DOI: 10.7860/JCDR/2023/64509.18672

Case Series

Internal Medicine Section

Bilateral Adrenal Masses with Different Aetiologies Presenting as Addisonian Crisis with Acute Kidney Injury: A Case Series

MOHINI[1], ROHIT PARSAD[2], SHAVETA DAHIYA[3], DIKSHA NAYAK[4], MANOJ MALIK[5]

ABSTRACT

An Addisonian Crisis (AC) is an endocrinological emergency associated with high mortality, resulting from an acute deficit of hormones from the adrenal glands. It can occur either in a patient with known Adrenal Insufficiency (AI) or as the initial presentation of the disease. Primary Adrenal Insufficiency (PAI), which can be caused by autoimmune adrenalitis or tubercular adrenalitis, is the most common cause worldwide and particularly prevalent in developing countries like India. Other causes of PAI include infiltrative pathology, drugs, haemorrhage, or, rarely, malignancy. Secondary Adrenal Insufficiency (SAI) often occurs due to abrupt steroid withdrawal or defects at the level of the pituitary or hypothalamus. The present case series highlights three cases (three male patients) in which patients presented with adrenal crisis despite no prior history of AI. Subsequently, they were diagnosed with bilateral adrenal masses of different aetiologies, including primary adrenal malignancy and granulomatous infiltration of the adrenals due to Tuberculosis (TB). One case involved bilateral primary adrenal malignancy with left perirenal and pararenal space infiltration, while the other two patients were diagnosed with disseminated TB with adrenal gland infiltration. The presentation of all three cases was characterised by non specific symptoms. Initial management for all three patients involved mineralocorticoid and glucocorticoid replacement, and they were discharged with corticosteroid supplements. However, the patient with bilateral adrenal malignancy was referred to the surgery and oncology department for further evaluation and management, whereas the remaining two patients were started on Antitubercular (ATT) drugs for definite treatment.

Keywords: Adrenalitis, Adrenal crisis, Glucocorticoid, Malignancy, Mineralocorticoid

INTRODUCTION

The adrenal or suprarenal glands play a pivotal role in maintaining the physiological stress response, as well as Blood Pressure (BP) and electrolyte homeostasis. They mainly secrete three corticosteroids: glucocorticoid (cortisol) and mineralocorticoid (aldosterone) from the cortex, and adrenal androgen precursors and catecholamines (epinephrine and norepinephrine) from the inner medulla. Glucocorticoids and sex steroids are under the feedback control of the Hypothalamo-Pituitary-Adrenal (HPA) axis, while mineralocorticoid levels are maintained by the Renin-Angiotensin-Aldosterone System (RAAS). AI can be caused by PAI or defects at the level of the pituitary or hypothalamus SAI. PAI can result from autoimmune adrenalitis, either isolated or as part of Autoimmune Polyglandular Syndromes (APS). It can also be genetic, caused by blocks in adrenal steroidogenesis like Congenital Adrenal Hyperplasia (CAH), or by adrenal gland destruction due to infections, haemorrhage, infiltration, or rarely, metastasis or malignancy. Secondary or central AI is caused by defects at the level of the hypothalamus or pituitary, which can be inherited structural defects or hormone mutations, or acquired causes like trauma, radiation damage, infiltrations, infections, vascular issues, neoplasia, or metastasis.

Addisonian Crisis occurs due to an acute insufficiency of adrenal hormones, either because of abrupt withdrawal of steroids or failure to increase their dose in response to any form of stress like surgery, infection, or trauma. The disease rapidly evolves from initial symptoms of fatigue, weakness, anorexia, nausea, asthenia, abdominal pain, and diarrhoea, eventually leading to acute abdomen, circulatory collapse, syncope, hypoglycaemia, mental obtundation, encephalopathy, or death. Risk factors include a previous episode of adrenal crisis, increasing age group, bacterial infections (most commonly gastroenteritis, followed by respiratory and urinary tract infections), and concomitant diabetes and bronchial asthma [1].

