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MINI-FOCUS ISSUE ON HEART FAILURE

BEGINNER

CASE REPORT: CLINICAL CASE

Reversible Biventricular Heart Failure Due to Primary Adrenal Insufficiency

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ABSTRACT

Adrenal insufficiency is a rare cause of heart failure. We describe a young patient who presented with new-onset biventricular systolic heart failure due to primary adrenal insufficiency. The patient was initiated on hydrocortisone, with rapid improvement of both left and right ventricular systolic function. (**Level of Difficulty: Beginner.**)
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HISTORY OF PRESENTATION

An otherwise healthy 23-year-old man presented to the emergency department with fatigue, lightheadedness, and progressive dyspnea on exertion for the past 3 months. He endorsed positional lightheadedness, worse when standing from a seated position, and significant dyspnea with minimal exertion, such as showering. He had no recent travel or sick contacts.

In the emergency department, his blood pressure was 97/51 mm Hg, heart rate was 109 beats/min, respiratory rate was 17 breaths/min, and oxygen saturation was 96% on room air. On physical examination, he was found to have diffuse skin hyperpigmentation relative to his baseline. No jugular venous distension or lower extremity edema was noted. His serum sodium was low at 121 mEq/l (normal range: 133 to 146 mEq/l), and serum potassium was elevated at 5.3 mEq/l (normal range: 3.5 to 5.1 mEq/l).

Because of his progressive dyspnea on exertion, an echocardiogram was obtained, which revealed global left ventricular systolic dysfunction (ejection fraction 35%), including severe anteroseptal hypokinesis and reduced right ventricular function (Videos 1 and 2).

LEARNING OBJECTIVES

- To recognize primary adrenal insufficiency as a cause of biventricular heart failure.
- To highlight the importance of glucocorticoid receptor signaling in maintaining normal cardiac function.
- To understand that prompt initiation of adrenal replacement therapy in an adrenal crisis rapidly improves cardiac function.

MEDICAL HISTORY

The patient had no significant medical history and took no medications or over-the-counter supplements. There was no family history of early myocardial infarction, heart failure, or sudden cardiac death. He had recently graduated from college and endorsed rare alcohol use with no illicit drug use.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, or patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

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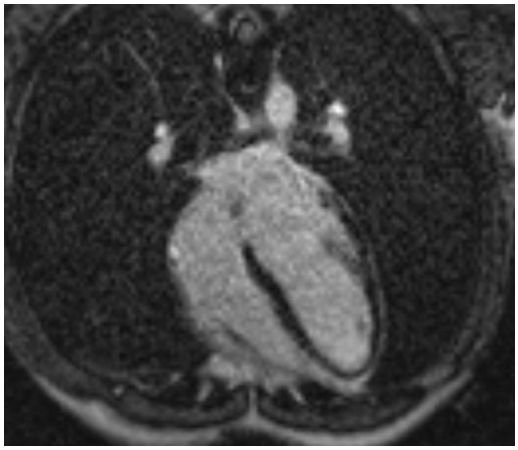
FIGURE 1 4-Chamber Phase-Sensitive Inversion Recovery TurboFLASH View From Post-Treatment Cardiac Magnetic Resonance Imaging Demonstrating No Late Gadolinium Enhancement



DIFFERENTIAL DIAGNOSIS

Because of the dyspnea on exertion, skin pigmentation, hyponatremia, hyperkalemia, and global systolic dysfunction, the leading diagnosis for our patient was primary adrenal insufficiency. Because of the young age of our patient and the rapid onset of symptoms, the differential diagnosis also included genetic cardiomyopathies (such as left ventricular noncompaction) and viral myocarditis.

INVESTIGATIONS

On admission, troponin level was 0.0 ng/ml (normal range: 0.00 to 0.04 ng/ml), and B-type natriuretic peptide level was 4 pg/ml (normal range: <100 pg/ml). Chest radiography was unremarkable. Twelve-lead electrocardiography showed sinus tachycardia with right-axis deviation and left posterior fascicular block.

His 8:00 AM cortisol level was found to be 1.3 μg/dl (normal range: 5.0 to 25 μg/dl), with minimal response to cosyntropin stimulation test (post-cosyntropin cortisol 1.5 μg/dl). Adrenocorticotropic hormone level was elevated at 1,047 pg/ml (normal range: 6 to 50 pg/ml). The patient was also noted to have a 21-hydroxylase antibody titer of 195 U/ml (normal range: <1 U/ml), confirming primary autoimmune adrenalitis (1).

