for the current patient's family, may be helpful to find the response. Adrenal hypoplasia congenita is a differential diagnosis for adrenal insufficiency. Undescended testis, especially in the absence of hypospadias, is a clue for diagnosis.

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Authors' Contributions

Fahimeh Soheilipour: Treatment of the case and supervision. Mohammad Ahmadi: Writing the article. Fatemeh Jesmi: Critical revision and rewrite.

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