Case 1

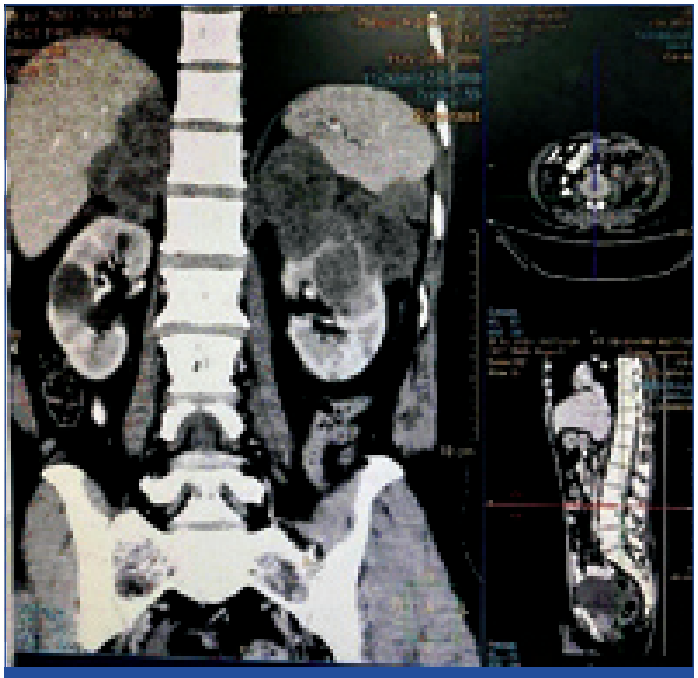
A 56-year-old male, who was not known to have any chronic illnesses, experienced mild, dull aching abdominal pain for one month, along with headaches and fatigue. However, he did not seek medical advice during this time. After one month of mild symptoms, he suddenly developed severe and diffuse abdominal pain. This was followed by an episode of syncope and loss of consciousness for approximately 5 to 10 minutes. As a result, the patient was brought to the hospital. During the general physical examination, the patient appeared drowsy and afebrile. His BP was 74/42 mmHg in the supine position, and his Pulse Rate (PR) was 120 beats per minute. His respiratory rate was 22 breaths per minute. Both the general physical and systemic examinations yielded normal results. Initially, the patient received an intravenous bolus of normal saline (0.9% crystalline) and later underwent Central Venous Pressure (CVP)-guided fluid administration while his vital signs were closely monitored. Routine blood investigations were conducted to rule out surgical emergencies such as visceral perforation.

The routine investigations revealed normocytic normochromic anaemia {Haemoglobin (Hb): 9.8 g/dL} and leucocytosis {Total Leukocyte Count (TLC): 14,200/mm^3 with 80% Polymorphonuclear Leukocytes (PMN)}. The patient's Renal Function Test (RFT) showed abnormal results, with blood urea of 116 mg/dL and serum creatinine of 2.9 mg/dL. Serum calcium was 8.9 g/dL, phosphorus was 3.6 mg/dL, uric acid was 6.3 mg/dL, and urine Complete Examination (CE) was normal. The patient's Liver Function Test (LFT) showed normal results, except for low serum albumin of 2.4 mg/dL. At the time of presentation, Arterial Blood Gas (ABG) analysis

