ATAXIA-TELANGIECTASIA OVERVIEW

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Ataxia-telangiectasia (A-T) is a rare degenerative disorder that first becomes apparent during childhood. It is a complicated illness that affects a number of different parts of the body, particularly the brain and the immune system.

A-T is a progressive disease, which means that symptoms worsen with time. Most individuals with A-T will eventually need a wheelchair and assistance with activities of daily living.

Although first noted in the scientific literature in 1926, A-T has only been systematically studied since the 1960s. New discoveries are being made, enabling us to better understand and manage the illness. Despite its rarity, A-T is of major interest to scientists, because its many different facets may yield clues about other major health problems including neurologic disease, cancer, immunodeficiency and aging.

Signs and Symptoms

A-T is characterized by a set of signs and symptoms that are distinctive yet vary widely in severity from person to person. The manifestations of A-T become worse over a period of years. However, the rate and nature of deterioration are not predictable.

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The constellation of signs and symptoms include the following:

- **Abnormal gait (ataxia) and posture:** The child with A-T typically appears normal until he/she begins to walk. The typical gait is wobbly, and the toddler may have great difficulty standing or sitting without swaying. These problems may be stable or even improve for a few years, but eventually the gait and posture deteriorate. Later, children with A-T may develop abnormal extra movements - tremors; uncontrolled jerking or fidgets of the hands and arms (chorea); larger twisting movements of the arms and legs (athetosis); or awkward and twisted postures (dystonia).

Signs and Symptoms

√ Abnormal gait and posture

√ Slurred speech

√ Difficulty with eye movements

√ Telangiectasia

√ Immune deficiency

√ Predisposition to cancer

√ Slow growth

- **Slurred speech (dysarthria) and drooling:** The child with A-T may have slurred speech from very early years, and the speech may worsen at a highly individual rate. Despite the slurred speech, the person with A-T still can communicate, although conversing can be a challenge.
- **Difficulty with eye movements (oculomotor apraxia):** Although vision is usually normal, persons with A-T develop difficulty with control and movement of the eyes. Eventually, many children have trouble reading and following moving objects.

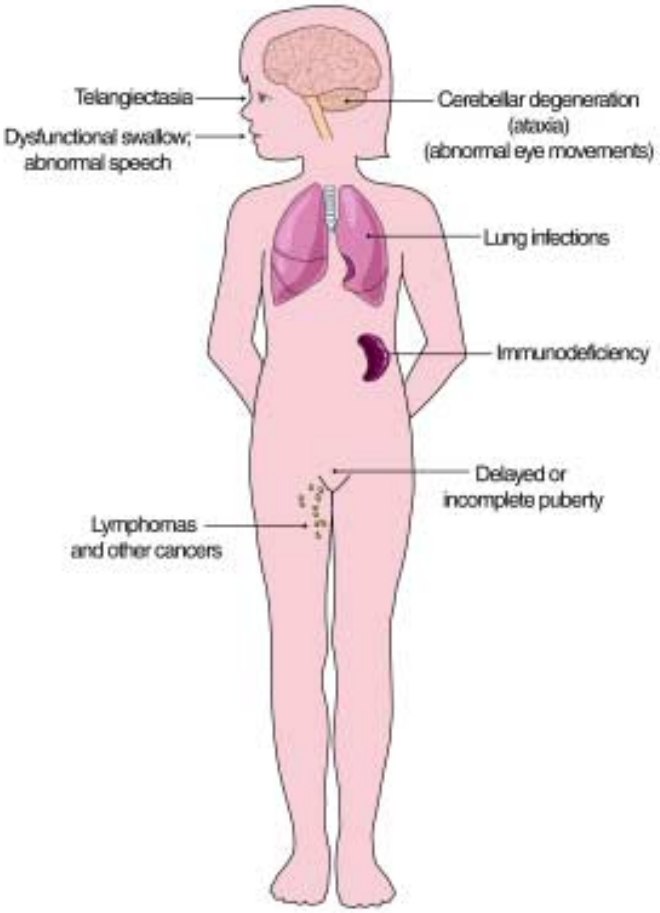

Fig. 1.1: Ataxia-telangiectasia affects a number of body systems.

- **Abnormal swallowing (dysphagia):** By the time children with A-T reach their teens, most have difficulty chewing food and swallowing liquids. In some cases, food or liquid will enter the windpipe (trachea).

- **Intellect:** Although intelligence is difficult to measure, some children with A-T do not do as well on standard testing as their peers. The disease may slow down brain processes and cause the person to need more time to think. In addition, A-T causes a characteristic dull facial expression that may convince others that the affected child is "slow" or not paying attention. Some children with A-T attend mainstream schools; others are in special school settings for part or all of the school day.

- **Skin:** Clusters of blood vessel (telangiectasia) usually appear on the whites of the eyes by the time the child is five to eight years old. Some children with A-T, however, do not develop these clusters until later, or not at all. These clusters make the eyes appear bloodshot or infected (pink eye). The skin, especially on sun-exposed areas, may show signs of premature aging (progeria). The skin of the face, hands and feet may develop light or dark spots that are most often seen on the skin of elderly persons. Children may develop grey hairs.

