The Role of Genetic Mutations in Gene DNMT1 in Autosomal Dominant Cerebellar Ataxia, Deafness, and Narcolepsy Syndrome

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Abstract

People with ADCADN syndrome have problems with the coordination of movements (ataxia) and hearing loss caused by internal ear disorder (sensory inferiority). ADCADN syndrome is caused by the mutation of the DNMT1 gene, which is based on the short arm of chromosome 19 as 19p13.2. The mutation in the DNMT1 gene, which causes ADCADN syndrome, affects the region of the DNA methyl transferase 1, which contributes to the proper DNA methylation process.

Keywords: ADCADN Syndrome; DNMT1 Gene; DNA Methyl Transferase 1; Brain Disorders

Generalizations of ADCADN syndrome

ADCADN syndrome is a neurodegenerative disorder characterized by symptoms that begin in the middle of adulthood and progressively worsen [1].

Signs and clinical symptoms of ADCADN syndrome

People with ADCADN syndrome have problems with the coordination of movements (ataxia) and hearing loss caused by internal ear disorder (sensory inferiority). These people often have dysentery (narcolepsy) daily. Narcolepia is usually accompanied by cataracts, which suddenly cause loss of muscle tone in response to strong emotions such as thrill, wonder or anger. This part of the muscle weakness can cause a person to fall while walking, which sometimes causes injury. These symptoms and symptoms of ADCADN syndrome usually start at age thirty [1].

Finally, people who have ADCADN also experience mental retardation (intellectual decline). Cognitive problems often begin with performance impairment, which is the ability to plan and execute operations and create problem solving strategies. Other features that can occur as a deterioration of the syndrome include: Nervous degeneration that carries information from the eyes to the brain (vision atrophy); cloudy eyes (cataracts); burning, tingling or pain in the arms and legs (sensory neuropathy); Swollen (lymph nodes) organs; Inability to control the intestines or urine flow (incontinence); Depression; Crying or laughter uncontrollably (pseudobulbar symptoms); or distorted vision of reality. The injured people usually die at age 40 or 50 [1,2].

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The etiology of ADCADN syndrome

ADCADN syndrome is caused by the mutation of the DNMT1 gene, which is based on the short arm of chromosome 19 as 19p13.2. This gene provides instructions for the synthesis of an enzyme called DNA methyl transferase 1. This enzyme is involved in DNA methylation, in which methyl groups including a carbon atom and three hydrogen atoms are added to DNA molecules. In particular, this enzyme helps to add methyl groups to cytosine nucleotides [1-3].

The DNA of methyl transferase 1 is active in the adult nervous system. Although its specific role in the nervous system is still not well understood, it may be possible to regulate neuronal puberty, differentiation, the ability of neurons to migrate in the areas where it is needed, the association of neurons with each other and the survival of the neurons help [1-3].

The mutation in the DNMT1 gene, which causes ADCADN syndrome, affects the region of the DNA methyl transferase 1, which contributes to the proper DNA methylation process. As a result, this mutation causes abnormal methylation, which in turn affects the expression of multiple genes. Ultimately, the maintenance of the neurons that make up the nervous system is disrupted and leads to signs and symptoms of ADCADN syndrome [1-4].

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ADCADN syndrome follows the dominant autosomal inheritance pattern. Therefore, a gene mutation of DNMT1 (parent or parent) is required to produce this syndrome and the chance of having a child with this syndrome in the dominant autosomal state is 50% for each possible pregnancy [1-4].
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Frequency of ADCADN syndrome

ADCADN syndrome is a neurogenic disorder whose frequency is not known in the world. So far, less than 24 cases of this syndrome have been reported in medical literature from around the world [1-4].

Diagnosis of ADCADN syndrome

ADCADN syndrome is diagnosed based on clinical and clinical findings of patients and some neurological and pathological tests. The most accurate method for detecting this syndrome is the molecular genetic testing of the DNMT1 gene to investigate the presence of possible mutations [1-5].

Figure 5: Schematic of the normal eye (pictured above) in front of the eye with cataract (photo below).

ADCADN syndrome treatment routes

The ADCADN syndrome treatment and management strategy is symptomatic and supportive. Treatment may be done by a team of experts including a neurologist, orthopedic specialist, physical medicine specialist, eye specialist, ears specialist, and other health care professionals. There is no valid treatment for this syndrome, and all clinical measures are needed to reduce the suffering of the sufferers. Genetic counseling is also needed for all parents who want a healthy baby [1-6].

Discussion and Conclusion

People with ADCADN syndrome have problems with the coordination of movements (ataxia) and hearing loss caused by internal ear disorder (sensory inferiority). ADCADN syndrome is caused by the mutation of the DNMT1 gene, which is based on the short arm of chromosome 19 as 19p13.2. The mutation in the DNMT1 gene, which causes ADCADN syndrome, affects the region of the DNA methyl transferase 1, which contributes to the proper DNA methylation process. There is no valid treatment for this syndrome, and all clinical

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measures are needed to reduce the suffering of the sufferers. In the future, gene therapy techniques will be used to reduce the suffering of the patients with this syndrome. The treatment of narcolepsy is directed toward the specific symptoms that are present in each individual. Various medications may help to alleviate certain symptoms associated with narcolepsy.

For individuals who experience excessive daytime sleepiness and sleep attacks, therapy may include administration of certain stimulants, such as modafinil (Provigil). Modafinil was approved by the Food and Drug and Administration (FDA) for the treatment of excessive daytime sleepiness in narcolepsy in 1999. Modafinil is now the most widely prescribed drug for excessive daytime sleepiness. The drug’s mechanism of action appears to differ from that of other stimulants and does not appear to affect alertness or memory. In addition, evidence suggests that modafinil therapy is not associated with dependency or symptoms of withdrawal and therefore may be an effective alternative to other treatments for excessive daytime sleepiness. Modafinil is generally associated with fewer side effects than previous drugs used to treat this condition.

Previous drugs that have been used to treat excessive daytime sleepiness in narcolepsy include methylphenidate (Ritalin, Methylin), methamphetamine, or dextroamphetamine. These drugs stimulate the central nervous system and are still used when modafinil is unsuccessful. Because such medications may be associated with certain side effects, including nervousness, insomnia, or irritability, careful monitoring by physicians is required to ensure appropriate dosage adjustments and effectiveness of such therapy. In addition, close monitoring and long-term follow-up by physicians may be required if therapy is withdrawn.

Additional stimulants that have been used to treat excessive daytime sleepiness and narcolepsy include mazindol, selegiline, and pemoline.

A variety of drugs have been used to treat cataplexy. The orphan drug Xyrem, manufactured by Jazz Pharmaceuticals, has been approved by the FDA to treat cataplexy, the sudden loss of muscular control and weakness that is associated with narcolepsy. Xyrem has also been effective in improving nighttime sleep in individuals with narcolepsy. Some individuals with narcolepsy treated with high doses of the drug showed improved of daytime sleepiness. However, Xyrem is potentially associated with serious side effects. The generic name for Xyrem is sodium oxybate and it is also known as gamma hydroxybutyrate or GHB.

**Bibliography**


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