Xia-Gibbs Syndrome

Subjects: Genetics & Heredity

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Xia-Gibbs syndrome is a neurological disorder characterized by weak muscle tone (hypotonia), mild to severe intellectual disability and delayed development.

genetic conditions

1. Introduction

Expressive language skills (vocabulary and the production of speech) are particularly affected; children with this condition usually do not speak their first word, a milestone typically achieved within the first year, until age two or later, and some never learn to talk. Development of motor skills, such as crawling and walking, can also be delayed.

Other signs and symptoms of Xia-Gibbs syndrome vary among affected individuals. Additional neurological features include poor coordination and balance (ataxia) and seizures. Feeding problems and sleep abnormalities can also occur in people with the condition, and many affected individuals experience short pauses in breathing while they sleep (obstructive sleep apnea). In some people with Xia-Gibbs syndrome, imaging tests of the brain show abnormalities in the brain's structure. For example, the tissue connecting the left and right halves of the brain (the corpus callosum) can be abnormally thin.

Xia-Gibbs syndrome can also affect physical development. Growth is usually impaired, and many affected individuals are shorter than their peers. Side-to-side curvature of the spine (scoliosis) is also a common feature. Some people with Xia-Gibbs syndrome have unusual facial features, such as a broad forehead, low-set ears or ears that stick out, widely space eyes (hypertelorism), eye openings that slant up or down (upslanting palpebral fissures or downslanting palpebral fissures), a flat bridge of the nose, or a thin upper lip. Other, less-common abnormalities involving the bones and skin include premature fusion of certain skull bones (craniosynostosis), unusually loose (lax) joints, and loose skin.

Behavior problems can also occur in Xia-Gibbs syndrome. Some affected individuals have features of autism spectrum disorder, which is characterized by impaired communication and social interactions, or of attention-deficit/hyperactivity disorder (ADHD). Other problems can include aggression, anxiety, poor impulse control, and self-injury.

2. Frequency

Xia-Gibbs syndrome is thought to be a rare disorder, although its prevalence is unknown. Doctors believe the condition is underdiagnosed, because many people with intellectual disability never have genetic testing to determine the underlying cause.

3. Causes

Xia-Gibbs syndrome is caused by mutations in a gene called *AHDC1*. This gene provides instructions for making a protein with an unknown function. Researchers suspect that the protein may be able to attach (bind) to DNA and control the activity of other genes. Most of the *AHDC1* gene mutations involved in Xia-Gibbs syndrome lead to production of abnormally short AHDC1 proteins. The effects of these changes in cells are unclear. The shortened proteins may be quickly broken down or be unable to function. Or, the abnormal proteins may interfere with the function of AHDC1 proteins produced from the normal copy of the gene. Researchers suspect that a reduction in the amount of functional AHDC1 protein impairs normal brain development, leading to intellectual disability, speech problems, and other neurological features of Xia-Gibbs syndrome. Abnormal development of other body systems caused by a shortage of AHDC1 protein may account for additional signs and symptoms of the condition.

3.1 The gene associated with Xia-Gibbs syndrome

- AHDC1

4. Inheritance

Xia-Gibbs syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

The condition results from new (de novo) mutations in the gene that occur either during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. Affected individuals have no history of the disorder in their family.

5. Other Names for This Condition

- AHDC1-related intellectual disability-obstructive sleep apnea-mild dysmorphism syndrome
- autosomal dominant intellectual disability 25
- XGS

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