National Ataxia Foundation

Ataxia with Oculomotor Apraxia (AOA)

What is AOA?

Ataxia with Oculomotor Apraxia (AOA) is a group of rare neurodegenerative disorders. There are many types of AOA, with the most common being AOA1, AOA2, and AOA4. Each type of AOA is caused by mutations in different genes.

- AOA1 is often associated with muscle twitching and jerky movements, as well as increased cholesterol levels. Symptoms usually begin around age 4.

- AOA2 is often associated with muscle twitching and jerky movements. Symptoms usually begin around age 15. People with AOA2 also have high amounts of the proteins alpha-fetoprotein and creatine phosphokinase (CPK) in their blood. It is unknown why AFP and CPK levels are elevated. Some people with AOA2 also have high cholesterol.

- AOA4 is often associated with repetitive muscle contractions, as well as muscle wasting in the hands and feet. Symptoms usually begin around age 4.

The frequency of AOA varies across the world. AOA1 is most common in Japan and AOA4 is most common in Portugal, though both forms are found across the world. AOA2 is the most common form of AOA worldwide, with an estimated prevalence of 1 in 900,000.

What are the symptoms of AOA?

Like many other forms of Ataxia, AOA is marked by poor balance and coordination. In fact, the word Ataxia means incoordination. There can also be problems coordinating muscles that control speech and swallowing.

Most people with AOA also have oculomotor apraxia, which means they have difficulty moving their eyes side-to-side. Instead, most people with AOA need to turn their head to see things on either side, rather than moving their eyes.

Neuropathy is also common for people with AOA. This slows down the connection between nerves, leading to impaired reflexes, limb weakness, and poor sensation in the hands and feet.

Intelligence is not usually impacted by AOA1 an AOA2. Some people with AOA4 have an intellectual disability.

What is the prognosis for AOA?

AOA symptoms usually begin in childhood. AOA1 and AOA4 usually begin around age 4. AOA2 symptoms usually begin around age 15. Most individuals with AOA will need to eventually use a wheelchair, typically 10 to 15 years after the start of balance and coordination issues. Lifespan generally is not shortened by the disease.

Due to increased cholesterol levels, people with AOA have an increased risk of developing heart disease. Following a low-cholesterol diet is recommended for most people with AOA, to reduce these risks. Treatments such as physiotherapy, occupational therapy, and speech-language therapy can also significantly improve the lives of people with AOA.

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Genetics of AOA

AOA are a group of genetic disorders, which means that they are inherited diseases. Each type of AOA is caused by mutations in different genes.

- AOA1 is caused by mutations in the APTX gene.
- AOA2: is caused by mutations in the SETX gene.
- AOA4: is caused by mutations in the PNKP gene.

Genes are microscopic structures within the cells of our bodies that contain instructions for every feature a person inherits from his or her parents. The abnormal gene responsible for different forms of AOA is passed along from generation to generation by family members who carry it. Most of the genes that cause AOA are involved in repairing damaged DNA.

AOA1, AOA2, and AOA4 are autosomal recessive diseases. This means that you need two copies of the gene that causes a specific form of AOA to develop this disorder. It also means that individuals of either sex are equally likely to inherit the gene and develop the disease.

Each child of a person with AOA has a 50 percent chance of inheriting the gene that causes AOA. However, since you need two copies of the AOA gene to develop the disorder, people with one AOA gene mutation do not get sick. We call these people carriers, since they have an AOA gene mutation and can pass it on to their children.

Gene tests can be performed for diagnostic purposes to determine what kind of Ataxia is within a person or family. Genetic testing also can be done, in some circumstances, even before there are symptoms to determine whether a person carries the abnormal gene or genes that cause Ataxia. This is called predictive or presymptomatic testing. A gene test also can be used to determine whether a fetus has an abnormal Ataxia gene. This is called prenatal testing. Anyone who is considering a predictive or prenatal test should consult with a genetic counselor to discuss the reasons for the test, the possible outcomes, and how those outcomes might affect the person emotionally, medically, or socially.

How is AOA diagnosed?

A neurologic examination can determine whether a person has symptoms typical of AOA. A neurologist is often the most helpful specialist in recognizing symptoms and diagnosing the disease that causes Ataxia. There are several potential follow-up tests. MRI brain imaging may be used to confirm the cerebellar atrophy. Blood tests can be used to detect increased levels of AFP, CPK, or cholesterol. An EMG can be used to confirm neuropathy.
A definitive diagnosis of AOA is established following genetic testing. This confirms that someone has the mutation that causes AOA1, AOA2, AOA4, or another type of AOA.

What kind of support is available after the diagnosis?

NAF provides accurate information for you, your family, and your physician about Ataxia. Please visit our website at www.ataxia.org for additional information, including a listing of Ataxia support groups, physicians who treat Ataxia, social networks, and more. For questions contact the NAF directly at (763) 553-0020 or naf@ataxia.org.