CLINICAL VIGNETTE

Acute Kidney Injury and Hyperkalemia as the First Presentation of Addison Disease

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Case Report

A 28-year-old male presents to emergency department with severe fatigue, generalized weakness and nausea. Symptoms started 2 to 3 weeks prior with worsening of the symptoms 2-3 days prior to presentation to emergency department. He denied fever or chills, and respiratory, cardiac, or musculoskeletal symptoms. He had no previous medical history, he was not taking chronic medications and had no previous hospitalization. Family history and social history unremarkable. Physical examination on presentation to emergency department showed a well-nourished, well developed young man in no distress or discomfort. Vital signs; blood pressure 102/62 mmHg with mild orthostasis on sitting position, heart rate 96 per minute, respiratory rate 14 and afebrile. Physical examination of lungs, heart and abdomen within normal limits. Patient's initial laboratory tests remarkable for a serum creatinine of 1.6 mg/dL, serum potassium of 8.2 mmol/L. Urine test including urine drug screen was negative. Chest X Ray normal. His hyperkalemia was treated with intravenous normal saline, insulin and glucose, sodium bicarbonate and calcium gluconate and was admitted. His initial diagnosis of acute kidney injury associated with hyperkalemia secondary to volume depletion and pre-renal azotemia. Patient continued to be hyperkalemic with serum potassium between 5.9- 6.8 moll/L, despite improvement of his renal function and treatment with intravenous insulin and glucose as well as oral sodium polystyrene sulfonate on several occasions over the next 48 hours. Given the persistent hyperkalemia and patient' symptoms a diagnosis of adrenal gland insufficiency was considered. Laboratory tests including serum cortisol, serum adrenocorticotropin, hormone, ACTH, aldosterone, plasma renin activity, serum and urine electrolytes were sent. The laboratory tests showed a low morning (8 A.M.) serum cortisol of 2mcg/dL; a high plasma ACTH of 1786 pg/mL; a low serum aldosterone of 1ng/d; and an elevated plasma renin activity of 18.4 ng/ml/hour. Patient's laboratory test results consistent with primary hypoadrenalism, Addison disease (AD). Patient was started on corticosteroid and mineralocorticoid with improvement of his symptoms and hyperkalemia. Patient was discharged on maintenance dose of prednisone and fludrocortisone for his Addison disease.

Discussion

Addison disease, AD, is a relatively rare endocrine disorder with a prevalence of one in 20,000 persons in United States and Western Europe,[1] and an incidence of 4.4 to 6.2 new cases/ million/year in Europe.[2,3] AD, or primary adrenal insufficiency, is a chronic disorder of the adrenal cortex resulting in inadequate production of glucocorticoid and mineralocorticoid.[4]

Patients with Addison disease usually present with non-specific, subtle symptoms including fatigue, generalized weakness, nausea, and muscle ache that make the diagnosis difficult for clinicians. These non-specific symptoms may deteriorate rapidly into life-threatening condition, Addissonian/Adrenal crises, if not treated promptly and appropriately. Therefore, high clinical suspicion is needed to avoid misdiagnosis of adrenal insufficiency.

The etiology of the AD has changed over the past few decades. Tuberculosis (TB) was the predominant cause (70%) of cases of AD in Europe in 1930s[5], but with improved diagnosis and treatment of tuberculosis, AD due to TB has significantly declined with 3% in Italy in a recent report.[6] The most common cause of AD in developed countries is autoimmune disease either in isolation or in association with autoimmune polyendocrinopathy syndromes. Worldwide, TB is still the most common cause of AD.[7]

Our patient received several liters of intravenous normal saline over the first 48 hours of his hospitalization for his low blood pressure, orthostatic symptoms, and reduced renal function. The lack of obvious evidence for fluid loss and volume depletion and relatively high level of serum potassium, 8.2 mmol/L, for mildly reduced renal function, creatinine 1.6 mg/dL, raised the suspicion for adrenal insufficiency. The patient was empirically treated for adrenal insufficiency with corticosteroid and mineral corticoid. Laboratory tests subsequently confirmed the diagnosis of AD.

