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A Case of Pediatric Adrenal Crisis, Not Just a Condition of Infancy

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Abstract

Pediatric adrenal insufficiency is often thought to mainly affect patient with congenital adrenal hyperplasia (CAH) in the newborn period. However, many cases occur outside of infancy and are not related to CAH. They often presents in an insidious nature with symptoms attributed to more common and often benign etiologies. Unfortunately, if not diagnosed early, adrenal insufficiency can lead to acute adrenal crisis with hemodynamic collapse. We present the case of a 15-year-old young man with a history of hypothyroidism who presented to an ED and developed hypotension and wide complex tachycardia due to hyperkalemia. After initial fluid resuscitation and treatment for his arrhythmia, he was then emergently transported to our hospital for further work up and care. Laboratory studies ultimately diagnosed him with Autoimmune Polyendocrinopathy Syndrome Type II leading to adrenal crisis.

Keywords: Autoimmune polyglandular syndrome; Adrenal crisis; Adrenal insufficiency; Shock

Introduction

Adrenal insufficiency and crisis can be potentially life threatening conditions leading to profound shock if not identified and treated rapidly. Pediatric teaching often focuses on adrenal insufficiency presenting early in life due to congenital adrenal hyperplasia. However, a large number of cases present outside of infancy with varied etiologies including iatrogenicity from overly rapid withdrawal of glucocorticoid therapy, autoimmune phenomenon, tuberculosis, adrenoleukodystrophy, adrenal hemorrhage (Waterhouse-Friedrichson syndrome), adrenal hypoplasia congenita, and Image syndrome [1-3]. A lack of awareness of the occurrence these diseases can lead to missed and delayed diagnosis and resulting increased morbidity and mortality. We discuss the case of a young man presenting with adrenal crisis who was ultimately diagnosed with Autoimmune Polyendocrinopathy Syndrome Type 2 (APS II). The case

illustrates important exam and laboratory findings that can tip of the clinician to the diagnosis of adrenal crisis and then discusses the diagnosis and management of adrenal crisis.

Case Presentation

A 15 year old male with a past medical history of hypothyroidism, attention deficit hyperactivity disorder, and chronic constipation initially presented to an outside emergency department (ED) with one month of worsening constipation, weight loss, decreased appetite, generalized mild abdominal pain, and subjective fevers. These symptoms were subacute to chronic in nature. Computed tomography (CT) imaging of his abdomen 6 days earlier performed as part of the workup for his constipation showed a large colonic stool burden. On arrival to the ED, his vital signs were within the expected range for his age and his abdominal exam was noted to be benign. Given the findings on his recent CT scan, manual disimpaction was performed and an enema was given to treat presumed constipation. Soon after this, his systolic blood pressure abruptly dropped to 56 mmHg at which time he was given two liters of IV fluid. Point of care blood glucose testing showed a level less than 40 mg/dL (ref 60-115 mg/dL). As a serum chemistry was being drawn, he developed a wide complex tachycardia. He was treated with lidocaine with restoration of sinus rhythm and was given a third liter of fluid. His labs returned which showed hyperkalemia to 7.1 mmol/L (ref 3.4-4.7 mmol/L) and hyponatremia to 110 mmol/L (ref 137-146 mmol/L). He was also noted to have significant renal insufficiency with a creatinine of greater than 4 mg/dL (ref 0.42-0.90 mg/dL). He was given calcium gluconate and sodium bicarbonate for the hyperkalemia. Given persistent hypotension he was placed on a dopamine infusion, started on a D5NS infusion, and transported by helicopter to our pediatric intensive care unit (PICU).

On arrival to our PICU, the patient remained hypotensive and repeat labs showed persistent hyperkalemia (4.9 mmol/L), hyponatremia (120 mmol/L), and renal insufficiency. Initial exam showed delayed capillary refill with normal mentation. No hyperpigmentation was noted. He received an additional normal saline bolus and was started on an epinephrine infusion in addition to the dopamine infusion for hypotension. Given concern for adrenal insufficiency, stress dose

hydrocortisone (100 mg IV) was given. As we could not rule out colonic perforation or GI bacterial translocation as a result of his constipation and disimpaction, empiric antibiotics were also initiated. He remained stable over the first night of the admission and workup including echocardiogram, infectious studies, and renal ultrasound showed no findings to explain his rapid decline. He was successfully weaned off of all pressor support on day one of hospitalization. He did have another episode of hyperkalemia (6.4 mmol/L) and he received calcium, insulin, and glucose with lowered potassium. Lab workup added to the blood drawn at initial presentation ultimately showed an undetectable cortisol level and a markedly elevated ACTH level of 180 pg/mL (ref range 6-55 pg/mL) consistent with primary adrenal insufficiency. Additionally, he had a TSH level of 63 U/mL (ref 0.5-4.4 U/mL) and Free T4 level of 0.97 ng/dL (ref 0.54-1.85 ng/dL). An aldosterone level was obtained the day after admission and was 3.7 ng/dL (ref 4-31 ng/dL). Several days later, 21-hydroxylase antibody testing returned with a value of >5000 U/mL (ref 0.0-1.0 U/mL) confirming an autoimmune etiology as the underlying cause of his adrenal insufficiency.

