Journal of Chitwan Medical College 2021;11(37):141-144
Available online at: www.jcmc.com.np

CASE REPORT

HEART FAILURE WITH LOW EJECTION FRACTION AS A PRESENTATION OF SEVERE PRIMARY ADRENAL INSUFFICIENCY

Saurav Khatiwada[1], Bishnu Singh[2], Laxman Mandal[1,*], Rahul Mittal[3], Rupesh Jaiswal[3]

[1]Department of Medicine Department of Medicine, Chitwan Medical College, Bharatpur-10, Chitwan, Nepal
[2]Medical Officer, Department of Medicine, Himal Hospital, Gyaneshwor, Kathmandu, Nepal
[3]Intern, Department of Medicine, Chitwan Medical College, Bharatpur-10, Chitwan, Nepal

Received: 15 Aug, 2021

Accepted: 1 Sep, 2021

Published: 30 Sep, 2021

Key words: Adrenal insufficiency; Glucocorticoid; Left ventrical ejection fraction; Mineralocorticoids.

***Correspondence to:** Laxman Mandal, Department of Medicine, Chitwan Medical College, Bharatpur-10, Chitwan, Nepal.*
Email: Drlaxmanmandal@gmail.com

Citation

Khatiwada S, Singh B, Mandal L, Mittal R, Jaiswal R. Heart failure with low ejection fraction as a presentation of severe primary adrenal insufficiency. Journal of Chitwan Medical College.2021;11(37):141-4.

ABSTRACT

Addison's disease or primary adrenal insufficiency is a condition where there is decreased production of glucocorticoid and mineralocorticoid from adrenal cortex and it's prevalance is around 100- 140 cases per millions in western societies. It has wide range of clinical features and is a serious condition. If diagnosed and treated in time, patient's condition can improve significantly. Here we present 37 years old female who presented with wide range of vague clinical features and was in shock and on investigation, her serum sodium was low and potassium level was high. With usual treatment of shock, patient condition didn't improve. So, echocardiography was done which showed global Left Ventricular wall hypokinesia with left ventrical ejection fraction of 25-30%. She was also taking treatment for hypothyroidism. Endocrinology consultation was done for her hypothyroidism, hyponatremia and possible adrenal crisis. Serum Cortisol was sent which was found low. With treatment with glucocorticoids and mineralcorticoids, patient improved significantly. She recovered from shock, her serum sodium and potassium became normal and after one month, left ventricular ejection fraction improved to 50%. So, with timely diagnosis and proper treatment, Addison's disease can be treated easily.

INTRODUCTION

Addison's disease or primary adrenal insufficiency, is a serious yet easily correctible endocrine disorder associated with subnormal production of glucocorticoids and mineralocorticoids from the adrenal cortex, with normal pituitary response of raised ACTH levels.

Common causes include autoimmune which comprises around 85% in Western Europe and rest includes tuberculosis, adrenal hemorrhage, genetic disorders and other infectious diseases.[1,3,7] Patient frequently presents with imprecise primary symptoms such as weakness, fatigue, anorexia, weight loss and likely hyperpigmentation.[2]. Hyperpigmentation is more obvious in palmar creases, vermilion border of the lips, mucosa of buccal cavity and around fresh scars and nipples.[4,5] Patients usually have hyponatremia, hyperkalemia, and metabolic acidosis.[6] The current prevalence of the condition in Western societies is around 100- 140 cases per million as assessed by Husebye et al.[3]

The diagnosis is established through a biochemical assessment of the hypothalamus pituitary-adrenal (HPA) axis in addition to mineralocorticoid function. Prompt diagnosis is critical so that early and adequate treatment can be initiated and patients can be followed up appropriately.[8]

The cardiovascular manifestations of Addison's disease include hypotension, syncope, and arrhythmias, while dilated cardiomyopathy and heart failure being rare life-threatening complication.[10-14]We describe a distinctive case of a middle-aged female with primary adrenal insufficiency complicated by acute adrenal crisis and severe myocardial dysfunction (cardiac failure) that promptly improved with the administration of steroids.

