Spastic Paraplegia Type 5A

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1. Introduction

Spastic paraplegia type 5A is one of a group of genetic disorders known as hereditary spastic paraplegias. These disorders are characterized by muscle stiffness (spasticity) and severe weakness in the lower limbs (paraplegia). Hereditary spastic paraplegias are often divided into two types: pure and complex. The pure types involve spasticity and weakness only in the lower limbs, while the complex types involve additional problems with other areas of the body; additional features can include changes in vision, changes in intellectual functioning, brain abnormalities, and disturbances in nerve function (neuropathy). Spastic paraplegia type 5A is usually a pure hereditary spastic paraplegia, although complex type features have been reported in some individuals, usually in those who have had the condition for many years.

In addition to spasticity and weakness, people with spastic paraplegia type 5A can lose the ability to sense the position of their limbs or detect vibrations with their lower limbs. They may also have muscle wasting (amyotrophy), reduced bladder control, or high arches of the feet (pes cavus). The signs and symptoms of spastic paraplegia type 5A usually appear in adolescence but can begin at any time between infancy and mid-adulthood. The condition slowly worsens over time, often leading affected individuals to require walking support or wheelchair assistance.

2. Frequency

Spastic paraplegia type 5A is a rare condition. Its prevalence is unknown.

3. Causes

Spastic paraplegia type 5A is caused by mutations in the *CYP7B1* gene. This gene provides instructions for making an enzyme called oxysterol 7-alpha-hydroxylase. In the brain, oxysterol 7-alpha-hydroxylase is involved in a pathway that converts cholesterol to hormones called neurosteroids. These neurosteroids increase nerve cell activity (excitability) and promote cell survival and communication between nerve cells. Oxysterol 7-alpha-hydroxylase helps maintain normal cholesterol levels in the brain and, by producing neurosteroids through altering existing hormones within the pathway, regulates the effects of neurosteroids on the brain.

CYP7B1 gene mutations that cause spastic paraplegia type 5A reduce or eliminate the activity of oxysterol 7-alpha-hydroxylase. In the brain, a decrease in enzyme activity results in an accumulation of cholesterol and alters neurosteroid production triggered by oxysterol 7-alpha-hydroxylase. Abnormal levels of neurosteroids impairs cell survival, likely leading to nerve cell death. The abnormal buildup of cholesterol in the brain probably also contributes to the death of nerve cells. The loss of these cells results in the deterioration of nervous system functions (neurodegeneration) and causes the movement problems, weakness, and other signs and symptoms of spastic paraplegia type 5A.

3.1 The gene associated with Spastic paraplegia type 5A

- CYP7B1

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- autosomal recessive spastic paraplegia 5A
- spastic paraplegia 5A
- SPG5A

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