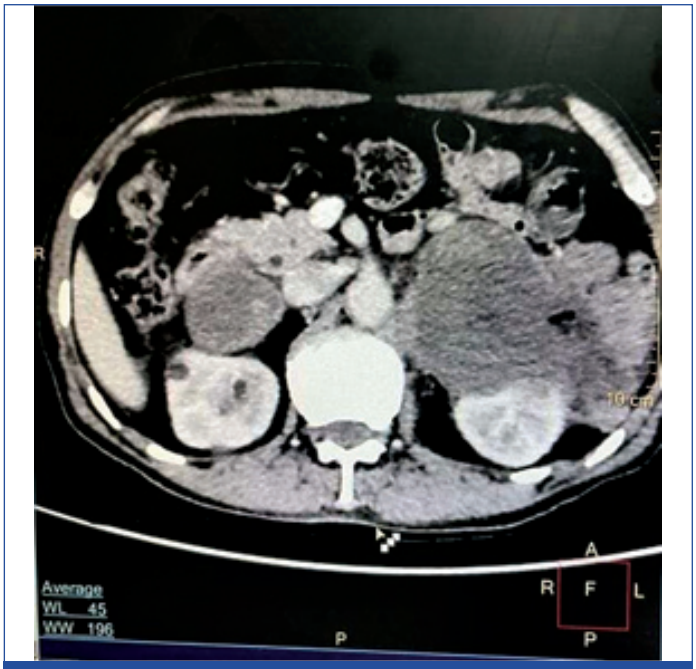
indicated uncompensated metabolic acidosis, with a pH of 7.21, bicarbonate (HCO_3-) of 13.1 mmol/L, sodium (Na+) of 125 mmol/L, and potassium (K+) of 7.24 mmol/L. Random Blood Sugar (RBS) measurements were on the lower side of the normal range, with values of 68 mg/dL and 65 mg/dL. Electrocardiogram (ECG) results were normal, without any findings suggestive of hyperkalaemia. X-ray imaging of the chest and abdomen did not reveal any pathology.

Based on the investigations conducted so far, there were indications of acute stress, as evidenced by the decreased serum albumin levels. Initially, sepsis leading to septic shock was considered as a possible cause of hypotension, hypoglycaemia, leukocytosis, deranged renal parameters, and electrolyte imbalance. Blood and urine cultures were sent for testing, but they later came back as sterile. However, the presence of anaemia and one month of abdominal pain suggested an underlying chronic pathology with a strong possibility of an autoimmune condition.

On the second day of admission, the cortisol level was measured at 8 am and was found to be in the intermediate range of 13.8 ug/dL, which was alarming as it should have increased in response to stress. The adrenocorticotrophin stimulation t-test was performed the next day, revealing a basal serum cortisol level of 11.94 µg/dL. After 30 minutes and 60 minutes of synthetic Adrenocorticotropic Hormone (ACTH) stimulation, the cortisol levels were 13.77 µg/dL and 14.04 µg/dL, respectively. An abdominal Ultrasonography (USG) showed bilateral adrenal masses. The serum aldosterone level was 5.52 ng/dL, which was at the lower limits of the reference range, and the serum renin level was significantly elevated at 98 µIU/mL. The serum Dehydroepiandrosterone Sulphate (DHEAS) level was subnormal at 10.4 µg/dL. Plasma metanephrines (45 pg/mL) and normetanephrines (151 pg/mL) were within the normal range. A Contrast Enhanced Computed Tomography (CECT) of the whole abdomen revealed well-defined lobulated heterogeneously enhancing mass lesions in the suprarenal region [Table/Fig-1,2]. The right mass measured 57×40 mm and caused compression of the inferior vena cava, while the left mass measured 98×64 mm and extended into the left perinephric and left anterior pararenal space. Enlarged lymph nodes were observed in the paraaortic, paracaval, and peripancreatic regions, suggestive of a malignant aetiology. There was no evidence of primary malignancy in the chest or abdomen.



[Table/Fig-1]: Contrast Enhanced Computed Tomography (CECT) abdomen with bilateral adrenal masses.



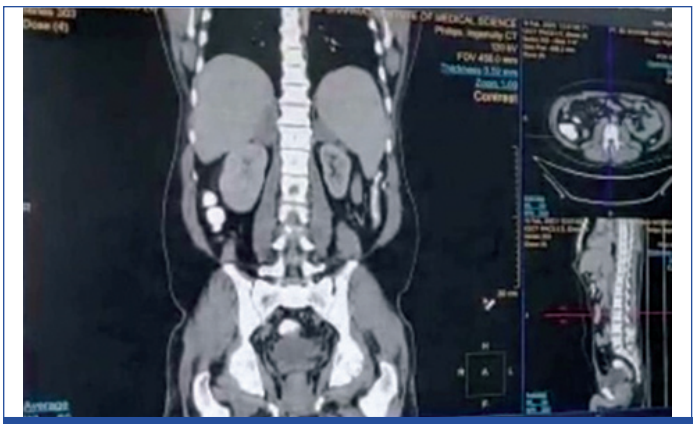
[Table/Fig-2]: Contrast Enhanced Computed Tomography (CECT) abdomen with bilateral adrenal masses with left side loss of renal tissue.