A-T is an autosomal recessive disorder caused by a defective gene on chromosome number 11.

- **Immune system:** Up to 80% of persons with A-T have a degree of immunodeficiency (low levels of immunoglobulin and/or white blood cells in the blood) that increases their susceptibility to infections. The degree of immunodeficiency can vary widely among persons with A-T, with some mildly affected while others have more severe problems. Immunodeficiency usually remains steady during life but may deteriorate over time.

- **Predisposition to develop cancer:** The lifetime risk for cancer is as high as 30 percent (one in three patients) in individuals with A-T. This may be as much as 1000 times more likely than in normal individuals of the same age. Most cancers involve the immune system (lymphoma), and the abnormal A-T gene may make treatment a little more difficult than in other individuals.

- **Growth and endocrine system:** Many children with A-T grow more slowly than their peers. Weight for height decreases in later years, in part due to difficulties with self-feeding and swallowing. Puberty may be delayed or incomplete.

How A-T is Diagnosed

As a rare disease, A-T may be difficult to diagnose. Often, children with A-T are first believed to have cerebral palsy or another neurological disorder such as Friedreich's ataxia. A-T is diagnosed by physical examination and laboratory tests. One important lab test is measurement of the serum alpha feto-protein (AFP) level, which is usually high in people with A-T. Laboratory tests may also be done to look for increased sensitivity to x-rays. The white blood cells of A-T patients are more likely to develop broken chromosomes or to die after laboratory x-ray exposure than the white blood cells of other individuals.

Incidence

A-T is an extremely rare disease, although it is known to occur in both genders, among all races, on all continents around the world. The incidence of A-T in the United States has been estimated to be between 1 in 300,000 and 1 in 40,000 persons. The A-T Children's Project knows of approximately 350 children with A-T in the United States.

The course of A-T varies widely. Individuals with A-T have grown up to attend college, live independently, and survive into their 50's and 60's.

Cause

A-T is an autosomal recessive disorder caused by a defective gene on chromosome number 11. In order to develop A-T, a person must inherit two abnormal copies of the gene, one from each parent. The gene responsible for A-T is called ATM, for Ataxia-Telangiectasia Mutated. The ATM gene produces a large protein that is called the ATM protein. People with A-T have defective genes on both copies of chromosome 11 and therefore do not produce the protein. Scientists are intensively studying the ATM gene and protein, trying to learn more about what it does, how it does it, and why its absence causes the problems observed in individuals with A-T.

Course of Illness

Among the earliest signs of A-T are difficulty with controlling body posture and movement. A-T often becomes apparent when a toddler first learns to walk. While all young children are unstable when first learning to walk, parents often notice that the child with A-T does not appear to improve. Some children with A-T may start to walk later than is normal. The child may have difficulty maintaining balance, be unable to stand without teetering back and forth, and fall or stumble more often.

The course of the neurologic problems in A-T is highly variable between individuals. Most seem to improve for a while in preschool years but at a slower place than is normal. This is the typical course for cerebral palsy, which is often misdiagnosed during these years because of the pattern of development. In late pre-school or early school years some aspect of functioning worsens. Children may have more difficulty with walking and balance, new problems with handwriting, the appearance of unusual movements of the eye or greater difficulty with speech. The new problems, or the appearance of the eye telangiectasia, often lead to new investigations and the proper diagnosis of A-T. With time, many of the problems become more prominent, and difficulties with uncontrollable limb or trunk movements arise.

Most people with A-T are susceptible to infections of the sinuses (sinusitis) and lung (bronchitis or pneumonia). They are also at greater risk of developing malignancies or cancers, particularly those affecting the immune system, such as lymphomas.

The course of A-T varies widely. Some ndividuals with A-T have grown up to attend college, live independently, and a few have survived into their 50's and 60's, but most do not do this well.

Treatment

There is at present no cure for A-T. Treatment is supportive in nature, to prevent infections and other illnesses, and to help the person remain as active and functional as possible. Children with A-T should be encouraged to attend school and maintain as normal a lifestyle as possible.

Medications may be prescribed to treat the extra movements of the arms and legs. However, no medication has yet been shown in a scientific way to help with the symptoms or the underlying disease. Parents and members of the health care team must remain vigilant to sinus and lung infections, and start appropriate treatment promptly. Special attention to nutrition and swallowing problems that arise may be helpful.

Persons with A-T may benefit from physical and occupational therapy, which can help them achieve their highest level of function. Speech and language therapy can help persons with A-T communicate more effectively. A variety of adaptive technology is available that can help enhance function and ability in the classroom or home. Overall, therapies work by helping children with strategy and practice on how best to use the motor abilities that they have, and to supply help in developing "work arounds" to allow for improved function despite a motor impairment. No form of therapy, even when done in a very intensive manner, appears to alter the rate of the underlying neurologic disease.

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