The patient's symptoms and hyperkalemia resolved after intravenous fluid administration and initiation of treatment for adrenal insufficiency with hydrocortisone and fludrocortisone.

The normal circadian rhythm of endogenous cortisol production, peak level of cortisol in the morning after waking, and gradual decline in the serum level during rest of the day to nothing at midnight, is not achieved with current corticosteroid regimen in treatment of AD. Modified- release hydrocortisone tablets that can mimic circadian rhythm has been proposed in this respect.[7,8] There is also a controversy in management with regard to other endogenous hormones that are normally produced by adrenal gland cortex that are not replaced in female

patients with AD at present, and that include androgenic hormones, Dehydroepiandrosterone (DHEA) and dehydro-epiandrosterone sulphate.[7,9] Further investigation is needed to address whether using the modified-release hydrocortisone tablet in patient with AD and replacing androgenic hormones in female patients with AD are beneficial. These may improve the quality of life and other outcomes in these patients.

REFERENCES

1. **Michels A, Michels N**. Addison disease: early detection and treatment principles. *Am Fam Physician*. 2014 Apr 1;89(7):563-8. PMID: 24695602.
2. **Chantzichristos D, Persson A, Eliasson B, Miftaraj M, Franzén S, Svensson AM, Johannsson G**. Incidence, prevalence and seasonal onset variation of Addison's disease among persons with type 1 diabetes mellitus: nationwide, matched cohort studies. *Eur J Endocrinol*. 2018 Jan;178(1):113-120. doi: 10.1530/EJE-17-0751. Epub 2017 Oct 24. PMID: 29066573.
3. **Kong MF, Jeffcoate W**. Eighty-six cases of Addison's disease. *Clin Endocrinol (Oxf)*. 1994 Dec;41(6):757-61. doi: 10.1111/j.1365-2265.1994.tb02790.x. PMID: 7889611.
4. **Arlt W, Allolio B**. Adrenal insufficiency. *Lancet*. 2003 May 31;361(9372):1881-93. doi: 10.1016/S0140-6736(03)13492-7. PMID: 12788587.
5. **Guttman PH**. Addison's disease-a statistical analysis of 566 cases and a study of the pathology. *Arch Pathol*. 1930;10:742, 896.
6. **Betterle C, Scarpa R, Garelli S, Morlin L, Lazzarotto F, Presotto F, Coco G, Masiero S, Parolo A, Albergoni MP, Favero R, Barollo S, Salvà M, Basso D, Chen S, Rees Smith B, Furmaniak J, Mantero F**. Addison's disease: a survey on 633 patients in Padova. *Eur J Endocrinol*. 2013 Oct 21;169(6):773-84. doi: 10.1530/EJE-13-0528. PMID: 24014553.
7. **Chakera AJ, Vaidya B**. Addison disease in adults: diagnosis and management. *Am J Med*. 2010 May;123(5):409-13. doi: 10.1016/j.amjmed.2009.12.017. PMID: 20399314.
8. **Debono M, Ghobadi C, Rostami-Hodjegan A, Huatan H, Campbell MJ, Newell-Price J, Darzy K, Merke DP, Arlt W, Ross RJ**. Modified-release hydrocortisone to provide circadian cortisol profiles. *J Clin Endocrinol Metab*. 2009 May;94(5):1548-54. doi: 10.1210/jc.2008-2380. Epub 2009 Feb 17. PMID: 19223520; PMCID: PMC2684472.
9. **Alkatib AA, Cosma M, Elamin MB, Erickson D, Swiglo BA, Erwin PJ, Montori VM**. A systematic review and meta-analysis of randomized placebo-controlled trials of DHEA treatment effects on quality of life in women with adrenal insufficiency. *J Clin Endocrinol Metab*. 2009 Oct;94(10):3676-81. doi: 10.1210/jc.2009-0672. Epub 2009 Sep 22. PMID: 19773400.