Ataxia-Telangiectasia (A-T)

What is ataxia-telangiectasia (A-T)?

A-T is a hereditary progressive neurodegenerative disorder that begins in early childhood. The most debilitating symptom is the progressively worsening ataxia or loss of balance. The underlying problem is a gradual and continual loss of certain types of cells in the cerebellum of the brain, which control and coordinate the movement of limbs, fingers, eyes, tongue, etc. It is thought that because the cells lack a protein named ATM (for ataxia-telangiectasia mutated), they do not recognize and repair breaks in the DNA (which carries the code for our genes). These DNA breaks occur all the time in all of us. But because the ATM protein controls over 700 other proteins that help cells to repair DNA, when there is not enough ATM protein, the DNA damage accumulates and eventually leads to the death of individual cells, especially in the central nervous system.

What are the symptoms of A-T?

An affected child usually begins to show signs of clumsiness shortly after learning to walk, around one year of age. This is followed slowly by increased loss of balance, slurring of words, and uncoordinated eye movements. Small, dilated blood vessels appear over the whites of the eyes, bridge of the nose, or ears, or elsewhere (i.e., telangiectasia); this is not seen in other kinds of early onset ataxias. Repeated infections of the sinuses and lungs occur due to an underlying immunodeficiency. A neurologist can document that the loss of balance is due to loss of cerebellar function within the brain. Occasionally, cancer is the first symptoms to appear, usually as a lymphoma or leukemia. This is a particularly dangerous situation because cancer in A-T patients must be treated differently. Later in life, muscles of the hands and feet become spastic. A persistent cough signals the onset of chronic lung failure.

What is the prognosis for A-T?

Many patients with A-T now live into their 30's or longer. The three most common causes of death are from: cancer, infection, and progressive lung failure. As the treatment of cancer has improved, the prognosis of A-T has improved. Similarly, for the prevention and treatment of infections. To date, little progress has been made in understanding or treating the chronic lung failure.

How is A-T acquired?

A-T is inherited as an autosomal recessive disorder. It is passed on by parents who are each carriers. When each parent passes on a single mutated copy of the ATM gene, their child will be affected. Mutations are changes in the DNA from the normal, healthy copy. The most common types of ATM mutations are: splicing (35%), nonsense (25%), and frameshift (25%). Each of these changes results in a deficiency of ATM protein in the nucleus of all cells in the body of an affected child.

How common is A-T?

In the U.S., A-T is the second most common recessive ataxia of childhood, Friedreich's Ataxia being the most common but usually occurs at a somewhat later age than A-T. In countries where marriage between cousins is uncommon, such as in the U.S., the incidence is about 1 in 40,000 live births. However, among ethnic groups where cousin-cousin marriages are common, the incidence increases significantly. The carrier frequency is approximately 1 in 100 persons.

How is the diagnosis made?

An alphafetoprotein (AFP) test is elevated in the blood in >95% of patients. Karyotyping usually reveals characteristic translocations between chromosomes 7 and 14. An MRI will show (after 7 or 8 years of age) that the cerebellum is shrinking in size. The absence of ATM protein and its various functions can be documented in the laboratory by a blood test. The sensitivity of A-T cells to ionizing radiation is also markedly increased. In an experienced laboratory, DNA sequencing can confirm the presence of mutations in both copies of the very large ATM gene. DNA sequencing can also be used to identify carriers; however, this is expensive because of the size of the gene. A more rapid method of carrier detection is being developed.

What kind of support is available after the diagnosis?

The National Ataxia Foundation offers support groups, chapters and ambassadors throughout the United States and Canada. These groups are excellent local resources for persons with ataxias and their families to learn, share, and network.
There is a patient support group that can be contacted through the A-T Children's Project website. Neurologists at A-T centers, such as Johns Hopkins or UCLA, can monitor progress and arrange speech and swallowing therapy, physical and occupational therapy, and adaptive equipment to minimize in-turning of the feet and hands, if these occur. They can prescribe drugs that reduce drooling, or cerebellar tremors. Because one of the most serious underlying problems of A-T cells is the inefficient repair of DNA damage, an antioxidant like alphalipoic acid (ALA) is usually prescribed to minimize the amount of DNA damage. Severe immunodeficiencies can be treated with intravenous immunoglobulin. These supportive treatments can greatly improve the quality of life for a patient. Because A-T patients are at an increased risk of developing cancer, any suggestive signs or symptoms should be quickly investigated so that an early diagnosis can be made and treatment initiated. Because the cells of A-T patients are extremely sensitive to the effects of ionizing radiation (such as X-rays), radiation therapy of cancer is dangerous and generally to be avoided. Radiological procedures, including dental X-rays, should be used only when no other diagnostic procedure is available. A careful record should be kept of each radiological procedure and the approximate dose of radiation that was received.

Although there is as yet no medicine that will reverse the progression of the disorder, drugs have been identified in the laboratory that can induce A-T cells with certain types of mutations to make ATM protein. However, these drugs have unacceptable side effects and new drugs are being pursued and tested.

National Ataxia Foundation
2600 Fernbrook Lane, Suite 119 • Minneapolis, MN 55447-4752
Phone: (763) 553-0020 • Fax: (763) 553-0167
Email: naf@ataxia.org • Website: www.ataxia.org