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Case Report

Rare Presentation of Adrenal Insufficiency as Cachexia: A Case Report

Ramy Ibrahim[1]*, Mehak Riaz[2], Sharathi Sirimanne[2], Aghapy Kirolos[2], Rishit Arnav Shaquib[2], Andrew Boulos[2] and Mark Basily[2]

[1]Medical Director of Premier Medical Associates and Head of Research Department, USA

[2]Research Volunteer, Premier Medical Associates, USA

***Corresponding Author:** Ramy Ibrahim, Medical Director of Premier Medical Associates and Head of Research Department, USA.

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Abstract

Adrenal insufficiency (AI) is an uncommon medical condition characterized by a disorder of the adrenal glands which results in insufficient secretion of glucocorticoids and mineralocorticoids, either in the basal state or during times of stress. Can be due to a primary cause like adrenal failure itself or secondary to a disturbance in the hypothalamic-pituitary-adrenal axis (HPA). The impact of the life-threatening condition of adrenal insufficiency in a stress response which is called Addisonian crisis, and the emergent significance of a proper treatment by optimizing cortisol replacement therapy is adopted in a case of 66-year-old female, who presented with an unexplained weight loss, lack of energy, failure to thrive and decreased appetite. She had lost close to 20% of her body mass, which was quite worrying. MRI of the pituitary gland showed a small adenoma.

Keywords: *Adrenal Insufficiency; Addison's Disease; Adrenal Crisis; Pituitary Adenoma*

Introduction

The adrenal glands, positioned atop the kidneys, consist of two primary sections: the cortex and the medulla. The cortex generates hormones regulating serum electrolytes (mineralocorticoids), serum glucose levels (glucocorticoids), and sex hormones (androgens). Meanwhile, the medulla secretes hormones that oversee the sympathetic and parasympathetic nervous systems (epinephrine and norepinephrine) [1].

Adrenal insufficiency (AI) is a significant disorder where the adrenal glands malfunction, resulting in inadequate secretion of glucocorticoids, mineralocorticoids, and adrenal androgens. This disruption in hormone production can negatively impact vital processes like energy regulation, fluid balance, and androgenic activity [2].

Primary adrenal insufficiency (PAI), also known as Addison's disease, is a key cause of AI. It is characterized by dysfunction or damage to the adrenal cortex, leading to insufficient hormone secretion.

Secondary adrenal insufficiency (AI) can arise from conditions affecting the pituitary gland's secretion of adrenocorticotropic hormone (ACTH) or the hypothalamus' secretion of corticotropin- releasing hormone (CRH) and other ACTH secretagogues, like vasopressin. One of the factors causing secondary AI is pituitary hemorrhage or infarction, termed Sheehan syndrome. This results from inadequate pituitary blood supply during childbirth, damaging pituitary tissue and causing deficiencies like ACTH deficiency and secondary AI [3-5].

Secondary AI causes also include pituitary tumors, hypophysectomy (pituitary removal surgery), and high-dose radiation affecting the pituitary gland or brain, leading to disrupted ACTH secretion and subsequent adrenal insufficiency [6].

Tertiary adrenal insufficiency (AI) when the dysfunction occurs at the hypothalamus level, it is termed Tertiary AI. Notably, central AI (encompassing secondary and tertiary forms) holds a higher prevalence, ranging from 150 to 280 cases per million, compared to primary adrenal insufficiency (PAI).