Hydrocortisone was continued at stress dosing until 24 hours after discharge. Given his low sodium and concern for overly rapid correction, it was felt the mineralocorticoid activity of stress dose hydrocortisone would be sufficient to allow safe correction of his electrolytes and additional mineralocorticoid replacement was not started until his sodium level had stabilized on hospital day 6. He was ultimately discharged on day 8 of hospitalization in good condition.

Discussion

APS II, also known as Schmidt syndrome, is defined by the presence of autoimmune adrenal insufficiency with the co-occurrence of autoimmune thyroid disease or type 1 diabetes mellitus [4,5]. Based on studies in the adult literature, adrenal insufficiency usually presents after 20 year of age; however, there are several reports of pediatric patients with the disease [1,6-9]. Approximately 40% to 50% of cases initially present with adrenal insufficiency, 30% to 40% present with thyroid dysfunction or diabetes, and the remainder present with concurrent endocrine dysfunction [6]. Common presenting symptoms include weakness, weight loss, nausea, vomiting, hypotension, hyperpigmentation, and mild hyponatremia and hyperkalemia [1-3,10]. While hypotension has been documented in adult patients, our patient's presentation with symptoms of shock is the first report of such a severe hemodynamic presentation of APS II in the pediatric age range [1,4].

Given the insidious nature of presentation of adrenal insufficiency, a high index of suspicion is needed, lest the disease progress and the patient present in adrenal crisis as in our patient's case. In the case of patients presenting in extremis with no other obvious source of shock, especially with the classic electrolyte disturbances of hyponatremia and hyperkalemia, adrenal insufficiency must be on the differential. For patients with other autoimmune

endocrinopathies and symptoms of adrenal dysfunction, screening cortisol and ACTH stimulation tests may uncover adrenal insufficiency. In the case of APS II, positive 21-hydroxylase antibody testing confirms the auto-immune nature of the disease and should be sent on patients with unexplained adrenal insufficiency [4,11,12]. For patients shown to have autoimmune adrenal insufficiency additional screening for thyroid disease and diabetes should be considered [4]. Our patient showed very low cortisol levels and markedly elevated ACTH consistent with primary adrenal insufficiency and the presence of 21-hydroxylase antibodies with a prior diagnosis of autoimmune hypothyroid confirmed his diagnosis of APS II.

Treatment of adrenal insufficiency is aimed first at hemodynamic stabilization in those presenting in acute adrenal crisis. In our patient's case he received fluid resuscitation and vasopressors followed immediately by stress dose hydrocortisone when the initial electrolyte panel was concerning for adrenal insufficiency. Given the relatively low risk of hydrocortisone therapy in patients with suspected adrenal insufficiency, steroid therapy should not be withheld while awaiting cortisol levels. Once stable, therapy is targeted at providing continued cortisol replacement and normalization of electrolytes. After the patient recovers from their acute presentation they can be transitioned to oral corticosteroids and fludricortisone to replace their cortisol and aldosterone needs. With our patient's extremely low sodium, fludricortisone was not started until near discharge when his sodium was back to the normal range as we were concerned that the potent aldosterone actions of fludricortisone on top of the mineralocorticoid effects of stress dose hydrocortisone would correct his sodium too quickly and place him at risk for central pontine myelinolysis. In patients with adrenal and hypothyroid disease it is imperative to treat the adrenal insufficiency prior to starting thyroid therapy, as thyroxine therapy can alter cortisol needs and metabolism thus precipitating or worsening adrenal crisis [4,13].

At discharge, patients should also be provided with a clear plan and medication supply for "sick days" requiring stress dosing of their steroid.

Conclusion

Adrenal insufficiency is a potentially lethal disease that affects patients across the pediatric age range. Because of its insidious onset, early symptoms are often missed and patients can present in extremis. In patients with shock of unknown etiology, the clinician must include adrenal insufficiency in the differential and should have a low threshold to give stress dose steroids.

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