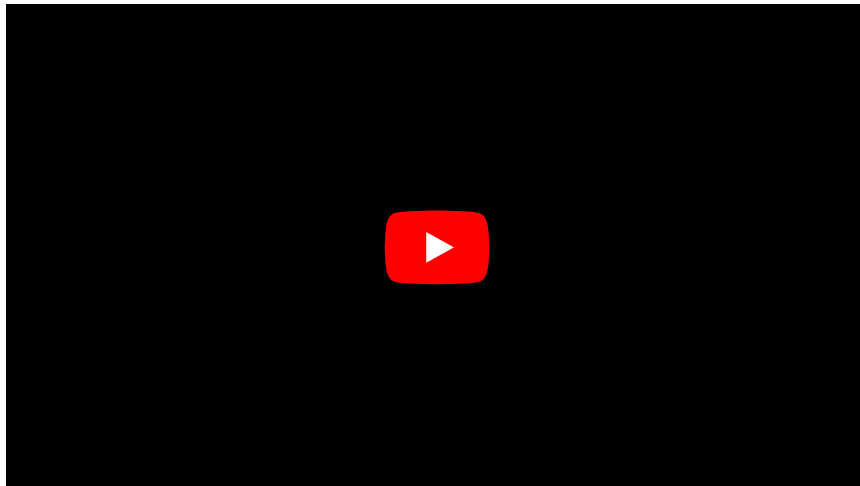


Hyperaldosteronism

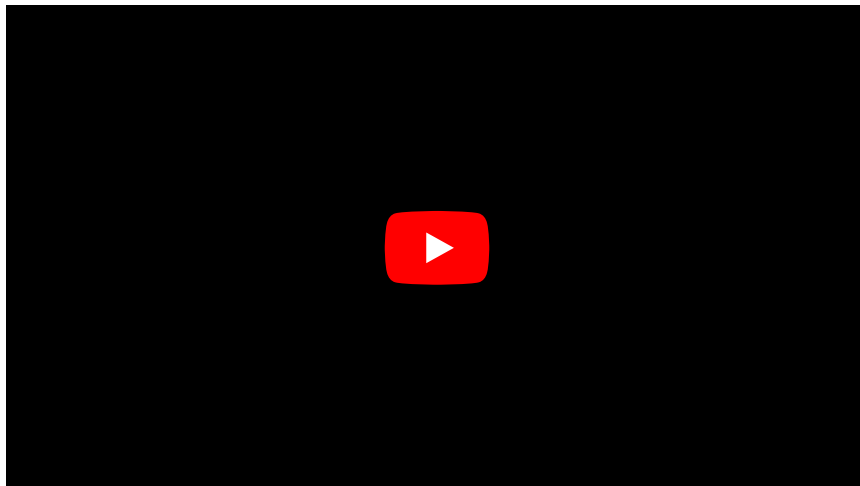
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Last update: Monday, 02 Oct 2023 at 8.17 pm.



Secondary hyperaldosteronism:



Definition of Disease:

Hyperaldosteronism, is defined as an excess of circulating aldosterone (McCance, Huether, Brashers, & Rote, 2010, p. 768). This causes physiologic hypertension (Young & Kaplan, 2014). Aldosterone is produced by the adrenal cortex of the kidneys. Hyperaldosteronism can be caused from a primary or a secondary etiology as described below (McCance et al., 2010).

Pathophysiology:

Aldosterone is a mineralocorticoid steroid that primarily affects the ion transport of the epithelial cells of the nephron collecting ducts of the kidneys (and to a lesser degree all other epithelial cells in the body) resulting in sodium and water retention with associated hydrogen and potassium ion loss (McCance, Huether, Brashers, & Rote, 2010, p. 717-718). Its normal serum level is typically between 5 to 30 ng/dL (McCance et al., 2010). The primary control mechanism of aldosterone secretion is the renin-angiotensin-aldosterone system, in which decreased blood

pressure or sympathetic stimulation of the kidneys causes renin release with resulting conversion of angiotensin I to angiotensin II which directly stimulates aldosterone secretion from the adrenal cortex (McCance et al., 2010). Although, angiotensin II is the primary stimulant for aldosterone synthesis and secretion; aldosterone secretion from the adrenal cortex is also directly affected to a lesser degree by the plasma concentrations of potassium, sodium, and ACTH levels (McCance et al., 2010).

