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Case Report

A case of tuberculosis of adrenal gland presenting as acute adrenal insufficiency following initiation of anti-tubercular therapy

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ABSTRACT

Adrenal tuberculosis is one important cause of acute or chronic adrenal insufficiency in developing countries like India. There are many random cases in literature describing various clinical situations of adrenal tuberculosis presenting with adrenal insufficiency, especially after initiation of anti-tubercular therapy. A 43-year-old male recently diagnosed patient with pulmonary tuberculosis and chronic coronary syndrome was admitted for acute decompensated heart failure with pulmonary edema. He was taking fixed dose combination anti-tubercular therapy. During admission, he had hyponatremia (serum sodium 96 mEq/L) and during treatment, he developed hypotension and shock, which were appropriately treated. Due to ischemic hepatitis, anti-tubercular treatment (ATT) was modified to streptomycin, ethambutol, and ofloxacin regimen to avoid further hepatotoxicity. Hyponatremia and shock recovered. Rifampicin and isoniazid were restarted. He again developed easy fatigability, nausea, vomiting, and hypotension. Suspecting adrenal insufficiency, fasting serum cortisol, and adrenocorticotropic hormone (ACTH) were done, which revealed a low serum fasting cortisol and high ACTH. Computed tomography abdomen showed enlarged left adrenal gland with calcifications. He was started on prednisolone 2 mg/kg/day with full dose fixed dose ATT, following which his symptoms resolved.

Keywords: Adrenal insufficiency, Rifampicin, Tuberculosis

INTRODUCTION

Infection of the adrenal gland is the second most common cause of primary adrenal insufficiency globally, next to autoimmune adrenalitis.[1] Among infections, tuberculosis of the adrenal gland remains one of the causes of primary adrenal insufficiency in developing countries. Thomas Addison, in his report on adrenal insufficiency, described 11 patients with tuberculosis of the adrenal gland.[2] The insufficiency can occur as a result of direct involvement or due to rifampicin containing anti-tubercular therapy, which can induce cortisol metabolism.[3] There are many random cases in the literature describing various clinical situations of adrenal tuberculosis with adrenal insufficiency, especially after initiation of anti-tubercular therapy.[3-5] We present one such case report.

CASE REPORT

A 43-year-old male was admitted in the Institute of Internal Medicine, Madras Medical College with c/o fever of 1 day duration and breathlessness for 4 days. The fever was high grade, intermittent fever, with no chills, and rigor. Breathlessness was initially exertional New York Heart Association (NYHA 2) which, then, progressed to breathlessness at rest (NYHA 4) during presentation.

He had presented with complaints of cough, expectoration, and exertional breathlessness 3 weeks back when he was diagnosed as pulmonary tuberculosis, coronary artery disease, and heart failure with ejection fraction of 45%. He was taking regular treatment for heart failure (Aspirin, atorvastatin, metoprolol, enalapril, and spironolactone) and was on fixed dose combination anti-tuberculous therapy (Isoniazid 225 mg, Rifampicin 450 mg, Pyrazinamide 1200 mg and Ethambutol 825 mg according to his weight). He was not a smoker or alcoholic.

Examination

Pulse rate was 104/min, regular rhythm. Blood pressure was 130/90 mm Hg. Saturation was 90% in room air, 98% with 6 L nasal oxygen.

Cardiovascular system – S1, S2 heard, Respiratory system – normal vesicular breath sounds heard. Bilateral basal

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crepitations heard. Abdomen was soft. Central nervous system examination was clinically normal.

Initial management

He was provisionally diagnosed as acute decompensated heart failure/acute pulmonary edema and was given back rest, nasal oxygen, fluid, and salt restriction and inj. Frusemide, T. Aspirin, T. Atorvastatin, T. Enalapril, and anti-tubercular treatment (ATT) were continued. The patient symptomatically improved in one day and was weaned to room air.

Investigations

Computed tomography (CT) chest showed patchy consolidation of apico-posterior segment of right upper lobe and segmental consolidation of right middle lobe. Bronchiectatic changes were seen in the right upper and middle lobe. The findings were suggestive of active infection. Electrocardiogram was normal.

Hemoglobin was 11.1 g/dL, total leukocyte count was 14,300/mm^3, platelet count was 6.4 lakhs/mm^3, urea was 13 mg/dl, and creatinine was 1.4 mg/dL.

Serum sodium was 96 mEq/L and potassium was 2.5 mEq/L.

Bilirubin and other liver function tests were normal.

Course in the hospital

He was given third-generation cephalosporin ceftriaxone, in addition to the initial prescription, considering the probability of secondary bacterial infection. As hyponatremia was thought to be euvolemic hyponatremia secondary to lung infection related syndrome of inappropriate anti diuretic hormone (SIADH), and since he was symptomatic, 3% hypertonic saline was given as correction targeting a daily sodium improvement of 6–8 mEq/day. Sputum was induced and sent for culture. His serum sodium improved over the next 3 days and total leukocyte count started decreasing.

