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## CASE REPORT

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# *Hyponatremic coma as a manifestation of Addison's disease*

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### Abstract

**Objective:** to show the importance of severe hydroelectrolytic disorder as a consequence of previously undiagnosed chronic disease.

**Description:** case report of hyponatremic coma caused by adrenal crisis in a child with previously undiagnosed Addison's disease despite suggestive clinical findings of this disease in the last four years. After correction of severe hyponatremia, mild hypovolemia, hypernatruria and hyperkalemia, the differential diagnosis of this hydroelectrolytic disorder revealed an adrenal crisis resulting from a primary chronic adrenal insufficiency. Oral treatment with hydrocortisone was efficient in correcting the metabolic disorder and the patient was then discharged.

**Comments:** it is very important to highly suspect of Addison's disease in order to avoid the dangerous consequences of late diagnosis such as severe hydroelectrolytic disorders and retarded growth and development.

*J Pediatr (Rio J) 2001; 77 (4): 337-40: Addison's disease, hyponatremia, hyponatremic coma; adrenal crisis, adrenal insufficiency.*

### Introduction

Addison's disease is the most common cause of chronic, primary adrenal insufficiency. It is frequently caused by progressive, autoimmune destruction of the adrenal cortex (autoimmune adrenalitis) and presents a prevalence of 39 to 60 cases per million in the general population.<sup>1,2</sup>

Most signs and symptoms of adrenal insufficiency are nonspecific and deceptive.<sup>1,2</sup> Hyponatremia is a frequent laboratory finding in adrenal insufficiency and, in cases of rapid establishment and more severity, it can cause seizures and coma. The causes of hyponatremia are varied. In

differential diagnosis of hyponatremia, it is important to consider volemia and natriuresis of patients. Hyponatremia in adrenal insufficiency concurs with hypovolemia and hypernatruresis.<sup>3</sup> Acute adrenal crisis are more frequently caused by infections. Addison's disease is not commonly diagnosed when it presents in the form of coma due to severe hyponatremia.

It is our objective to report a case of Addison's disease diagnosed by acute adrenal crisis and hyponatremic coma. Considering the patient's previous history and the acute level of malnutrition, it is possible that adrenal insufficiency had established itself for a long time. We also carried out a brief review of the literature and did not find reports of other cases of Addison's disease with the same form of manifestation. Moreover, it is also our objective to discuss the importance of symptomatology and early diagnosis.

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### Case report

Nine-year old boy, white, born to family of farmers from the rural area of a small town in the Taquari valley, state of Rio Grande do Sul, Brazil. Patient was admitted to the Pediatric Intensive Care Unit (ICU) of the Hospital Bruno Born, city of Lajeado, Rio Grande do Sul, presenting with seizures followed by coma since the night prior to hospitalization. Patient was born by normal delivery and at term, with birthweight of 2,000 g and without intercurrents. Parents and sister of patient were normal.

Approximately four years ago, patient started presenting frequent episodes of vomit and repeated pneumonia. He also presented important anorexia, asthenia, adynamia and severe weight loss; at times, he was reported not having strength to get out of bed for up to 15 days. In school, patient presented high absenteeism and poor learning. He was reported with extreme difficulty to tolerate low temperatures. Patient presented with results of exams carried out at two different teaching hospitals of Porto Alegre, capital of Rio Grande do Sul, which were carried out during the past three years. The conclusion of investigations were of gastroesophageal reflux and chronic bronchitis. Patient was transferred from the hospital in his hometown, where he had been hospitalized for the past 25 days, to our services receiving intravenous antibiotics for treatment of pneumonia.

Physical examination indicated weight 16 kg (less than P3); height 1.0 m (less than P3); fever; first-degree dehydration; characteristics of severe malnutrition; and coma with hyperextension of the limbs, no neck stiffness, and isochoric pupils responsive to light; colored mucosa and darkening of the skin. Patient was normal for cardiac and pulmonary auscultation, with decreased left-side vesicular murmur. He did not present with abnormalities to abdominal examination. Testicle size was normal for age. Patient extremities were cold and femoral pulse was symmetric and adequate.