Genetics:

Primary familial hyperaldosteronism

There are three uncommon types of primary familial hyperaldosteronism that are caused from a dominantly expressed genetic mutation (Young & Kaplan, 2014). • Type I familial hyperaldosteronism is due to a chimeric gene of CYP11B1/CYP11B2 (Young & Kaplan, 2014). This is also referred to as a glucocorticoid-remediable aldosterone (GRA) since it can be treated with glucocorticoid administration (Young & Kaplan, 2014). The prevalence of type I familial hyperaldosteronism is only 0.66% but should be ruled out in a hypertensive patient under the age of 21 (Young & Kaplan, 2014). • Type II familial hyperaldosteronism's exact mutation location is not known. However, it resides somewhere within chromosomes 7p 22 (Young & Kaplan, 2014). This mutation causes bilateral idiopathic hyperplasia of the adrenal glands or an aldosterone producing adenoma (Young & Kaplan, 2014). The prevalence of type II familial hyperaldosteronism is also only 0.66% (Young & Kaplan, 2014). • Type III familial hyperaldosteronism is caused from a germline mutation affecting the KCNJ5 subunit of the potassium channel complex and is the rarest of the three (Young & Kaplan, 2014). Type III familial hyperaldosteronism typically presents at an early age and is associated with massive hyperplasia of the adrenal glands (Young & Kaplan, 2014).

Secondary aldosteronism

Bartter syndrome is the only known genetic cause of secondary hyperaldosteronism (McCance et al., 2010). It is an autosomal recessive heterogeneous genetic disorder that causes disrupted salt transport by the ascending loop of Henle (McCance et al., 2010). This results in symptomatic diuresis from salt wasting with resulting hypokalemia, hypovolemia, hypercalciuria, and metabolic acidosis (McCance et al., 2010).

Epidemiology:

The age of onset of hypertension is an important piece of information to help decipher between the different ideologies of primary hyperaldosteronism (Funder et al., 2008). If primary aldosteronism is detected in someone before the age of 20 a familial genetic etiology is possible (Funder et al., 2008). Disease described

Primary hyperaldosteronism

Primary aldosteronism, which is defined as a non-suppressible hyper secretion of aldosterone from the adrenal glands, can occur through several etiologies but the two most common are: • An aldosterone producing adenoma • Bilateral idiopathic hyperaldosteronism (Young & Kaplan, 2014). More rare causes of primary aldosteronism include: • Unilateral hyperplasia (otherwise known as primary adrenal hyperplasia) of the adrenal gland • Bilateral adrenal hyperplasia that can be either macr nodular or micronodular • One of the three types of familial hyperaldosteronism as described above • An ectopic aldosterone secreting tumor or a pure aldosterone producing adrenocortical carcinoma (Young & Kaplan, 2014).

Secondary hyperaldosteronism

Secondary aldosteronism is defined as any pathophysiology that results in an up regulation of the renin angiotensin aldosterone feedback system (McCance, Huether, Brashers, & Rote, 2010). As expected, any situation in which circulating blood volume is decreased such as shock, dehydration, or hypoalbuminemia will result in renin secretion by the kidneys with subsequent hyperaldosteronism (McCance et al., 2010). Additionally since the kidneys are the source of renin, any pathology resulting in a compromise blood flow to the kidneys will result in renin excretion such as heart failure, hepatic cirrhosis, or renal artery stenosis (McCance et al., 2010). However the most common cause of secondary hyperaldosteronism is from diuretic administration (McCance et al., 2010). Congestive heart failure is a particular instance in which this feedback system worsens the pathology and is why angiotensin converting enzyme (ACE) inhibitors are recommended in these patients (McCance et al., 2010). A lesser common etiology is a renin secreting adenoma from the kidney (McCance et al., 2010). Additionally a patient should be asked if they consume excessive amounts of licorice or chronically chewed tobacco as this can increase mineralocorticoid levels within the body causing aldosteronism (McCance et al., 2010). Increases in aldosterone levels will also be seen in women who are pregnant or are using oral contraceptives (McCance et al., 2010). In Bartter syndrome, hypokalemia causes excess prostaglandin (specifically PGE2) production which causes excess renin secretion by the renal cells (McCance et al., 2010).