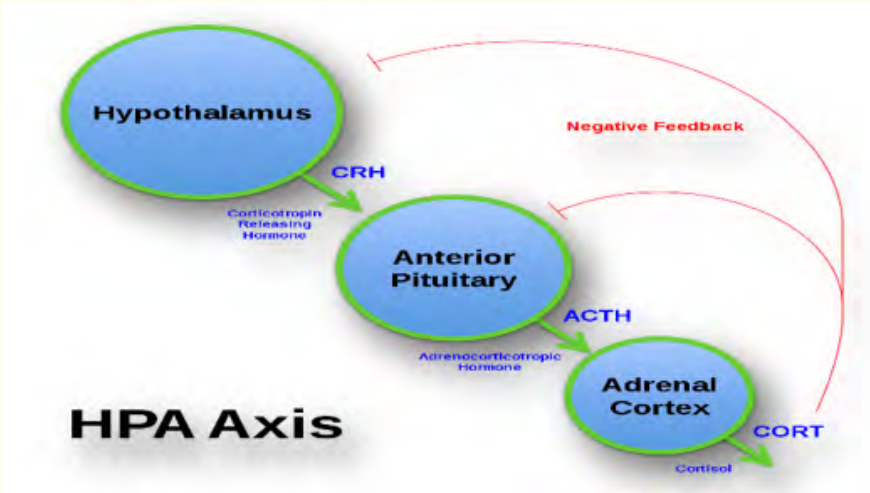
Adrenal crisis refers to sudden, severe health decline marked by symptoms like low blood pressure, abdominal distress, and significant lab test abnormalities. Intravenous glucocorticoid administration can resolve this critical condition. In primary adrenal insufficiency (PAI), adrenal crisis symptoms may be more intense due to concurrent mineralocorticoid deficiency. Often seen in PAI but less common in central adrenal insufficiency; pituitary apoplexy, characterized by pituitary hemorrhage or infarction, illustrates adrenal crisis in central AI [7].

"Functional adrenal insufficiency" or "relative adrenal insufficiency" describes subnormal corticosteroid production during critical illness, without structural hypothalamic-pituitary-adrenal axis defects. Presently, no consensus exists on diagnostic criteria for this entity [8].

Pituitary adenomas, non-cancerous tumors from the anterior pituitary's five cell types, make up around 10% of intracranial neoplasms. Occurring in the third and fourth decades, these tumors are classified based on size: microadenomas (under 10 mm) and macroadenomas (over 10 mm). Autopsies and imaging reveal asymptomatic microadenomas in 10 - 20% of the population [9]. Most pituitary tumors are benign, slow growing. Clinically, they can cause hyperfunction due to hormone overproduction or hypofunction due to glandular destruction from tumor growth or inhibitory hormonal effects [10].

Clinical manifestation of AI

Adrenal insufficiency's clinical presentation varies, including fatigue, weakness, weight or appetite loss, low blood pressure, hyperpigmentation, salt cravings, gastrointestinal issues, and sexual dysfunction. Symptoms usually emerge gradually over months, and the condition's slow progression might lead individuals to overlook initial symptoms. Stressors like illness, injury, dehydration, or abrupt cessation of long-term steroid treatment can trigger adrenal crisis, a life- threatening state necessitating immediate medical attention.



Figure

This case illustrates a patient's progression with a pituitary adenoma and isolated adrenocorticotropic hormone (ACTH) deficiency, culminating in secondary adrenal insufficiency, a rare condition within this context.

Diagnosing AI (Adrenal insufficiency)

Evaluation of serum cortisol concentration: The accurate diagnosis of adrenal insufficiency, regardless of origin, hinges on identifying inadequately low cortisol synthesis. Most diagnostic assessments rely on total serum cortisol levels. However, careful interpretation is necessary when assessing patients with anomalies in cortisol-binding globulin (CBG) or albumin levels, such as those with cirrhosis, nephrotic syndrome, or individuals using oral estrogens [11].

In such cases, abnormal CBG or albumin levels can lead to erroneous diagnoses, either in the form of reduced or elevated cortisol levels. While salivary or serum-free cortisol measurements have been proposed as alternatives, their availability is limited, and criteria for evaluating responses are yet to be established.

Adrenocorticotropic hormone (ACTH) levels: ACTH, a hormone released by the pituitary gland, stimulates cortisol production. Low cortisol and high ACTH levels suggest primary adrenal insufficiency (adrenal gland failure). Conversely, low cortisol and low to normal ACTH levels may indicate secondary adrenal insufficiency (arising from pituitary or hypothalamic dysfunction).

If serum cortisol and plasma ACTH levels are inappropriately low, the patient likely suffers from secondary (pituitary-related) or tertiary (hypothalamus-related) adrenal insufficiency. However, prompt identification of primary adrenal insufficiency is crucial, especially in emergent situations like shock. A strategy to ascertain this involves stimulating the adrenal gland with synthetic ACTH and measuring plasma ACTH and serum cortisol levels before administration. Although cortisol response suffices for diagnosing adrenal insufficiency and determining immediate treatment, the later-available ACTH value aids in characterizing the extent of the defect.

