Syndrome Of Apparent Mineralocorticoid Excess (SAME)



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Pathophysiology

11 Beta-Hydroxysteroid Dehydrogenase Deficiency
(1)(1) Wands Beta-fish Hydras-Steroid-stairs dehydrator (deficiency) broken
This syndrome is due to a deficiency of the enzyme 11-beta-hydroxysteroid dehydrogenase type 2. This enzyme is located at aldosterone-binding sites and causes degradation of cortisol, which binds as avidly to the mineralocorticoid receptor as aldosterone, to inactive cortisone. Inhibition of the enzyme leads to increased stimulation of mineralocorticoid receptors via pathologically persistent cortisol.

Elevated Cortisol
Up-arrow Court-of-Sol
Cortisol is a steroid hormone that is produced in the zona fasciculata of the adrenal cortex. It has multiple important effects including stimulation of gluconeogenesis, immunosuppression, increased insulin resistance, the elevation of blood pressure, among others. At elevated levels, it may stimulate mineralocorticoid receptors. Normally the enzyme 11-beta-hydroxysteroid dehydrogenase type 2 converts cortisol to cortisone, which is inactive on the mineralocorticoid receptors. A deficiency in this enzyme leads to reduced cortisone levels and elevated cortisol levels.

Low Renin
Down-arrow Wrenches
Renin is an enzyme that is normally secreted by the renal juxtaglomerular cells in response to low renal blood pressure, beta 1 adrenergic receptor activation, and NaCl deficiency. It works by hydrolyzing (breaking down) angiotensinogen to angiotensin 1 which is further broken down by the endothelial-bound angiotensin-converting enzyme (ACE) into angiotensin II, a potent vasoconstrictor. Since in the syndrome of apparent mineralocorticoid excess, there is elevated mineralocorticoid activity which results in hypertension and metabolic alkalosis, the renin-angiotensin-aldosterone is inhibited and therefore renin levels are decreased. This can be useful for the diagnostic process.

Low Aldosterone
Down-arrow Aldo-stereo
Aldosterone is a steroid hormone that increases renal reabsorption of water and sodium, as well as the secretion of potassium. Since in the syndrome of apparent mineralocorticoid excess, there is elevated mineralocorticoid activity which results in hypertension and metabolic alkalosis, the renin-angiotensin-aldosterone is inhibited and therefore aldosterone levels are decreased. This can be useful for the diagnostic process.

Causes

Autosomal-Recessive
Recessive-chocolate
This syndrome can be inherited in an autosomal recessive pattern, which means that to get the disease, the patient needs to inherit both copies of the defective gene coding for the enzyme 11-beta hydroxysteroid dehydrogenase.

Licorice (glycyrrhetinic acid) Ingestion
Liquor-Rice
Licorice is a popular sweetener found in many soft drinks, food products, snacks, and herbal medicines. Licorice contains a steroid, glycyrrhetinic acid, that inhibits (both competitively and by reducing gene expression) 11-beta-hydroxysteroid dehydrogenase enzyme and therefore is an acquired cause of SAME.

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Signs & Symptoms

Hypertension

Hiker-BP

Cortisol can avidly bind and activate the mineralocorticoid receptors, which is normally prevented by the enzyme 11-beta hydroxysteroid dehydrogenase by breaking it into cortisone. In SAME, cortisol activates the mineralocorticoid receptors leading to sodium reuptake by renal cells and increased water reabsorption, ultimately leading to hypertension. Elevated cortisol levels can cause hypertension by mechanisms independent of the mineralocorticoid receptor. It activates the renin-angiotensin system, enhances vasoactive substances and causes suppression of the vasodilatory systems. One of the main clinical signs in a patient with SAME is therefore hypertension.

Hypokalemia

Hippo-banana

Cortisol can avidly bind and activate the mineralocorticoid receptors, which is normally prevented by the enzyme 11-beta hydroxysteroid dehydrogenase by breaking it into cortisone. In SAME, cortisol activates the mineralocorticoid receptors leading to sodium reuptake by renal cells and potassium secretion, which leads to hypokalemia. Hypokalemia is the decreased potassium level in serum, defined by <3.5 mEq.

Metabolic Alkalosis

Metal-ball Elk-loser

Metabolic alkalosis is defined as an increase in the serum concentration of bicarbonate which results in a pH greater than 7.45. In the context of SAME, it is caused by increased mineralocorticoid receptor activity that causes loss of hydrogen ions by the renal cells. The mechanism of loss of hydrogen ions is due to the increased activity of the apical proton pump in the collecting duct. When a hydrogen ion is secreted into the tubular lumen, a bicarbonate ion is gained into the systemic circulation by the basolateral chloride/bicarbonate exchanger. The hypokalemia present in SAME also contributes to the metabolic alkalosis by the efflux of potassium from intracellular to extracellular space in exchange for hydrogen ions and by the increased secretion of hydrogen in the kidney in order to enable potassium reabsorption.

Treatment

Potassium-Sparing Diuretics

Bananas Shooting Dice-rockets

Potassium sparing diuretics are a class of diuretics consisting of aldosterone receptor antagonists (spironolactone, eplerenone) and epithelial sodium channel blockers (e.g., triamterene, amiloride). All agents in this class reduce the reabsorption of sodium and the excretion of potassium and are therefore useful in the treatment of SAME.

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