Evaluation and Treatment of Adrenal Dysfunction in the Primary Care Environment

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KEYWORDS

• Cushing's syndrome • Adrenocorticotropic hormone • Sympathetic nervous system • Pheochromocytoma

KEY POINTS

- Adrenal Insufficiency is the clinical manifestation of deficient production or action of glucocorticoids or mineral corticoids.
- Adrenal Insufficiency is often disabling and occasionally lethal; however, it can be successfully treated if diagnosed early.
- Hypercortisolism, commonly called Cushing's Syndrome is caused by the overproduction of ACTH and consequent bilateral hyperplasia and overproduction of cortisol.
- The most common cause of Cushing's Syndrome is caused by prolonged exposure to glucocorticoids prescribed for inflammation.
- The primary care clinician should have knowledge related to the signs and symptoms, predisposing factors, diagnostic tests and treatment options for adrenal disorders.

INTRODUCTION

Adrenal dysfunction is an uncommon clinical disorder that occurs when there is interference with the normal functioning of the adrenal gland.[1–3] Adrenal disorders are classified by either hyperproduction or hypoproduction of cortisol and may be congenital or acquired. Adrenal insufficiency occurs when there is an inadequate level of basal or stress level cortisol. Conversely, Cushing's syndrome is characterized by an overproduction of adrenocorticotropic hormone (ACTH) with consequent bilateral adrenal hyperplasia and overproduction of cortisol.

The adrenal glands, located at the superior poles of the kidneys, produce hormones that regulate metabolism, the immune system, blood pressure, and other essential functions. Each gland is composed of 2 distinct parts, the adrenal medulla and the adrenal cortex. The adrenal medulla is regulated by the sympathetic nervous system and secretes the catecholamines, epinephrine, and norepinephrine. The adrenal cortex secretes 2 types of adrenocortical hormones, mineralocorticoids and glucocorticoids, along with a small amount of androgenic hormones. For the primary care clinician,

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the treatment of adrenal cortex disorders is more common; however, recognizing adrenal medullary dysfunction is also essential to ensure that patients are referred for appropriate specialty care.

ADRENAL MEDULLA

Disorders of the adrenal medulla arise primarily from neoplasms. Pheochromocytoma, the most common neoplasm, originates from chromaffin cells and excretes catecholamines. These neoplasms may also be of neural lineage, such as neuroblastomas and ganglioneuromas.[4,5] Fewer than 10% are malignant and the triad of symptoms include headache, diaphoresis, and palpitations. The classic sign is hypertension that is often refractory to treatment. In about 50% of patients, hypertension is sustained; however, some patients have relatively normal blood pressure with surges of elevations. Paroxysmal symptoms may vary from several times daily to weekly or monthly. The classic triad of symptoms include headache, diaphoresis, and palpitations. Less common symptoms include anxiety, pain in the chest or abdomen, fatigue, and weight loss. Given the life-threatening nature of labile hypertension, a high index of suspicion is imperative. Typically, pheochromocytoma is diagnosed with evidence of catecholamines or their metabolites in the urine. After a positive urine test a computed tomography scan, MRI, or ultrasound examination (when radiation must be minimized in pregnancy, infants, and children) may be used to visualize a tumor.

Diseases of the adrenal medulla are fortunately rare; however, they are potentially life threatening. The primary care clinician must be able to recognize the signs and symptoms of adrenal medullar dysfunction. Proper treatment is managed by endocrinology, surgery, and oncology (for the <10% of cases that are malignant).

ADRENAL CORTEX

The adrenal cortex, the outer layer of the adrenal gland, is composed of 3 distinct zones and is responsible for the production of vital hormones, cortisol and aldosterone. The outer zone, the zona glomerulosa, produces the mineralocorticoid aldosterone, which is responsible for sodium reabsorption and potassium excretion, which regulates extracellular fluid volume and arterial blood pressure. Dysfunction of the zona glomerulosa may result in death owing to retention of high levels of potassium and excess loss of sodium.[6] The zona fasciculata and the zona reticularis produce glucocorticoids. Cortisol, the most important glucocorticoid, regulates metabolism and mediates the response to stress. It is essential when the body experiences stress such as with surgery, trauma, or serious infection. Without proper amounts of cortisol, the body is unable to cope with major stress, which can lead to crisis and death. **Table 1** lists the adrenal hormones and their potencies secreted by the adrenal cortex.

ADRENAL INSUFFICIENCY

Adrenal insufficiency is the clinical manifestation of deficient production or action of glucocorticoids and/or mineralocorticoids. It is a potentially life-threatening disorder that can result from primary adrenal failure or secondary adrenal disease owing to impairment of the hypothalamic–pituitary axis.[7–10] Although often disabling and occasionally lethal, adrenal insufficiency can be treated successfully if diagnosed early. The primary care clinician should have knowledge related to signs and symptoms, predisposing factors, diagnostic tests, and treatment modalities. **Box 1** lists symptoms, clinical signs, and laboratory results associated with adrenal insufficiency.