MANAGEMENT

The patient was started on 50 mg of hydrocortisone every 12 h and carvedilol 3.125 mg twice a day. To assess improvement in cardiac function and to rule out alternative etiologies of cardiac dysfunction, cardiac magnetic resonance imaging with contrast and stress imaging was obtained on day 3 of treatment and demonstrated an improved left ventricular ejection fraction from 35% to 55%, resolution of regional wall motion abnormalities, normal right ventricular function, and no evidence of trabeculations, delayed enhancement, or ischemia (**Figure 1**).

At discharge, the patient's sodium level had improved to 129 mEq/l and his potassium level to 4.5 mEq/l. His blood pressure had also increased to 114/67 mm Hg. He was transitioned to a daily oral regimen of 20 mg hydrocortisone and 0.1 mg fludrocortisone in the morning and 10 mg hydrocortisone in the evening and discharged home with outpatient cardiology and endocrinology follow-up appointments.

DISCUSSION

Patients with primary adrenal insufficiency, also known as Addison's disease, have variable cardiac presentations, ranging from no symptoms to cardiac arrest (2). First described in 1963, primary adrenal insufficiency is a rare cause of new-onset heart failure (3). Of the few case reports describing adrenal insufficiency-mediated heart failure, the unifying theme is reversibility of cardiac dysfunction with glucocorticoid and mineralocorticoid replacement therapy (3–6).

The pathophysiology of heart failure due to primary adrenal insufficiency is not well understood. Contributing factors include electrolyte imbalances, hemoconcentration with subsequent poor coronary blood flow, and the direct effects of the loss of steroid hormones on the myocardium. In a surgical model of adrenal insufficiency, adrenalectomy in rats led to decreased papillary muscle contractile force, which was reversed with dexamethasone replacement therapy (7). In a genetic model of glucocorticoid deficiency, cardiomyocyte-specific deletion of the glucocorticoid receptor in mice led to spontaneous systolic heart failure and hypertrophy, with decreased expression of genes responsible for cardiac contractility and cardiomyocyte survival and increased expression of genes involved in inflammatory processes and cardiac hypertrophy (8).

In our case, glucocorticoid deficiency likely caused decreased myocardial and papillary muscle contractility as well as activation of proinflammatory genes, leading to acute systolic heart failure. It is likely that a secondary stressor (e.g., social stressors or a viral illness) also contributed to the patient's left ventricular dysfunction, thus culminating in heart failure with

reduced ejection fraction. Because of his young age and lack of comorbidities and the early identification of heart failure, our patient presented in compensated heart failure without signs of fluid overload.

The rapid reversibility of cardiac function in our case is notable. After 96 h of therapy, the patient exhibited significant improvement in left ventricular ejection fraction, from 35% to 55%, and normalization of right ventricular function. This demonstrates the importance of rapid identification and treatment of adrenal insufficiency to restore cardiac function and the role of glucocorticoid and mineralocorticoid signaling as a potential therapeutic target in heart failure.

Our case is also unique in that right ventricular dysfunction coexisted with left ventricular dysfunction during the patient's initial presentation. To our knowledge, biventricular dysfunction due to adrenal insufficiency has not been previously described. The patient's right ventricular function also rapidly recovered with steroid replacement therapy, which strongly suggests that the biventricular dysfunction was due to acute adrenal insufficiency. Further research is needed on how adrenal hormones affect right ventricular function and if the molecular mechanisms are distinct from those affecting left ventricular function.

It is important to note that chronic treatment of adrenal insufficiency is also associated with heart failure. In a group of 22 patients with Addison's disease, 7 developed heart failure over a follow-up period of 30 years. Decreasing or discontinuing fludrocortisone, as well as discontinuing salt supplementation, resulted in subsequent improvement of their cardiac symptoms (9). Therefore, adrenal hormones exert both positive and negative effects on the myocardium.

FOLLOW-UP

The patient has had no episodes of fatigue, lightheadedness, or dyspnea on exertion since being initiated on oral hydrocortisone and fludrocortisone. Repeat echocardiography after 3 months showed preserved recovery of left ventricular (ejection fraction 53%) and right ventricular systolic function, with normal global left ventricular longitudinal strain (18.8%; normal range >18%) (Videos 3 and 4).

CONCLUSIONS

Primary adrenal insufficiency contributes to cardiovascular dysfunction and may present as new-onset systolic heart failure. Initiation of adrenal replacement therapy in patients with adrenal failure leads to a rapid improvement in cardiac function. Further studies are needed to investigate the molecular mechanisms of glucocorticoid and mineralocorticoid effects on the myocardium.

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KEY WORDS autoimmune, echocardiography, systolic heart failure

APPENDIX For supplemental videos, please see the online version of this paper.