After 3 days of admission, the patient developed hypotension and shock. He was started on vasopressor support, initially with noradrenaline and then on dual inotrope support of noradrenaline and dopamine.

During the course of inotrope treatment, the patient developed an increase in serum transaminases, probably due to ischemic hepatitis. To avoid further hepatotoxicity, ATT was modified to streptomycin, ethambutol, and ofloxacin regimen.

Sputum culture was negative. Sputum acid-fast bacillus was positive. Hence, another sputum sample was sent for culture of *Mycobacterium* with sensitivity testing.

After 14 days of inotropic support, the patient's shock improved and was weaned off from inotrope support. The patient was able to maintain saturation in room air. He was also asymptomatic.

Repeat investigations now showed a normal total count, renal function tests, liver function tests, and serum electrolytes. ATT was now initiated as half dose of pyrazinamide and ethambutol and full dose of rifampicin and isoniazid.

He started to have symptoms such as easy fatigability, nausea, vomiting, and his blood pressure again dropped to a hypotensive range.

Considering the initial presentation of hyponatremia and hypotension and other symptoms, adrenal insufficiency was suspected and fasting serum cortisol and serum adrenocorticotropic hormone (ACTH) were sent. Cortisol was 4 mg/dL (reference range 6.02–18.4) and ACTH was 62 pg/mL (reference range 12–58).

Cosyntropin stimulation test could not be performed due to logistic issues.

CT abdomen was done with the suspicion of tuberculous adrenalitis, which showed enlarged left adrenal gland with chunky calcifications.

He was started on steroid replacement initially as Inj. Hydrocortisone 100 mg iv q6h, following which his symptoms of nausea, vomiting, and fatigability recovered. Prednisolone was substituted in place of hydrocortisone in the dose of 2 mg/kg/day, considering the enzyme inducer activity of rifampicin and considering recovery from sickness He did not develop symptoms after that.

He was restarted on full dose ATT before discharge.

He was discharged with stable vitals. His discharge prescription consisted of full dose ATT, T. Prednisolone 80 mg/day in two divided doses (based on body weight), antiplatelets, statins, and heart failure drugs (enalapril and metoprolol and spironolactone).

He was followed up after discharge. His 3 months follow-up was normal. The patient did not tolerate tapering of steroids and hence 80 mg/day of prednisolone was continued. The mycobacterial culture of the sputum sample given during admission showed sensitivity to rifampicin. Repeat chest imaging showed resolution of consolidation.

He planned to reduce the steroid dose after completion of ATT and assess response. However, he lost to follow-up after the 4th month of ATT.

DISCUSSION

Adrenal insufficiency due to tuberculosis can present in two ways: (1) Acute adrenal insufficiency, where the gland is bilaterally enlarged. (2) Chronic adrenal insufficiency where the gland is atrophied or calcified.

Chronic adrenal insufficiency usually presents with non-specific symptoms and signs, which are usually underdiagnosed or overlooked.[1] Chronic adrenal insufficiency can present

as acute adrenal insufficiency in the presence of a triggering factor such as fever, infection, or surgery.[1,3]

Drug therapy with rifampicin can precipitate adrenal crisis in both groups of patients, by inducing the metabolism of cortisol through CYP450 and reducing the serum cortisol levels. Hence, textbooks mention that corticosteroid replacement doses should be double or triple that of the usual weight-based dose.[6,7]

Acute adrenal insufficiency is usually misdiagnosed due to its similarities with other conditions such as hypovolemic shock, SIADH, septic shock, and acute abdomen.[1]

This patient initially had a diagnostic confusion due to the underlying chronic coronary syndrome, which led us to consider cardiogenic shock as the primary diagnosis. The initial presentation of hyponatremia in this patient was thought of as SIADH due to pneumonia. We did not have few manifestations such as hyperkalemia and hypoglycemia.

Textbook literature mentions that hyponatremia and hypotension are the two most common presenting features of adrenal crisis.[1]

The patient's initial presentation of hypotension and hyponatremia could be explained by the adrenal crisis precipitated by the rifampicin-based ATT or the acute pulmonary edema. He would have improved in between due to the switching of the ATT regimen to a non-rifampicin containing regimen. He developed symptoms again due to re-introduction of rifampicin.

CONCLUSION

This case report highlights the fact that rifampicin, even though the key drug in managing tuberculosis, can sometimes precipitate adrenal crisis and treating physicians should be aware of this. Also the steroid replacement dose in such patients is higher than the usual dosage used in adrenal insufficiency.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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