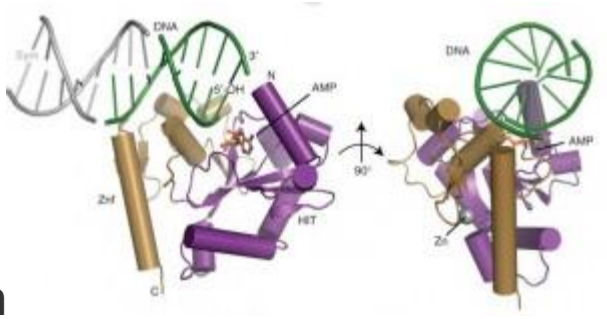
AOA1

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) causing wasting of the hand and foot muscles and some numbness tends to occur in the later stages of the condition.

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 (small jerking movements), athetosis (twisting movements), dystonia (stiff, twisted postures), myoclonus (jerks) and tremor. Fortunately, the movement disorders tend to settle with age.

Slurred speech (dysarthria)

This is very common and may progress with time. Most patients, however, can make themselves understood. The lack of co-ordination 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

Significant learning difficulties are not associated with AOA1 but there may be a mild slowing in thought processes. Some people with the condition 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_{10}.

Laboratory findings and diagnosis

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_{10}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.

(With grateful thanks to: Dr N Davies, Department of Neurology, Queen Elizabeth Hospital, Birmingham and Professor A M R Taylor, Institute for Cancer Studies, University of Birmingham)

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