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LIDDLE SYNDROME: PATHOPHYSIOLOGY, CLINICAL FEATURES, TREATMENT.

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Abstract

Liddle syndrome is a rare autosomal dominant disorder characterized by early-onset hypertension, hypokalemia, and metabolic alkalosis. It results from gain-of-function mutations in epithelial sodium channel (ENaC) subunits. This expanded review covers detailed molecular mechanisms, clinical manifestations, diagnostics, differential diagnosis, and modern treatment approaches.

Introduction

Liddle syndrome, first described by Grant Liddle in 1963, is a form of pseudohyperaldosteronism. Despite clinical similarity to hyperaldosteronism, patients have suppressed renin and aldosterone levels.

Genetics and Molecular Basis

Mutations in SCNN1A, SCNN1B, and SCNN1G genes encode ENaC subunits. These mutations disrupt PY motifs, preventing binding to NEDD4-2 ubiquitin ligase, resulting in decreased degradation of ENaC and increased channel activity.

Pathophysiology

Increased ENaC activity leads to sodium retention, volume expansion, and hypertension. Enhanced sodium reabsorption drives potassium and hydrogen ion secretion, causing hypokalemia and metabolic alkalosis. RAAS suppression occurs due to volume overload.

Clinical Features

Patients present with early-onset hypertension, hypokalemia, fatigue, muscle weakness, and sometimes arrhythmias. Severe cases may lead to cardiovascular complications including left ventricular hypertrophy.

Diagnosis

Diagnosis includes detection of hypertension with low plasma renin activity and low aldosterone levels, hypokalemia, metabolic alkalosis, and confirmation via genetic testing.

Differential Diagnosis

Includes primary hyperaldosteronism, congenital adrenal hyperplasia, apparent mineralocorticoid excess, and Cushing syndrome.

Treatment

Treatment involves ENaC inhibitors such as amiloride and triamterene. Spironolactone is ineffective. Salt restriction and monitoring electrolytes are essential.

Prognosis

With proper treatment, prognosis is good. Untreated cases may result in severe cardiovascular complications.

Conclusion

Liddle syndrome is an important and treatable cause of secondary hypertension. Early recognition and targeted therapy improve outcomes significantly.

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References

1. Liddle GW et al. A familial renal disorder simulating primary aldosteronism. J Clin Invest. 1963.
2. Gormley K et al. Liddle syndrome mechanisms. Hypertension. 2003.
3. Warnock DG. Liddle syndrome overview. Kidney Int. 2001.
4. Snyder PM. ENaC regulation. J Clin Invest. 2002.
5. Hanukoglu I. ENaC mutations. Endocr Dev. 2016.
6. Rossier BC et al. ENaC physiology. Physiol Rev. 2015.
7. Funder JW et al. Mineralocorticoid receptors. Endocr Rev. 2017.
8. Lifton RP et al. Genetic basis of hypertension. Nature. 2001.
9. Palmer LG. Ion transport mechanisms. Kidney Int. 2004.
10. Soundararajan R et al. ENaC and hypertension. Am J Physiol. 2010.