Liddle syndrome

Description

Liddle syndrome is an inherited form of high blood pressure (hypertension). This condition is characterized by severe hypertension that begins unusually early in life, often in childhood, although some affected individuals are not diagnosed until adulthood. Some people with Liddle syndrome have no additional signs or symptoms, especially in childhood. Over time, however, untreated hypertension can lead to heart disease or stroke, which may be fatal.

In addition to hypertension, affected individuals can have low levels of potassium in the blood (hypokalemia). Signs and symptoms of hypokalemia include muscle weakness or pain, fatigue, constipation, or heart palpitations. The shortage of potassium can also raise the pH of the blood, a condition known as metabolic alkalosis.

Frequency

Liddle syndrome is a rare condition, although its prevalence is unknown. The condition has been found in populations worldwide.

Causes

Liddle syndrome is caused by mutations in the *SCNN1B* or *SCNN1G* gene. Each of these genes provides instructions for making a piece (subunit) of a protein complex called the epithelial sodium channel (ENaC). These channels are found at the surface of certain cells called epithelial cells in many tissues of the body, including the kidneys, where the channels transport sodium into cells.

In the kidney, ENaC channels open in response to signals that sodium levels in the blood are too low, which allows sodium to flow into cells. From the kidney cells, this sodium is returned to the bloodstream (a process called reabsorption) rather than being removed from the body in urine.

Mutations in the *SCNN1B* or *SCNN1G* gene change the structure of the respective ENaC subunit. The changes alter a region of the subunit that is involved in signaling for its breakdown (degradation) when it is no longer needed. As a result of the mutations, the subunit proteins are not degraded, and more ENaC channels remain at the cell surface. The increase in channels at the cell surface abnormally increases the reabsorption of sodium (followed by water), which leads to hypertension. Reabsorption

of sodium into the blood is linked with removal of potassium from the blood, so excess sodium reabsorption leads to hypokalemia.

Learn more about the genes associated with Liddle syndrome

- SCNN1B
- SCNN1G

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- Pseudoaldosteronism
- Pseudoprimary hyperaldosteronism

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Liddle syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0221043/)

Genetic and Rare Diseases Information Center

- Liddle syndrome (https://rarediseases.info.nih.gov/diseases/7381/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Liddle syndrome%22)

Catalog of Genes and Diseases from OMIM

- LIDDLE SYNDROME 1; LIDLS1 (https://omim.org/entry/177200)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Liddle+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2880+days%22%5Bdp%5D)

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