CASE REPORT

A 37-year-old female presented to gastroenterology OPD with complaints of generalized weakness for five months and vomiting for last 10 days. Weakness was described as both lack of energy to perform chores like washing clothes and walking more than one flight of stairs without resting as well as easy fatigability. She had amenorrhea of six months duration which had not been investigated or managed. Her medical history in last three months was complicated with iatrogenic hypothyroidism resulting from inadvertent use of carbimazole at 10mg/day for 2 months for suppressed TSH (TSH of 0.3 mIU/ml). She had empirically received anti-thyroidal agent while she had sub-acute thyroiditis. This was then rectified with cor-

rectional levothyroxine use at dose of 50ug/day for 16 days prior to presentation at our hospital. Meanwhile, she revealed history of orthostatic dizziness and multiple brief pre-syncopal episodes for past four months especially on abrupt standing. She had sought medical attention for her symptoms over last 10 days which were worsening anorexia with nausea, recurrent non-projectile vomiting, and increased sleepiness.

On examination, she was disoriented and in shock with blood pressure of 80/50 mm of Hg in right arm supine position with a pulse of 90 beats per minute. Her GCS was E3V5M6. Periphery was cold and clammy. Her height was 149 cm and weight was 40 kg. Systemic examination including bilateral lung fields and cardiac auscultation were unremarkable.

She was admitted, and managed based on history, examination and preliminary investigations. Her detailed reports are listed in Table 1. It was remarkable for serum sodium of 109 meq/l (normal range 133-146meq/l) and serum potassium of 5.8 meq/l (normal range 3.5- 5.5meq/l). WBC count was 14100 /mm3 with microcytic hypochromic anemia (Hb: 8.5 g/dl) and mild transaminitis. Thyroid function test revealed hypothyroidism with serum fT4 of 0.85 ng/dl (0.89-1.76 ng/dl) and TSH of 105.3 5µIU/ml (0.45-5.5 uIU/ml). Urine pregnancy test was negative. A 12 lead ECG and chest X-ray were unremarkable.

She was started on iv crystalloids and broad-spectrum antibiotics. For her severe symptomatic hyponatremia, she had been on intermittent hypertonic saline use for five days in intensive care unit. BP was persistently low and did not improve with fluid administration, so she was put on nor-adrenaline since the day of admission. An echocardiography was conducted to rule out cardiogenic shock. It revealed global left ventricular wall hypokinesia, mild tricuspid regurgitation with TRPG of 20 mmHg. There was grade I diastolic dysfunction with left ventricular ejection fraction of 25-30%. Levothyroxine (75 mcg) supplementation had also been escalated for her iatrogenic hypothyroidism.

Serum cortisol was sent due to suspicion of adrenal insufficiency and endocrinology consultation was sought for her hypothyroidism, hyponatremia and possible adrenal crisis.

On our further probing, there was history of loss of appetite with significant weight loss of around 15 kg in last six months. There was history of darkening of skin complexion for last six months. There was no history of tuberculosis or similar history of skin pigmentation or consanguinity in family. Focused physical examination revealed subtle hyperpigmentation over knuckles, palmar creases and oral mucosa. Her random serum cortisol was low (0.5 ug/dl) which suggested adrenal insufficiency.

Pt was administered with IV hydrocortisone (she was started on hydrocortisone supplementation (100mg stat followed by 50mg qid)) along with IV crystalloids and broad-spectrum antibiotics. Her BP was persistently low and did not improve with fluid administration so the patient was supported with vasopressors (nor-adrenaline 3.75 ml/hr) for 3 days. Therefore, an echocardiography was conducted to rule out cardiogenic shock. It revealed global LV wall hypokinesia, mild Tricuspid regurgitation with TRPG of 20 mmHg. There was grade I diastolic dysfunction with left ventricular ejection fraction of 25-30%. Levothyroxine (75 mcg) supplementation was given to counter iatrogenic hypothyroidism. Laboratory results which depicted severe hyponatremia and hyperkalemia as mentioned above in addition to cardiovascular collapse raises the suspicion of adrenal crisis.

Table 1: Summary of Blood Tests

Parameter		Refrence range	Encounter	
			At the time of admission	At the time of discharge
CBC	Hb %	12-16 gm/dl	8.5	
	WBC	4000-11000/cumm	14100	
	Platelet	150000- 400000/cumm	177000	
BMC	Na	135-150 mmol/L	109	136
	K	3.5-5.5 mmol/L	5.8	4.1
	Urea	15-45 mg/dl	50	19
	Creatinine	0.4-1.4 mg/dl	1.07	0.58
TFT	FT3	2.30-4.20 pg/dl	2.03	2.49
	FT4	0.89-1.76 pg/ml	0.85	0.91
	TSH	0.35- 5.50 microIU/ml	105.32	7.28