Initially, the differential diagnosis included sepsis with septic shock, adrenal crisis, and chronic duodenal ulcer with perforation peritonitis. However, all the investigations supported the diagnosis of PAI secondary to bilateral adrenal malignancy, which presented with adrenal crisis and Acute Kidney Injury (AKI). The patient received fluid resuscitation with 1.5 L of 0.9% normal saline and 1.5 L of 5% dextrose over the initial 12 to 15 hours, successfully correcting their hypotension. CVP-guided fluid administration was followed. Antihyperkalemic measures were implemented, including injection calcium gluconate, injection dextrose 25% W/V with 12.5 units of regular insulin, and nebulisation with salbutamol. Analgesics were administered for pain management. Definitive management began on the second day with an intravenous bolus of 100 mg hydrocortisone, followed by 200 mg over four divided doses. Subsequent days involved doses of 200 mg, 100 mg, and 50 mg, gradually transitioning to oral hydrocortisone (20 mg in the morning and 10 mg in the evening) on the 6th day of admission. The patient's abdominal pain and fatigue completely resolved, and they experienced a dramatic improvement with no residual sequelae. Upon discharge, the patient was prescribed Tablet (Tab.) hydrocortisone 10 mg at 8 am, 5 mg at 1 pm, and 5 mg at 5 pm, Tab. fludrocortisone 100 mg OD, and Tab. Dehydroepiandrosterone 25 mg OD. They were referred to a specialised Endosurgery Department in a higher centre for adrenal surgery and further management.

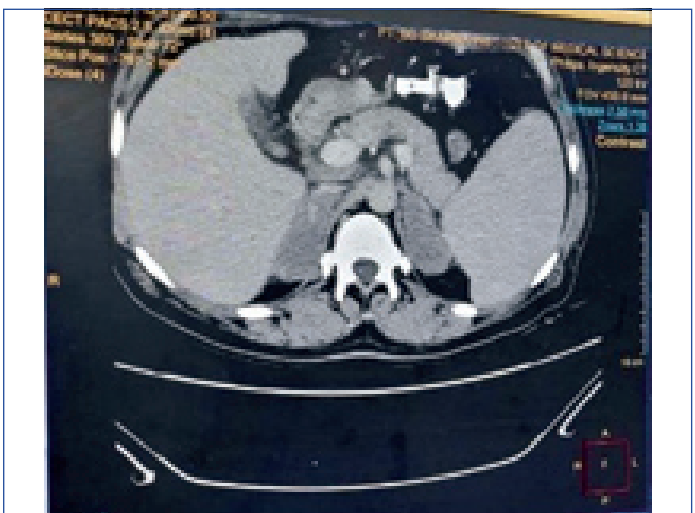
Case 2

A 53-year-old male, known diabetic for five years on Oral Hypoglycaemic Agents (OHAs), was brought to the medicine emergency with chief complaints of dizziness associated with tremor, sweating, irrelevant talk, and palpitation for five hours. On examination, the patient was hypotensive with a BP of 80/60 mmHg, heart rate of 110/minute, and oxygen saturation of 98% at room air. The patient's RBS was 45 mg/dL, for which he was immediately transfused with injection dextrose 25% weight/volume along with fluid therapy using 0.9% Normal saline initially as an intravenous bolus, then central venous guided. The patient regained consciousness within a few hours, his vitals became stable, and all his systemic examinations were normal. Initially, this seemed to be an episode of hypoglycaemia secondary to OHA. However, later the patient revealed that he had been experiencing mild diffuse, dull aching abdominal pain for the past 20 days and had been self-medicating for symptomatic relief. His abdominal ultrasound revealed hypoechoic lesions measuring 6.3×2.4 cm over