Sign and Symptoms:

The manifestations of primary aldosteronism are directly related to the renal effects of aldosterone (McCance et al., 2010; Young & Kaplan, 2014). Primary signs are hypertension, metabolic alkalosis, and hypokalemia (Young & Kaplan, 2014). Other signs and symptoms include a new steady-state involving mildly increased volume and decreased potassium, a lack of edema, mild hyponatremia, metabolic alkalosis if hypokalemia is present, hypomagnesemia, an increase in the glomerular filtration rate, muscle weakness related to hypokalemia, increased urinary albumin wasting, and increased cardiovascular risk (Young & Kaplan, 2014). Initial sodium and water retention reaches a maximum intensity after a few days of increased aldosterone levels then diuresis ensues due to increasing atrial natriuretic peptide secretion and hypertension driven diuresis from increased renal perfusion pressure (pressure natriuresis) (Young & Kaplan, 2014). This process is referred to as the aldosterone escape phenomenon and establishes the new steady-state (Young & Kaplan, 2014). Signs and symptoms of secondary hyperaldosteronism are similar to primary hyperaldosteronism in that patients typically express hypertension, hypokalemia, and metabolic alkalosis however unlike primary aldosteronism there may be edema present (McCance et al., 2010). Also signs and symptoms will reflect the specific etiology that is causing the secondary hyperaldosteronism.

Diagnosis

If hyperaldosteronism is suspected in a patient aldosterone and renin levels should be measured (McCance et al., 2010). A measured serum aldosterone level greater than 15 ng/dL is indicative of hyperaldosteronism (McCance et al., 2010). Serum renin levels less than 1 ng/mL per hour is associated with primary aldosteronism (McCance et al., 2010). Secondary sources would see a much higher level of renin in the serum. Primary hyperaldosteronism evidence-based guidelines for treatment were published by the endocrine Society in 2008 (Funder et al., 2008). These guidelines recommend evaluating patients for primary hyperaldosteronism if they present with the following history: • Stage II or stage III or drug-resistant hypertension as defined by the joint national commission, • “hypertension and spontaneous or diuretic induced hypokalemia”, • “hypertension with adrenal incidentaloma”, • “hypertension in a family history of early onset hypertension or cerebrovascular accident in a young age (<40 yr)”, • case detection is also recommended “for all hypertensive first-degree relatives or patients with PA” (Funder et al., 2008). These guidelines recommend evaluating all these patients listed above using a renin to aldosterone serum ratio to decipher if hyperaldosteronism is present and contributing to their symptoms (Funder et al., 2008). If the ARR ratio is positive (>20-40) these guidelines recommend confirmatory tests for primary hyperaldosteronism (Funder et al., 2008). Once primary aldosteronism is confirmed, adrenal computed tomography (CT) scan should be ordered to evaluate for masses or carcinoma (Funder et al., 2008). Bilateral versus unilateral adrenal disease should be distinguished before surgical intervention is applied (Funder et al., 2008). This can be accomplished through an adrenal venous sampling (Funder et al., 2008). If the patient is 20 years of age or younger and has a family history of hyperaldosteronism or a family history of strokes under the age of 40 genetic testing is recommended (Funder et al., 2008).

Treatment

Treatment is aimed at mitigating the effects of hypertension, renal toxicity, cardiovascular damage, and hypokalemia (Young & Kaplan, 2014). Due to the many different etiologies of hyperaldosteronism, treatments must be tailored towards the specific underlying cause. For unilateral adrenal hyperplasia, laparoscopic adrenalectomy is recommended (Funder et al., 2008). If surgical intervention is not a possibility mineralocorticoid receptor antagonist treatment is recommended (Funder et al., 2008). If the patient has bilateral adrenal hyperplasia, treatment with a mineralocorticoid receptor antagonist is recommended (Funder et al., 2008). Spironolactone is recommended as first-line treatment (Funder et al., 2008). Patients with glucocorticoid receptive aldosteronism should be treated with the lowest effective dose of glucocorticoid to stabilize blood pressure and serum potassium levels (Funder et al., 2008).

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