In order to assess the cause of severe hyponatremia with accompanying cardio vascular collapse, serum morning cortisol level were assessed and was found to be 0.5µg/dL.(normal range:3.7 – 19.4µg/dL). Adrenocorticotrophic hormones level were elevated at 190pg/ml(normal value:<46.0pg/ml). This findings led to the diagnosis of primary adrenal insufficiency. Minealocorticiods 21-hydroxylase antibody titer was not done due to financial constraints. A noncontrast CT scan of abdomen and pelvis was unrevealing and showed normal bilateral suprarenal glands without any focal lesions. Tuberculosis as a cause of Primary Adrenal Insufficiency was ruled out by normal chest x ray findings, negative family history of TB and normal Ct abdomen findings. Supplementary causes of Primary Adrenal Insufficiency such as malignancy, hemochromatosis, infiltrative diseases, adrenoleukodystrophy are ruled out. USG abdomen was normal. N-terminal brain natriuretic peptide was not done due to financial restraints. Through the Echocardiography finding of acute heart failure

due to primary adrenal insufficiency, the patient was treated for medical treatment with parenteral diuretics, Angiotensin receptor blocker, beta blockade along with fluid and salt restriction.

Patient was started on hydrocortisone 100 mg IV stat followed by 50 mg four times a day for 2 days and was then switched to oral prednisolone. She also received Fludrocortisone 100 µg once daily. Patient blood pressure values improved 2 days after admission, hence vasopressor support was withdrawn. To assess improvement in cardiac function Echocardiography was performed after 5 days of initiation of therapy which showed improvement in LVEF (from 25-30% to 35%).

At discharge of the patient, sodium and potassium values were within normal limits. Her blood pressure was 100/60 mm Hg. She was switched to oral prednisolone 5 mg once daily after breakfast and 100 µg Fludrocortisone in the morning and discharged home with advice for follow up in cardiology and endocrinology departments. After 1 month follow up, transthoracic echocardiography was done which showed improvement in LVEF to 50 %.

DISCUSSION

To our knowledge this is the first reported case of reversible cardiomyopathy as a complication of primary adrenal insufficiency from Nepal. We present a case of primary adrenal insufficiency in a 37-year-old female which was complicated with heart failure (REVERSIBLE cardiomyopathy) wherein a near complete recovery of normal cardiac function was achieved after the initiation of Hydrocortisone.

Due to varied clinical signs and symptoms, the diagnosis of Addison's disease is often delayed while many a times the diagnosis of Addison's disease is made when patient presents with symptoms of acute adrenal insufficiency.[3]

Cardiac manifestation of this disease is variable ranging from no symptoms to cardiac arrest.[9] Cardiovascular manifestation of primary adrenal insufficiency involve hypotension, syncope and arrhythmias while dilated cardiomyopathy and heart failure being rarer life threatening entities.[10-14] With prompt glucocorticoid and mineralocorticoid replacement therapy, the cardiac dysfunction can be reversed as described in few case reports illustrating adrenal insufficiency mediated cardiac failure.[12-15]

The exact cause of heart failure in Addisons disease is not clear. Some of the factors include diminished blood volume, hemoconcentration leading to perhaps insufficient coronary blood flow, dyselectrolytemia, decreased activity of one or more cortical hormones on cardiac muscle, poor elimination with decreased glycogen reserves.[8]

Glucocorticoid has a major role in cardiac contractility. Study shows a correlation between diminished endogenous glucocorticoid with development of myocardial dysfunction. Study shows that adrenalectomized rats have impaired myocardial contractility, which was associated with a depletion of microsomal phosphorylase activity and marked reduction in calcium uptake in the sarcoplasmic reticulum.[16-17] These can result in impaired glycogenolysis and reduced cardiac contractility. Likewise, glucocorticoid modulates sympathetic activity too. Glucocorticoid deficiency is associated with downregulation of adrenergic receptors, decreased adrenaline synthesis and decrease cardiovascular reactivity to catecholamines. Study shows that Glucocorticoid deficiency may also result in the loss of protective effects against catecholamine. These underlying mechanisms could explain the association between severe myocardial dysfunction and adrenal insufficiency.[18,19]

Despite having a low EF, our patient did not present with edema, possibly due to the impaired renin-angiotensin-aldosterone system caused by Addison's disease. Therefore, it is important to note that Addison's disease could mask the accompanying heart failure, and we suggest performing heart echography in patients with Addison's disease if heart dysfunction is suspected by history or physical examination.