the upper lobe of the right kidney and 7.6×3.4 cm over the left kidney, suggestive of adrenal pathology. His ABG analysis on presentation showed uncompensated metabolic acidosis with a pH of 7.19 and HCO_3- of 12.0 mmol/L, hyponatraemia (Na+126 mmol/L), and hyperkalaemia (K+7.15 mmol/L), indicating AI. Other investigations, such as a complete blood count, LFT, and urine examination, were normal, but the patient had deranged renal function tests with blood urea of 110 mg/dL and serum creatinine of 2.2 mg/dL. Signs of hyperkalaemia were evident on the ECG with tall T waves and a prolonged PR segment. The patient was started on antihyperkalemic measures along with monitoring of vital signs and RBS levels. The measurement of 8 am cortisol was 1.8 µg/dL, confirming AI. Meanwhile, his sensorium deteriorated again due to hyponatraemia (Na+112 mmol/L) with recurrent episodes of hypoglycaemia, and the patient was started on injection hydrocortisone 100 mg as an intravenous bolus and 200 mg over 4 divided doses. This was followed by 200 mg, 100 mg, and 50 mg on subsequent days, and he was switched to oral hydrocortisone 20 mg in the morning and 10 mg in the evening. A CECT of the abdomen was performed when his serum creatinine improved to 1.3 mg/dL, confirming ill-defined mildly enhancing hypodense lesions in the bilateral adrenal glands, likely adrenal deposits with the possibility of granulomatous or tubercular aetiology [Table/Fig-3,4]. The Mantoux test came out positive with a raised Erythrocyte Sedimentation Rate (ESR) of 60 mm in the first hour, and mycobacterium TB was detected in the sputum Cartridge Based Nucleic Acid Amplification Test (CBNAAT). Initially, the differential diagnoses considered were OHA-induced hypoglycaemia, sepsis with septic shock, adrenal crisis secondary to tubercular infiltration of adrenal glands, and myocardial infarction. However, the final diagnosis was pulmonary tuberculosis with PAI due to tubercular adrenalitis with bilateral adrenal masses presenting with adrenal crisis and AKI. The patient improved dramatically and was discharged on ATT, Tab. hydrocortisone 10 mg, 5 mg, and 5 mg at 8 am, 1 pm, and 5 pm respectively, and Tab. fludrocortisone 100 µg once daily. Now the patient is on Outpatient Department (OPD) follow-up, continuation phase of ATT, and has improved symptomatically.



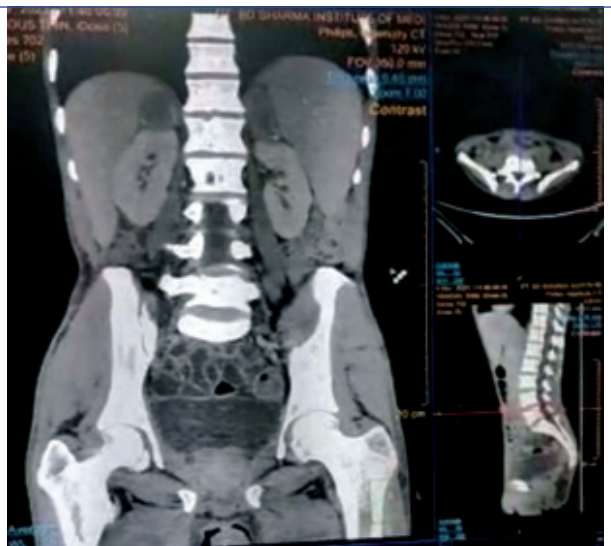
[Table/Fig-3]: Contrast Enhanced Computed Tomography (CECT) abdomen with bilateral adrenal glands enlarged.



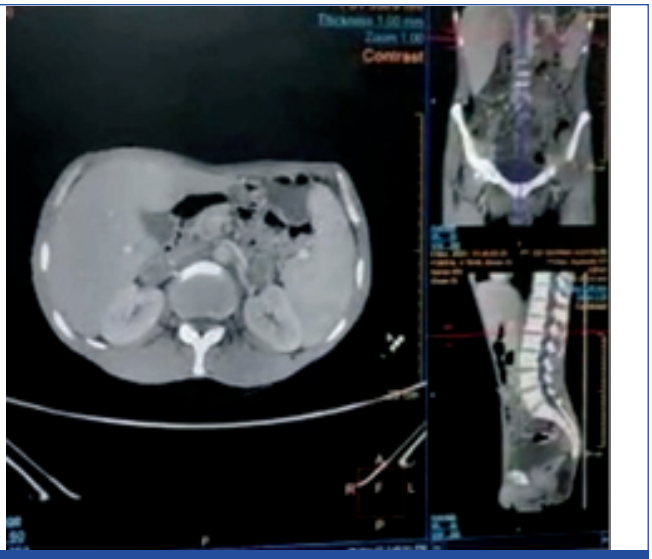
[Table/Fig-4]: Contrast Enhanced Computed Tomography (CECT) abdomen with bilateral masses.