Morning serum cortisol concentration: In individuals without adrenal insufficiency, early morning (around 6 AM) serum cortisol levels range from 10 to 20 mcg/dL (275 to 555 nmol/L), surpassing levels observed at other times of the day. A morning cortisol concentration lower than three mcg/dL (80 nmol/L) strongly indicates adrenal insufficiency. Similar considerations extend to elevated serum cortisol values. A morning concentration exceeding 15 mcg/dL (415 nmol/L) predicts a normal cortisol response to insulin-induced hypoglycemia or a short ACTH test [12]. A morning serum cortisol exceeding 18 mcg/dL offers even greater reassurance, obviating the need for further testing, barring suspected elevated CBG levels (e.g. due to estrogen use) [13,14].

Electrolyte levels: Adrenal insufficiency can disrupt electrolyte equilibrium, impacting sodium and potassium levels. Abnormal electrolyte levels can provide diagnostic support.

Imaging studies: Employing CT scans or MRIs, healthcare providers can evaluate the adrenal glands, pituitary gland, and hypothalamus for structural anomalies.

Adrenal crisis consideration: Adrenal crisis should be suspected when confronted with a patient exhibiting peripheral vascular collapse (vasodilatory shock), regardless of whether adrenal insufficiency is previously known. Additionally, isolated corticotropin (ACTH) deficiency, though rare, should be considered if a patient presents with unexplained severe hypoglycemia or hyponatremia. Consequently, the diagnosis of adrenal insufficiency relies on a potent combination of clinical vigilance, laboratory assessments, and hormonal stimulation tests.

Case Presentation and Discussion

A 66-year-old female with PMHx HTN, HLD, Sjogren syndrome, and autoimmune hypothyroidism presented in the hospital on 11/19/22 with nausea, vomiting, diarrhea, abdominal cramping with eating from the past 1-2 months, and she had been losing weight

(total 30 lbs) with 16 lbs lost in the past two months, unintentionally. She also had decreased appetite and night sweats over the past two weeks. A Gastroenterologist then saw her for evaluation of gastric ulcers and treated with PPIs for GERD. She was also evaluated by a Cardiologist for low BP as well, with no apparent cardiac cause.

Physical examination of the abdomen was within normal limits; no rash/ discoloration was noticed on skin examination. She was not in any acute distress at that time.

Weight: 11/19/22-->52.6 kg (116 lbs).

Weight: 11/12/21-->62.1 kg (137 lbs).

BMI: 18.17 kg/m^2 on 04/14/2023, 52 kg (115 lb).

BMI: 17.54 kg/m^2 on 04/19/2023, 50 kg (112 lb).

The patient later developed cachexia, but blood parameters were not consistent with severe malnutrition, as she did not have profound electrolyte abnormalities, and her weight loss was out of proportion with her metabolic components. She had positive fecal elastase and was diagnosed with pancreatic insufficiency, for which she was started on creon. However, the patient did not have the symptoms of indigestion or malabsorption. It was also possible that the patient had adapted her diet to prevent the discomfort from indigestion.

ACTH stimulation test (09/22/2022): ACTH was 32 (normal range), cortisol went from 9.9 to 19.4, a normal response.

Labs (01/04/2023) showed pancreatic elastase 123.

Labs (03/22/2023) showed TSH 3.59, TPO 72, T3 2.9, and cortisol 1.1.

She started on 20 mg in the morning, hydrocortisone, and 10 mg in the afternoon with the plan to recheck cortisol levels.

On 04/3/2023: After holding hydrocortisone for 24 hours, fasting/AM cortisol was only 3.5, and ACTH was within standard limit. Hydrocortisone decreased to 15 mg in the morning and 5 mg in the afternoon.

CT brain (04/18/2023): Showed no acute findings.

MRI pituitary (04/19/2023): A small 3 mm focus of non-enhancement and T2 hyperintensity was noted within the region of left pars intermedia/posterior adenohypophysis that may represent a pars intermedia/Rathke's cleft cyst. Additional differential consideration included cystic pituitary microadenoma.