Laboratory examinations indicated hemogram with 11.5 g/dl hemoglobin; 35% hematocrit with 8.700 leukocytes/dl and 1% eosinophiles. Arterial gasometry with pH 7.23 and 24 mEq/l bicarbonate. Serum sodium 102 mEq/l; serum potassium 5.1 mEq/l; serum ionic Ca 1.02 mMol/l; glycemia 186 mg/dl; serum urea 16 mg/dl; serum creatinine 0.8 mg/dl; urine sodium 74 mEq/l; and urine potassium 24.7

mEq/l (isolated sample). Chest x-ray indicated extensive parenchymatous consolidation on the left side.

We started antibiotic treatment with intravenous ampicillin. Early and initial rapid correction of serum sodium was carried out with NaCl at 3% in six hours, and we calculated slow correction for 125 mEq/l in 48 hours (this concentration was attained only on the fifth day of hospitalization). Table 1 shows the evolution of values of serum sodium and potassium.

Due to the status of severe malnutrition, severe hyponatremia with high urine sodium levels, and darkening of the skin, we verified the possibility of diagnosis of Addison's disease. Thus, we measured serum cortisol. Patient came out of the coma soon after natremia greater than 110 mEq/l was attained; realimentation began progressively. The boy maintained a constant tendency to hyponatremia. On the second day of hospitalization, cortisol serum results indicated less than 1.2 µg/dl at 8 a.m., and less than 1 µg/dl at 4 p.m. (reference values for 8 a.m. 5-23 µg/dl and for 4 p.m. 3-15 µg/dl). We measured adrenocorticotrophic hormone (ACTH) and antiadrenal antibodies, which indicated 2,900 pg/ml (normal = up to 46 pg/ml) and less than 1:2 (normal = less than 1:2), respectively.

X-ray and CT-scan of the abdomen indicated normal adrenals and no signs of calcification.

With these findings, we confirmed the initial hypothesis of acute adrenal crisis caused by pneumonia and secondary to Addison's disease. We started hormone replacement with hydrocortisone at 15 mg/m<sup>2</sup> orally (2/3 at 8 a.m. and 1/3 between 4 and 6 p.m.) and serum sodium was definitively normalized.

Patient was discharged after 14 days of hospital stay, weighing 17 kg and receiving oral hydrocortisone; patient was indicated to return in 2 weeks for an outpatient examination.

### Discussion

Insufficient production of adrenal hormones can be a result of diseases of the adrenal cortex (primary adrenal insufficiency) or of the hypothalamus-pituitary system due to insufficient secretion of corticotrophin releasing hormone

**Table 1 -** Evolution of serum sodium and potassium levels

	Hospital admission	1 <sup>st</sup> day discharge	2 <sup>nd</sup> day	3 <sup>rd</sup> day	4 <sup>th</sup> day	5 <sup>th</sup> day	6 <sup>th</sup> day	Hospital
<b>Sodium (mEq/l)</b>	102	105	114	115	113	125	137	142
<b>Potassium (mEq/l)</b>	5.1	5.1	4.8	3.6	3.2	4.5	3.9	4.5

(central adrenal insufficiency) or of the ACTH (secondary adrenal insufficiency).<sup>4</sup>

There are two forms of primary adrenal insufficiency, congenital or acquired. The congenital forms are very rare and usually manifest during the neonatal period or the first months of life.<sup>5-8</sup> The exception being adrenoleukodystrophy, that appears at the end of the first 10 years of age and concurs with severe neurological alterations such as blindness, deafness, dementia, quadriplegia and with death.<sup>9</sup>