Case 3

A 55-year-old male chronic smoker with 40 pack years, who is not known to have any other chronic illness, presented to the medicine casualty with complaints of fever. The patient had experienced eight episodes of loose stools one day ago, followed by a two hour period of altered sensorium accompanied by dizziness and irrelevant talk. The patient's attendant reported decreased appetite, weight loss, and diffuse, dull, aching abdominal pain of insidious onset that had been present for the past two years but was non progressive. On examination, the patient was found to be hypotensive with a blood pressure of 60/44 mmHg, a pulse rate of 108/minute, a saturation level of 97% on room air, and a blood sugar level of 34 mg/dL. General physical examination revealed pallor and bilateral enlarged inguinal lymph nodes, while the rest of the systemic examinations were within normal limits. The patient's sensorium improved after receiving a transfusion of one unit of injection dextrose 25% W/V. Simultaneously, an i.v. bolus of 0.9% normal saline was initiated, followed by an infusion of injection noradrenaline due to persistent hypotension. Routine examination revealed anaemia (Hb 9.0 g/dL), leukopenia (TLC 2600/mm^3), and deranged RFT (blood urea 81 mg/dL and serum creatinine 2.5 mg/dL). LFT, lipid profile, urine CE, X-ray chest, and ECG were all normal. An Arterial Blood Gas (ABG) analysis revealed uncompensated metabolic acidosis with a pH of 7.05 and HCO_3-10.8 mmol/L, hyponatraemia (Na+120 mmol/L), and hyperkalaemia (K+5.9 mmol/L) for which anti-hyperkalemic measures were administered. An abdominal USG showed normal findings except for mild fatty changes in the liver and bulky adrenal glands. The patient's sensorium again deteriorated, and he remained in a state of refractory hypotension that did not respond to fluids and ionotropes. Considering the strong possibility of AI leading to a crisis, a serum cortisol test was performed at 8 am, which confirmed the diagnosis with a value of 2.5 µg/dL. The patient was immediately started on injection hydrocortisone 100 mg i.v., followed by 200 mg in four divided doses. With adequate fluid resuscitation, his creatinine levels decreased to 1.2 mg/dL, and a CECT scan of the abdomen revealed bilateral enlarged adrenal glands with smooth borders, peripheral calcification, minimal peripheral enhancement, and central hypoattenuating areas, indicative of adrenal TB with a few lymph nodes in the periportal and peripancreatic regions [Table/Fig-5,6]. Initially, the differentials considered were sepsis with septic shock, Addison's crisis, and malignancy (haematological or solid).



[Table/Fig-5]: Contrast Enhanced Computed Tomography (CECT) abdomen with bilateral enlarged adrenal with peripheral calcification.



[Table/Fig-6]: Contrast Enhanced Computed Tomography (CECT) abdomen with right adrenal 61×35×32 mm and left 55×44×26 mm.

Later, his Mantoux test came out positive, with an elevated ESR of 40 mm in the first hour. Fine Needle Aspiration Cytology (FNAC) from the aspirate of the right inguinal lymph node revealed a large number of macrophages, lymphocytes, histiocytes, and a few degenerated neutrophils amidst necrotic material. Staining for Acid Fast Bacilli (AFB) yielded highly positive results, suggesting tubercular inflammation. His sensorium and hypotension improved dramatically with steroids. Thus, the final diagnosis was extrapulmonary TB with PAI, accompanied by Addison's crisis due to TB adrenalitis, which presented as an adrenal crisis likely triggered by acute gastroenteritis with AKI. Like the previous patient, he was discharged on Tab. hydrocortisone 10 mg, 5 mg, and 5 mg at 8 am, 1 pm, and 5 pm respectively, Tab. fludrocortisone 100 µg, and antitubercular drugs. However, after leaving the hospital, the patient did not take his medications and was subsequently lost to follow-up.

