



Ataxia-Telangiectasia:(A-T) An Overview

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Ataxia-Telangiectasia (“A-T”) is a very rare, familial neurodegenerative disorder.

Other features of the disorder include:-

* *Frequent infections* * *Thin build* * *An increased risk of cancers*

The most striking laboratory finding is an increased sensitivity to high doses of ionising radiation. Initial diagnosis may be difficult because of the disorder’s slow onset and its rarity.

CLINICAL FEATURES

1. Introduction

The first signs of A-T usually occur in the toddler years. These first signs are of difficulty with control of the body, posture and body movement (truncal ataxia). The child may start to walk later than usual (after 18 months), may be reluctant to let go of supporting people or objects, may continue to walk unsteadily for longer than normal, may be unable to stand still without tottering back and forth and may fall frequently.

Prominent blood vessels in the whites of the eyes usually occur by the age of 5 years. These are the ocular telangiectasia of the condition and resemble those vessels seen in the eyes of much older people. They can occasionally be present at birth yet in others may not develop until the teenage years. Although potentially a cosmetic problem they do not bleed or itch. It is their constant nature, not changing with time or weather or emotion, which marks them as different from other eye blood vessels.

Initially it may be hard to be sure that anything is amiss and some children seem to improve from 3 to 5 years, but eventually it becomes obvious that balance control is abnormal. Walking becomes more strenuous and appears awkward, doors and walls are frequently used for support. Running may, for a while, seem less affected; this is because less balance is needed for quick movements than slower graceful ones. Most children with A-T start to use a wheelchair around their 10th year (some even earlier).

Towards the end of the first decade and the start of the second other problems come to light; these can become as disabling as the loss of body balance control.

2. Co-ordination of Limbs

Co-ordination of the limbs becomes abnormal (peripheral ataxia). Involuntary movements may start in some children but not all. These are:-

- Little jerks of the hands and feet which look like fidgeting (chorea)
- Slower, larger twisting movements of the neck, face and shoulders (athetosis)
- The adoption of rather stiff and twisted postures (dystonia)
- Occasional uncontrolled jerks of limbs (such as we all get sometimes when going to sleep)
- Shaking episodes of a limb which are like shivering (tremors).

3. Slurred Speech (Dysarthria)

Slurring of speech may develop in the first decade, getting worse for 5 to 10 years and then remaining a static problem. We know of no-one who cannot be understood, although conversation can be a slow process.

4. Eye Movements

Eye movements become restricted (vertical and horizontal saccadic apraxia). Reading and following moving objects becomes difficult.

5. Intellect

Learning difficulties are not seen in A-T. However, many children seem to have a slowing-down in their thinking speed. Some children are in mainstream while others are in special schools; a few have attended university.

6. Immune Problems

About half the people with A-T have immune problems. These usually take the form of repeated colds and runny noses (sinopulmonary infections).

The immune system is complex and difficult to assess, but if the child is suffering more than his/her fair share of infections an immunologist should undertake this assessment. Some people with A-T need additional immunisations (DPT, Hib, Prevenar and Pneumovax), others need continual antibiotics to provide a “background cover” and some need injections of immunoglobulins (proteins that the body makes to fight infections). Others are never troubled. The impression is that it is bacterial rather than viral infections that are the most trouble.

7. Thin Build

Thinness, sometimes to an excessive degree, is a part of A-T. Some of this is due to a poor appetite, some to the energy expended with involuntary movements and some must be inherent in the disorder. Some children have a mild form of A-T, the disorder starting later and all the features being less marked.

Some people with A-T, both males and females have a delayed puberty. This seems more common in those who are thin or are prone to infections.

8. Adults with A-T

Young adults with A-T may develop difficulties with swallowing and food ‘going down the wrong way’. This may exacerbate any tendency for lower respiratory tract infections like pneumonia. Weight loss may also occur and so patients will need some extra monitoring. The A-T Clinic at Papworth Hospital is specifically for adults

DRUGS

No single drug, medicine, herbal remedy etc. can help all people with A-T. Most drugs which act on the nervous system can cause problems in A-T. Drug therapy requires specialised attention.

LABORATORY FINDINGS AND DIAGNOSIS

The tests that are of use in the diagnosis of A-T are shown in table 1. The most useful tests are a combination of serum AFP level, the response of white blood cells to X-rays or gamma rays and measurement of the level of ATM protein (the protein affected in the cells of A-T patients). If these tests indicate A-T, then identification of the mutations in the ATM gene will be attempted. These tests can only be carried out in specialist centres. The individual patient's symptoms and signs are what determine the clinical diagnosis. Diagnosis is more difficult before the disorder has fully developed when the child may be 'a bit wobbly on his/her feet'. The laboratory findings are confirmatory, of the clinical diagnosis of A-T.