The patient was taking hydrocortisone replacement therapy with regular follow-up with her endocrinologist. The patient also consulted a dietician for GERD and malnutrition. The primary care provider will closely follow up on the pituitary gland with a hormonal panel.

Management of AI

The presentation of AI can vary, ranging from asymptomatic hormonal dysfunction to a potentially life-threatening adrenal crisis. It is crucial to promptly diagnose and manage AI to prevent serious complications. Treatment for adrenal insufficiency typically involves hormone replacement therapy to replenish the deficient hormones. It usually includes oral corticosteroids, such as hydrocortisone or prednisone, which mimic the effects of cortisol. In some cases, mineralocorticoid and androgen replacement therapies may also be necessary. Proper management and regular medical follow-ups are required to ensure adequate hormone levels and prevent complications associated with adrenal insufficiency. Administering fludrocortisone and glucocorticoids is the mainstay treatment.

Conclusion

In conclusion, adrenal insufficiency represents a complex interplay of endocrine dysfunction with far-reaching consequences. Primary and secondary forms, along with the concept of "functional adrenal insufficiency," highlight the intricate mechanisms involved. Clinical symptoms underscore the significance of diagnosing and managing this condition effectively.

The diagnostic journey involves cortisol and ACTH evaluations, supported by imaging and electrolyte assessment. Management hinges on hormone replacement, requiring a careful balance of glucocorticoids and mineralocorticoids. The presented case illustrates practical challenges in diagnosis and treatment.

Understanding adrenal insufficiency's nuances, diagnostic intricacies, and tailored management is pivotal for optimal patient care. Collaboration across medical disciplines is essential to navigate this complex terrain successfully.

Bibliography

1. Kumar R and Wassif WS. "Adrenal insufficiency". *Journal of Clinical Pathology* 75 (2022): 435- 442.
2. Mason AS., *et al*. "Epidemiological and clinical picture of Addison's disease". *Lancet* 2 (1968): 744-747.
3. Bates AS., *et al*. "The effect of hypopituitarism on life expectancy". *The Journal of Clinical Endocrinology and Metabolism* 81 (1996): 1169-1172.
4. Nilsson B., *et al*. "Pituitary adenomas in Sweden between 1958 and 1991: incidence, survival, and mortality". *The Journal of Clinical Endocrinology and Metabolism* 85 (2000): 1420-1425.
5. Regal M., *et al*. "Prevalence, and incidence of hypopituitarism in an adult Caucasian population in northwestern Spain". *Clinical Endocrinology* 55 (2001): 735-740.
6. Shivaprasad C. "Sheehan's syndrome: newer advances". *Indian Journal of Endocrinology and Metabolism* 15.3 (2011): S203-S207.
7. Alexandraki KI., *et al*. "Adrenal Insufficiency". In: Feingold KR, Anawalt B, Blackman MR, *et al*., editors. Endotext South Dartmouth (MA): MDText.com, Inc (2000).
8. Kazlauskaite R., *et al*. "Corticotropin test for Hypothalamic-Pituitary-Adrenal Insufficiency: A Metanalysis". *The Journal of Clinical Endocrinology and Metabolism* 93.11 (2008): 4245-4253.
9. Lovas K and Husebye ES. "Replacement therapy for Addison's disease: recent developments". *Expert Opinion on Investigational Drugs* 17.4 (2008): 497-509.
10. Reimondo G., *et al*. "Secondary hypoadrenalism". *Pituitary* 11.2 (2008): 147-154.
11. Lebbe M and Arlt W. "What is the best diagnostic and therapeutic management strategy for an Addison patient during pregnancy?" *Clinical Endocrinology* 78 (2013): 497-502.
12. Hagg E., *et al*. "Value of basal plasma cortisol assays in the assessment of pituitary-adrenal insufficiency". *Clinical Endocrinology* 26 (1987): 221-226.
13. Dickstein G., *et al*. "Adrenocorticotropin stimulation test: effects of basal cortisol level, time of day, and suggested new sensitive low dose test". *The Journal of Clinical Endocrinology and Metabolism* 72 (1991): 773-778.
14. Schlaghecke R., *et al*. "The effect of long-term glucocorticoid therapy on pituitary-adrenal responses to exogenous corticotropin-releasing hormone". *The New England Journal of Medicine* 326 (1992): 226-230.

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