DISCUSSION

The AI can be primary or secondary due to acquired or inherited causes. The condition may remain undetected in a compensated state until an acute illness or any form of stress precipitates it into a state of adrenal or AC [1]. The prevalence of adrenal crisis ranges from 5.2 to 8.3 per 100 patient-years [2,3]. TB was the most common cause (70%) during the 1930s. Currently, autoimmune adrenalitis (Addison's disease) is the most common cause of PAI in developed countries, while TB remains the leading cause of AI in developing countries [4]. However, in many cases, the cause may remain unidentified. The clinical presentations start with vague symptoms like fatigue, abdominal pain, and anorexia, progressing into syncope, confusion, encephalopathy, etc. Upon evaluation, these patients usually have normocytic anaemia, eosinophilia, lymphocytosis, hypotension, hypoglycaemia, AKI, hyperkalaemia, hyponatraemia, and metabolic acidosis. The definitive diagnosis of AI requires the demonstration of low serum cortisol. High serum ACTH with no rise in cortisol levels on ACTH stimulation suggests PAI, while low ACTH levels with normal mineralocorticoid levels are seen in SAI. The next step is to establish if the cause is treatable and manage it.

Mineralocorticoid deficiency can be established with low or normal serum aldosterone and increased serum renin. A prospective study involving 364 patients over two years concluded that AC-associated mortality is around 6% of the total patients who had a crisis and can occur even in educated patients [3]. Thus, in acutely ill patients, treatment should be started without delay, and meanwhile, blood samples could be sent or kept for diagnostics.

An adrenal incidentaloma refers to a mass lesion with a diameter greater than 1 cm, typically unilateral, benign, and non functioning. However, it can also be bilateral, malignant, and secretory. Bilateral adrenal masses can be associated with cortical adenomas, lymphoma, Adrenocortical Carcinomas (ACC), metastasis, infections (such as TB or fungal), haemorrhage, amyloidosis, or infiltrative diseases. Primary adrenal malignancy is much less common than secondary metastasis to the adrenals, with an estimated incidence of 7.4 cases per million population, most of which are ACC. In rare cases, adrenal malignancy can result in adrenocortical hypofunction instead of hormone excess [5]. This occurs when more than 90% of the adrenal glandular tissue is destroyed, leaving the remaining tissues unable to compensate through hypertrophy or hyperplasia [6]. AI can also rarely occur due to pituitary metastasis with hormone deficits, adrenalitis, immunotherapies for certain malignancies like melanoma, or as an iatrogenic effect of adrenolytic agents such as mitotane used in ACC treatment [7,8].

In a retrospective study by Lubomski et al., which analysed 15,376 patients with adrenal malignancies from 2006 to 2017, 182 cases of AI were reported, with 21 (11%) being primary and the majority 161 (88.5%) being secondary to malignancy. Similarly, out of a total of 24 AC, 5 (20.8%) were primary and 19 (79.2%) were associated with secondary malignancy [9]. Patient with bilateral adrenal malignancy is a scarce finding and those presenting with AC is equally unique. CT, MRI, Positron Emission Tomography (PET) scan, fine needle aspiration biopsy are the investigation modalities used to define the type, nature (benign or malignant) and extent of the disease [10].

In all three of our cases, adrenal masses were initially detected using USG and later confirmed to be bilateral adrenal malignancy or bilateral tubercular deposits through CECT scans of the abdomen. Nevertheless, the occurrence of bilateral adrenal malignancy or bilateral adrenal masses secondary to tubercular adrenalitis presenting with acute adrenal crisis and AKI is extremely rare in Rohtak, Haryana region and possibly the first of its kind.

