

## **What is Ataxia-Oculomotor Apraxia (AOA)?**

AOA 1 and 2 are rare degenerative disorders of the nervous system. As in Ataxia-Telangiectasia (A-T), the ataxia refers to lack of coordination and the oculomotor apraxia describes difficulty in moving the eyes. Telangiectasiae are not usually seen.

AOA1 tends to start a year or so later than A-T but the onset of AOA2 is usually much later (teens). There is no associated weakening of the immune system and at present there is no known increased risk of cancer with AOA 1 or 2.

## **Clinical features of AOA1**

### **Introduction**

AOA1 may come on at the toddler stage or a bit later. The child may be labelled as a little clumsy and may start to walk later than their brothers or sisters. Balance gradually declines and it may be noticed that running is easier than walking i.e. the child falls less. By 10-11 years after onset a wheelchair may be required.

As in some patients with A-T, fidgety movements of arms and face (chorea) may occur early on in AOA1 but may disappear as the condition progresses. Peripheral nerve damage (neuropathy) giving rise to wasting of the hand and foot muscles and some numbness tends to occur in the later stages of the condition.

**Incidence:** approximately the same as A-T of 3 per million.

### **Co-ordination of limbs**

This becomes abnormal and patient may have trouble reaching for objects. Involuntary movements include those described above in A-T. These include chorea, athetosis, dystonia, myoclonus (jerks) and tremor. Fortunately, the movement disorders tend to settle with age.

### **Slurred speech (dysarthria)**

This very common and may progress with time. Most patients, however, can make themselves understood. The lack of coordination of speech can also occasionally involve the swallowing mechanism.

### **Eye movements (oculomotor apraxia)**

Patients have difficulty in moving their eyes (side to side mainly) and may adapt by moving their head to change focus. This can interfere with reading but often may not be noticed by the patient and is picked up by other family members.

### **Intellect**

Marked mental retardation is not seen in AOA1 but there may be a mild slowing in thought processes. Some may continue in mainstream schools but others may prefer the setting of a special school.

### **Muscle wasting and numbness (peripheral neuropathy)**

Later in the condition sensation in the feet and hands may be reduced and wasting of the foot and hand muscles can be seen. Attention to foot care and foot wear is required in a similar way to the follow up of patients with diabetic nerve damage.

### **Drugs**

No single drug can help all people with AOA1. Certain symptoms can be reduced with medication. One family seemed to improve a little with a vitamin called co-enzyme Q<sub>10</sub>.

### **Laboratory findings and diagnosis (AOA1)**

<b>Test</b>	<b>Results</b>	<b>Usefulness</b>
Albumin in blood	Decreased	Good but not specific to AOA1
Immunoglobulin levels	Normal	Good but not in all and may be abnormal in other conditions
Alpha-fetoprotein	Normal	Very reliable
Chromosome breaks and rearrangements	Normal	Very reliable
Ionising irradiation sensitivity	Normal	Very reliable

AOA1 is a clinical diagnosis but there are some useful laboratory tests that can be carried out. The main point of testing is to exclude A-T and to try to distinguish from AOA2. Patients with AOA1 do not have the DNA repair problems or sensitivity to irradiation seen in A-T and their alpha-fetoprotein is normal. The blood albumin, if low, in a patient with good nutrition tends to point to AOA1.

The diagnosis can now be confirmed by a blood test looking at DNA. Genetic abnormalities (mutations) in a gene called aprataxin cause the disorder. This gene test is only available via Professor Taylor's laboratory in Birmingham.

### **Genetics and incidence**

AOA1 is a genetic disorder which does tend to run in families. It is an autosomal recessive condition which means brothers and sisters may have it but the parents are often unaffected. If a child in a family has the condition there is a 1 in 4 chance that other offspring will be affected. Prenatal diagnosis is possible but is not an NHS service at present.

The estimated incidence of AOA1 is similar to A-T at 3 per million.

### **Treatment**

Patients should probably be considered for a trial of a vitamin called co-enzyme Q<sub>10</sub> but no proper studies have confirmed a positive response seen in one AOA1 family. As with A-T, speech therapy, physiotherapy and possibly orthopaedic assessment should also be considered in dealing with the different aspects of AOA1.

## **Clinical features of AOA2**

### **Introduction**

AOA2 tends to start in late adolescence or early teens. Balance gradually declines and it may be noticed that running is easier than walking i.e. the child falls less. By 16-17 years after onset of the condition a wheelchair may be required.

As in some patients with A-T and AOA1, choreoathetoid (fidgety) movements of arms and face may occur early on and unlike AOA1 they tend to persist into adulthood. Peripheral nerve damage (neuropathy) giving rise to wasting of the hand and foot muscles and some numbness tends to occur in the later stages of the condition.

**Incidence:** probably more than A-T, >3 per million.

### **Co-ordination of limbs**

This becomes abnormal and patient may have trouble reaching for objects. Involuntary movements include those described above in A-T. These include chorea, athetosis, dystonia, myoclonus (jerks) and tremor. Fortunately, the movement disorders tend to settle with age.

### **Slurred speech (dysarthria)**

This very common and may progress with time. Most patients, however, can make themselves understood. The lack of coordination of speech can also occasionally involve the swallowing mechanism.

### **Eye movements (oculomotor apraxia)**

Patients have difficulty in moving their eyes (side to side mainly) and may adapt by moving their head to change focus. This can interfere with reading but often may not be noticed by the patient and is picked up by other family members.

### **Intellect**

Marked mental retardation is not seen in AOA2 but there may be a mild slowing in thought processes. Some may continue in mainstream schools but others may prefer the setting of a special school.

### **Muscle wasting and numbness (peripheral neuropathy)**

Later in the condition sensation in the feet and hands may be reduced and wasting of the foot and hand muscles can be seen. Attention to foot care and foot wear is required in a similar way to the follow up of patients with diabetic nerve damage.

### **Drugs**

No single drug can help all people with AOA2. Certain symptoms can be reduced with medication.

## Laboratory findings and diagnosis (AOA2)

Test	Results	Usefulness
Albumin in blood	Decreased	Not reliably so and not specific
Immunoglobulin levels	Increased	Good but not in all and may be seen in other conditions
Alpha-fetoprotein	Increased	Very reliable but requires distinction from A-T
Chromosome breaks and rearrangements	Normal	Very reliable
Ionising irradiation sensitivity	Normal	Very reliable

AOA2 is a clinical diagnosis but there are some useful laboratory tests that can be carried out. The main point of testing is to exclude A-T and to try to distinguish from AOA1. Patients with AOA2 do not have the DNA repair problems or sensitivity to irradiation seen in A-T but their alpha-fetoprotein is nearly always increased. The diagnosis can now be confirmed by a blood test looking at DNA. Genetic abnormalities (mutations) in a gene called senataxin cause the disorder. This gene test is only available via Professor Taylor's laboratory in Birmingham.

### Genetics and incidence

AOA2 is a genetic disorder which does tend to run in families. It is an autosomal recessive condition which means brothers and sisters may have it but the parents are often unaffected. If a child in a family has the condition there is a 1 in 4 chance that other offspring will be affected. Prenatal diagnosis is possible but is not an NHS service at present. The estimated incidence of AOA2 is probably greater than A-T which is known to be 3 per million.

### Treatment

As with A-T and AOA1, speech therapy, physiotherapy and possibly orthopaedic assessment should also be considered in dealing with the different aspects of AOA2.

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