GENETICS, PRENATAL DIAGNOSIS AND INCIDENCE

A-T is usually familial, that is, it runs in families. The mode of inheritance is autosomal recessive ('AR'). In AR families there is a 1 in 4 chance of each child born to the parents having the disorder.

Prenatal diagnosis can be carried out in most families, but this is complex and requires arrangement before conception. Further information can be obtained about this from the A-T Society or the A-T Clinic, Nottingham (please see separate leaflet).

The incidence of A-T in Caucasians is about 3 per million so the disorder is very rare, with probably fewer than 200 affected people in the U.K.

CANCER

People with A-T have an increased incidence (probably 1% per year) of tumours, particularly lymphomas and leukaemia. The treatment of these tumours may require the use of ionising radiation in large doses. As this can be dangerous, careful discussion with the relevant doctor is needed.

There is evidence of a moderate increased risk of breast cancer in mothers of children with A-T that may be greater in those under 50 years of age. They should discuss possible screening methods with their GP.

RADIATION

It is important to put the radiation sensitivity into context. Although people with A-T have an increased sensitivity to ionising radiation (X and gamma rays), they cope with other forms of radiation normally, i.e. obtaining a suntan from ultraviolet light.

Also, the tumours seen in A-T are not thought to be radiation induced. Finally, normal X-rays of arms and chest and any necessary dental X-rays do not produce enough radiation to be harmful.

TREATMENT

Presently there is no cure for A-T, but thanks to advances in clinical management, life expectancy is improving. There are many things that can be done to help those with the disorder. Some of these are listed in Table 2. The A-T Society is the most up-to-date source of information and its contact details are on the front cover of this information sheet.

THE CAUSE OF A-T

The neurological findings in A-T are of selective nervous system damage (of the cerebellum, brain stem, basal ganglia and spinal cord). The laboratory findings suggest a defect in the cellular response to damage to DNA, particularly breaks across both strands of DNA. This damage can occur spontaneously but is also caused by x-rays and gamma rays. Precisely how this defect leads on the one hand to the neurological problems and on the other to an increased risk of lymphoid cancer is not fully understood.

RECENT AND FUTURE RESEARCH

Research has led to a better understanding of how A-T progresses and the differences that there are between patients. However, there is still no treatment. Different drugs have been tried and continue to be tried. The systematic screening for candidate drugs will hopefully make more likely the prospect of an effective treatment. It is also possible that in the long term an answer may come from new technologies such as stem cell transfer.

A-T NATIONAL CLINICS

Thanks to advances in clinical management, life expectancy in A-T is improving. All families who have a family member with A-T should take the opportunity (via their GP, specialist or the A-T Society) to attend the A-T specialist clinics at Nottingham and Papworth.

Nottingham City Hospital The multi-disciplinary team (involving neurologist, immunologist, geneticist, dietitian and therapists) has seen many families with one or more children with A-T. At present the clinic is held 3 times a year and is aimed at being complimentary to local care arrangements. It allows all the concerns of the family to be addressed at a 'one stop shop' by interested, experienced staff.

Papworth Hospital The multi-disciplinary clinic (involving immunologist, chest physician, social worker, dietitian, therapists) is for people over the age of 16 with A-T. Its aim is to address the health problems associated with this age group.

There are close links between the A-T Society, the clinics and the various research groups.

TABLE 1

Test	Result	Usefulness
Alpha-fetoprotein in blood	Increased	Good, but not specific to A-T
Chromosome breaks/rearrangements	Increased	Good, but may be normal
X-ray/gamma ray sensitivity	Increased	Good, but may be normal
ATM protein level	Absent or reduced	Very reliable - only done in a few centres
ATM mutations	Present in A-T	Gold standard - only done in a few centres
Immunoglobulin levels (IgM, IgG, IgA)	Decreased	Not always low, also low in other conditions

TABLE 2

Action	Reason
Exercise and physiotherapy	Makes best use of muscle control, should be fun-stretches muscles and ligaments
Antibiotics, immunoglobulins, vaccinations and chest physiotherapy	To treat chest infections and prevent permanent chest problems
Speech therapy	Of great help with diction, especially in the second decade
Orthopaedic referral/assessment	Corrective procedures can be helpful for joint or postural problems particularly in the lower limbs or spine.

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