The acquired forms of primary adrenal insufficiency have Addison's disease as their basis. This disease, in turn, had tuberculosis as its most common cause. Currently, most cases of Addison's disease are related autoimmune destruction of the adrenals (autoimmune adrenalitis) or are idiopathic.<sup>10</sup> The most specific sign of chronic, primary adrenal insufficiency is hyperpigmentation of the skin and mucosae due to high circulating levels of ACTH. Common laboratory findings are hyponatremia (frequent), hyperpotassemia, acidosis, and mild increase in serum creatinine. Diagnosis is confirmed by presence of low serum concentrations of cortisol, combined with high levels of ACTH, in addition to nonresponsiveness to stimulation with ACTH.<sup>11</sup>

The literature also reports other types of primary acquired adrenal insufficiency that also present autoimmune characteristics:

1. Type I polyglandular autoimmune disease (PGA) is associated with chronic mucocutaneous candidiasis and/or acquired hypoparathyroidism. The age of onset is predominately in childhood or in the early adult years. Insulin requiring diabetes and/or autoimmune thyroid disease are infrequent.
2. Type II PGA is associated with insulin requiring diabetes and/or autoimmune thyroid disease(s). It occurs predominately in the middle years of life and it is not associated with hypoparathyroidism.<sup>12</sup>

Primary acquired adrenal insufficiency may also be associated with HIV infection or opportunistic infections,<sup>13</sup> and with other microorganisms and certain drugs.<sup>4</sup>

Our patient presented, for approximately four years, signs and symptoms highly suggestive, though nonspecific, of adrenal insufficiency, including nausea, vomit, anorexia, asthenia, severe weight loss, and difficulty to tolerate low temperatures.

Patient was hospitalized in a state of coma with no meningeal signs nor history of head trauma. He had neither a family history of epilepsy nor history previous seizures. Patient was not exposed to toxic substances or drugs, or medications that might have caused seizures and coma or anticipated acute adrenal crisis. In our early examination of the boy, the finding that most called our attention was darkening of the skin.

Patient history, physical examination, and early laboratory findings allowed for the hypotheses of acute adrenal crisis anticipated by pulmonary infection and, probably, secondary to Addison's disease. We measured serum cortisol and, due to the extremely low levels, we also measured ACTH; next, we started hormone replacement with hydrocortisone.

The very high levels of ACTH confirm the initial hypothesis of chronic, primary adrenal insufficiency. We have to emphasize, however, that stimulation with ACTH was not carried out. This test is the most adequate for final diagnosis of the disease.<sup>4</sup>

Due to the unfeasibility of continuing etiologic investigation of the patient, we indicated the boy to carry out diagnosis complementation elsewhere.

Paterson<sup>14</sup> reports two cases of delay in diagnosis of Addison's disease in a 20-year old patient (four days to diagnosis) and in a 70-year old patient (five weeks to diagnosis; patient evolved to death). The author concluded that early clinical manifestations of adrenal insufficiency are nonspecific, and that alterations in laboratory findings usually are not severe. Both these factors can contribute to delay in diagnosis.

In patients with adrenocortical insufficiency, rapid diagnosis and treatment, even without final diagnosis confirmation, are fundamental and, often, can save lives. Thus, it is important to keep in mind that hyponatremia with elevated urine sodium is not always an indication of inappropriate secretion of the antidiuretic hormone. In this sense, the possibility of Addison's disease should always be taken into consideration, especially in cases of associated hypercalcemia.<sup>15</sup>

It is also important to underscore that normal serum sodium does not necessarily exclude the diagnosis of Addison's disease; though, evidently, it indicates lesser probability of the disease and, thus, may contribute to delay in diagnosis.<sup>16</sup>

In the hypothesis of late diagnosis, this delay may cause severe consequences to patient growth and development. It is important to beware and suspect the possibility of adrenal insufficiency in patients who present with hyponatremia, even without associated hypocalcemia and especially in cases with no clinical and laboratory findings compatible with association of kidney failure. In these situations, emergency hormone treatment should be started promptly, even without laboratory confirmation of cortisol deficiency - based solely on abnormal serum and urine electrolytes.

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