CONCLUSION

Addison's disease might present with features of severe myocardial dysfunction. So, any patient presenting with severe myocardial dysfunction with low serum Sodium level and high Potassium level, not responding to usual treatment and where cause is not obvious, adrenal insufficiency should be also considered which is easily treatable condition. With proper treatment, patients' condition can improve significantly.

REFERENCES:

1. Nieman LK, Turner ML. Addison's disease.Clin Dermatol. Jul-Aug 2006;24(4):276-80. [DOI]
2. Nicolaides NC, Chrousos GP, Charmandari E. Adrenal Insufficiency. [Updated 2017 Oct 14]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: [LINK]
3. Husebye ES, Allolio B, Arlt W, Badenhoop K, Bensing S, Betterle C, et al. Consensus statement on the diagnosis, treatment and follow-up of patients with primary adrenal insufficiency. J Intern Med. 2014 Feb;275(2):104-15. [DOI]
4. Hellesen A, Bratland E, Husebye ES. Autoimmune Addison's disease–An update on pathogenesis. Ann Endocrinol (Paris). 2018 Jun;79(3):157-63. [DOI]
5. Michels A, Michels N. Addison disease: early detection and treatment principles. Am Fam Physician. 2014 Apr 1;89(7):563-8. [PMID]
6. Brooke AM, Monson JP. Addison's disease. Medicine. 2009;37(8):416-9. [DOI]
7. Barthel A, Benker G, Berens K, Diederich S, Manfras B, Gruber M, et al. An update on Addison's disease. Exp Clin Endocrinol Diabetes. 2019 Feb;127(2-03):165-175. [DOI]
8. Goodof II, Macbryde CM. Heart failure in Addison's disease with myocardial changes of potassium deficiency. The Journal of Clinical Endocrinology. 1944 Jan 1;4(1):30-4. [DOI]

9. Krug JJ. Cardiac arrest secondary to Addison's disease. Ann Emerg Med. 1986 Jun;15(6):735-7. [DOI]

10. Bhattacharyya A, Tymms DJ. Heart failure with fludrocortisone in Addison's disease. J R Soc Med. 1998 Aug;91(8):433-4. [DOI]

11. Krishnamoorthy A, Mentz RJ, Hyland KA, McMillan EB, Patel CB, Milano CA, Hernandez AF. A crisis of the heart: an acute reversible cardiomyopathy bridged to recovery in a patient with Addison's disease. ASAIO J. Nov-Dec 2013;59(6):668-70. [DOI]

12. Cushner GB, Zahler SF, Hills AG. Untreated Addison's disease complicated by pulmonary congestion due to left ventricular failure. Ann Intern Med. 1963;58:341-6. [DOI]

13. Afzal A, Khaja F. Reversible cardiomyopathy associated with Addison's disease. Can J Cardiol. 2000;16:377-9. [PMID]

14. Wolff B, Machill K, Schulzki I, Schumacher D, Werner D. Acute reversible cardiomyopathy with cardiogenic shock in a patient with Addisonian crisis: a case report. Int J Cardiol. 2007;116:e71-e73. [DOI]

15. Mozolevska V, Schwartz A, Cheung D, Shaikh B, Bhagirath KM, Jassal DS. Addison's disease and dilated cardiomyopathy: a case report and review of the literature. Case Rep Cardiol. 2016;2016:4362514. [DOI]

16. Narayanan N. Effects of adrenalectomy and in vivo administration of dexamethasone on ATP-dependent calcium accumulation by sarcoplasmic reticulum from rat heart. J Mol Cell Cardiol. 1983;15:7—15. [DOI]

17. Rao MK, Xu A, Narayanan N. Glucocorticoid modulation of protein phosphorylation and sarcoplasmic reticulum function in rat myocardium. Am J Physiol Heart Circ Physiol. 2001;281:H325—33. [DOI]

18. Collins S, Caron MG, Lefkowitz RJ. Beta-Adrenergic receptors in hamster smooth muscle cells are transcriptionally regulated by glucocorticoids. J Biol Chem.1988;263:9067—70. [PMID]

19. Orlowski J, Lingrel JB. Thyroid and glucocorticoid hormones regulate the expression of multiple Na, K-ATPase genes in cultured neonatal rat cardiac myocytes. J Biol Chem. 1990;265:3462—70. [PMID]