Costeff Syndrome

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Costeff syndrome is an inherited condition characterized by vision loss, delayed development, and movement problems. Vision loss is primarily caused by degeneration (atrophy) of the optic nerves, which carry information from the eyes to the brain. This optic nerve atrophy often begins in infancy or early childhood and results in vision impairment that worsens over time. Some affected individuals have rapid and involuntary eye movements (nystagmus) or eyes that do not look in the same direction (strabismus).

Keywords: genetic conditions

1. Introduction

Development of motor skills, such as walking, is often delayed in people with Costeff syndrome. Affected individuals may also have speech difficulties (dysarthria). While some people with Costeff syndrome have mild to moderate intellectual disability, many have normal intelligence.

Movement problems in people with Costeff syndrome develop in late childhood and include muscle stiffness (spasticity), impaired muscle coordination (ataxia), and involuntary jerking movements (choreiform movements). As a result of these movement difficulties, individuals with Costeff syndrome may require wheelchair assistance.

Costeff syndrome is associated with increased levels of a substance called 3-methylglutaconic acid in the urine (3-methylglutaconic aciduria). The amount of this substance does not appear to influence the signs and symptoms of the condition. Costeff syndrome is one of a group of metabolic disorders that can be diagnosed by the presence of 3-methylglutaconic aciduria. People with Costeff syndrome also have high levels of another acid called 3-methylglutaric acid in their urine.

2. Frequency

Costeff syndrome affects an estimated 1 in 10,000 individuals in the Iraqi Jewish population, in which at least 40 cases have been described. Outside this population, only a few affected individuals have been identified.

3. Causes

Mutations in a gene called *OPA3* cause Costeff syndrome. The *OPA3* gene provides instructions for making a protein whose exact function is unknown. The OPA3 protein is found in structures called mitochondria, which are the energy-producing centers of cells. It is thought to play a role in the organization of the shape and structure of mitochondria and in controlled cell death (apoptosis).

OPA3 gene mutations that result in Costeff syndrome lead to a loss of OPA3 protein function. Cells without any functional OPA3 protein have abnormally shaped mitochondria. These cells likely have reduced energy production and die prematurely, decreasing energy availability in the body's tissues. Cells in the eyes and brain have high energy demands, and it is likely that they are particularly vulnerable to cell death due to dysfunctional mitochondria and reduced energy production.

3.1. The Gene Associated with Costeff Syndrome

- OPA3

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

- 3-methylglutaconic aciduria type 3
- 3-methylglutaconic aciduria type III
- autosomal recessive OPA3
- autosomal recessive optic atrophy 3
- Costeff optic atrophy syndrome
- infantile optic atrophy with chorea and spastic paraplegia
- Iraqi Jewish optic atrophy plus
- MGA, type III
- MGA3
- OPA3 defect
- optic atrophy plus syndrome

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