CONCLUSION(S)

The AC is a medical emergency that requires early identification of the condition and immediate management. Many patients may lack prior knowledge of their disease and present for the first time, so a high degree of vigilance is required to avoid missing them. Early supportive management should be followed by treatment with corticosteroid replacement. After stabilisation, the cause of AI (Addison's disease) - primary or secondary - can be evaluated, which might lead to the discovery of rare conditions like bilateral adrenal masses due to malignancy or TB.

Addison's crisis is a common disease that requires a high level of suspicion, early diagnosis, and treatment to prevent mortality. Patient education is necessary to explain the need for compliance with medications and increasing their dose during acute illness to prevent future crises. In conclusion, AC may be the first presenting manifestation of bilateral adrenal masses attributed to various causes, including primary bilateral malignancy, granulomatous lesions like TB and sarcoidosis, which can be devastating for a patient if not diagnosed and treated in a timely manner.

REFERENCES

[1] Rushworth RL, Torpy DJ. A descriptive study of adrenal crises in adults with adrenal insufficiency: Increased risk with age and in those with bacterial infections. BMC Endocrinol Disord. 2014;14:79. Doi: 10.1186/1472-6823-14-79.
[2] Smans LC, Van der Valk ES, Hermus AR, Zelissen PM. Incidence of adrenal crisis in patients with adrenal insufficiency. Clin Endocrinol (Oxf). 2016;84(1):17-22.
[3] Hahner S, Spinnler C, Fassnacht M, Burger-Stritt S, Lang K, Milovanovic D, et al. High incidence of adrenal crisis in educated patients with chronic adrenal insufficiency: A prospective study. J Clin Endocrinol Metab. 2015;100(2):407-16.
[4] Omori K, Nomura K, Shimizu S, Omori N, Takano K. Risk factors for adrenal crisis in patients with adrenal insufficiency. Endocr J. 2003;50(6):745-52.
[5] Chandrasekar T, Goldberg H, Klaassen Z, Wallis CJD, Woon DTS, Herrera-Caceres JO, et al. The who, when, and why of primary adrenal malignancies: Insights into the epidemiology of a rare clinical entity. Canc. 2019;125(7):1050-59.

[6] Patrova J, Jarocka I, Wahrenberg H, Falhammar H. Clinical outcomes in adrenal incidentaloma: Experience from one center. Endocr Pract. 2015;21(8):870-77.
[7] Salinas C, Renner A, Rojas C, Samtani S, Burotto M. Primary adrenal insufficiency during immune checkpoint inhibitor treatment: Case reports and review of the literature. Case Rep in Oncol. 2020;13(2):621-26.
[8] Lin CH, Chen KH, Chen KY, Shih SR, Lu JY. Immune checkpoint inhibitor therapy-induced hypophysitis~a case series of Taiwanese patients. J of the Formos Med Assoc. 2019;118(1):524-29.
[9] Lubomski A, Falhammar H, Torpy DJ, Rushworth RL. The epidemiology of primary and secondary adrenal malignancies and associated adrenal insufficiency in hospitalised patients: An analysis of hospital admission data, NSW, Australia. BMC Endocrinol Disord. 2021;21(1):141. Doi: 10.1186/s12902-021-00787-6.
[10] Fassnacht M, Dekkers OM, Else T, Baudin E, Berruti A, De Krijger RR, et al. European Society of Endocrinology Clinical Practice Guidelines on the management of adrenocortical carcinoma in adults, in collaboration with the European Network for the Study of Adrenal Tumors. Eur J of Endocrinol. 2018;179(4):G1-G46.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of General Medicine, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India.
2. Postgraduate, Department of General Medicine, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India.
3. Assistant Professor, Department of General Medicine, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India.
4. Postgraduate Student, Department of General Medicine, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India.
5. Postgraduate Student, Department of General Medicine, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Rohit Parsad,
Postgraduate, Department of General Medicine, Pt. B.D. Sharma PGIMS,
Rohtak-124001, Haryana, India.
E-mail: rohitparsad77@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 08, 2023
- Manual Googling: Jun 17, 2023
- iThenticate Software: Jul 28, 2023 (5%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 06, 2023**
Date of Peer Review: **Jun 09, 2023**
Date of Acceptance: **Jul 31, 2023**
Date of Publishing: **Nov 01, 2023**