The Clinical Manifestations, Diagnosis, and Treatment of Adrenal Emergencies

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KEYWORDS

- Adrenal emergencies • Primary adrenal insufficiency (Addison disease)
- Secondary adrenal insufficiency • Tertiary adrenal insufficiency • Adrenal crisis
- Pheochromocytomas

KEY POINTS

- Adrenal insufficiency occurs because of a disruption in the hypothalamic-pituitary-adrenal axis. The resultant hormonal deficiencies cause a myriad of nonspecific symptoms, complicating the clinical picture and delaying diagnosis.
- The hallmark of adrenal crisis is hypotension and shock refractory to fluid resuscitation and vasopressors. Adrenal crisis is a life-threatening condition and treatment should not be delayed for confirmatory testing.
- Hydrocortisone is the drug of choice for treating cases of adrenal crisis or insufficiency because of its glucocorticoid and mineralocorticoid effects.
- Pheochromocytoma is a rare, catecholamine-secreting tumor of the adrenal medulla, which may precipitate life-threatening hypertension and lead to multiorgan system failure.

INTRODUCTION

With his perfectly tanned, boyish good looks, athleticism, intelligence, and wit, John F. Kennedy (JFK) was the picture of vitality. Even 50 years after his assassination, his presidential administration, still referred to as Camelot, embodies the hopes, dreams, and exuberant idealism of many Americans. Yet beneath the facade, JFK was plagued by the myriad of health problems seen in patients with adrenal insufficiency and those on chronic steroids. JFK's medical records reveal that he was diagnosed with adrenal insufficiency in 1947 and hypothyroidism in 1955. Experts now believe that JFK suffered from autoimmune polyendocrine syndrome type 2. Unlike the participants of more recent political campaigns, JFK's health issues remained largely hidden from the public domain. Decades later, we know that JFK's physicians prescribed him

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numerous medications but the extent to which his illness impacted his presidential decision-making and the course of American history remains largely unknown.[1,2]

Emergency medicine physicians should be able to identify and treat patients whose clinical presentations including key historical, physical examination, and laboratory findings are consistent with diagnoses of primary, secondary, and tertiary adrenal insufficiency, adrenal crisis, and pheochromocytoma. Failure to make a timely diagnosis leads to increased morbidity and mortality. As great mimickers, adrenal emergencies often present with a constellation of nonspecific signs and symptoms that can lead even the most diligent emergency physician astray. As discussed in this article, the emergency physician must include adrenal emergencies in the differential diagnosis when encountering such clinical pictures.

EMERGENCIES OF THE ADRENAL CORTEX

Primary Adrenal Insufficiency (Addison Disease)

Epidemiology

In the United States, the prevalence of Addison disease is 40 to 60 cases per 1 million population. Internationally, the occurrence is equally rare. The reported prevalence in countries where data are available is 39 cases per 1 million population in Great Britain, 60 cases per 1 million population in Denmark, and 144 cases per million in Norway.[3,4] It is more common in women and diagnosis peaks during the fourth to sixth decades of life. In the United States, roughly 80% of cases are caused by autoimmune disorders.[5] These autoimmune disorders can occur as an isolated process or as part of an autoimmune polyendocrine syndrome known as the polyglandular autoimmune syndrome types I and II. Type I polyglandular autoimmune syndrome is associated with candidiasis, hypoparathyroidism, and adrenal failure. Type II polyglandular autoimmune syndrome consists of Addison disease plus either an autoimmune thyroid disease or type 1 diabetes mellitus associated with hypogonadism, pernicious anemia, celiac disease, or primary biliary cirrhosis.[6] Causes of Addison disease are shown in **Table 1**.

Anatomy and physiology

The adrenal glands are encapsulated, retroperitoneal organs comprised of an outer cortex and an inner medullary zone. The cortex is subdivided into three zones: the zona fasiculata and zona reticularis, which secrete glucocorticoids and androgens, and the zona glomerulosa, which produces mineralocorticoids.[7] The most clinically important glucorticoid produced by the adrenal cortex is cortisol. Aldosterone and dehydroepiandrosterone acetate (DHEA) are the most clinically important mineralocorticoid and androgen, respectively. Aldosterone functions in the setting of hypovolemia and regulates blood pressure by acting on the distal tubules and collecting ducts of the nephron to cause the conservation of sodium, secretion of potassium, which leads to increased water retention and blood pressure. DHEA acts as a metabolic intermediate in the biosynthesis of the androgen and estrogen sex steroids.[7] **Table 2** reviews the actions of the adrenal hormones and the target systems they affect. The inner medullary zone produces catecholamines including epinephrine and norepinephrine. Adrenal function and secretion of hormones is maintained by the body until approximately 80% to 90% of the glands are destroyed.

Released during periods of stress including trauma and infection, cortisol is vital to the body's response and impacts immune function; vascular tone; and lipid, protein, and carbohydrate metabolism. Its release is regulated by the hypothalamic-pituitary-adrenal (HPA) axis (**Fig. 1**). Signals from the body (eg, cytokine release, tissue injury, pain, hypotension, hypoglycemia, hypoxemia) are sensed by the central nervous