Dentatorubral pallidoluysian atrophy (DRPLA)

Dentatorubral pallidoluysian atrophy (DRPLA) is a rare type of inherited progressive late-onset cerebellar ataxia. It is caused by a defect in a gene and results in damage to a part of the brain known as the cerebellum, and to its connections within the central nervous system that control movement and coordination. The name of this condition refers to a detailed specific site in the brain. 'Atrophy' means wasting away.

What are the symptoms?

DRPLA has a wide variety of symptoms and patients often present differently. The severity and time of onset of these symptoms varies between individuals. Some patients may experience all these symptoms while others will experience only a few. The order in which symptoms appear differs from one person to another. Symptoms include progressive memory loss and personality change (dementia), impaired control of bodily movements (ataxia), spasmodic jerky contraction of groups of muscles (myoclonus), affecting especially the shoulders, hips and face (chorea), fits, which can result in loss of consciousness, convulsions (epilepsy) and psychiatric disturbance.

What causes DRPLA?

DRPLA is caused by a defect in a gene. The abnormal gene is located on the 12th chromosome (Each person has 23 pairs of chromosomes). All genes are made up of nucleotides that are held together in a chain. Each nucleotide is identified by a letter (A, T, C or G). The gene that causes DRPLA is extended because of extra copies of a C-A-G repeat in atrophin-1 (ATN1) on chromosome 12.

How is DRPLA inherited?

DRPLA is inherited in an autosomal dominant fashion i.e. there is a strong chance of the condition passing to the next generation. For more information see Ataxia UK's leaflet 'Ataxia: what's that'.

When do symptoms start?

This can be highly variable. The onset of symptoms within one study was found to be between 34-60 years of age. However, symptoms can become apparent in childhood. There is a clear relationship between the onset of symptoms and the repeat length of the abnormal gene. As a general rule the more repeats there are, the earlier symptoms tend to begin. [Wardle *et al.* JNNP 2007]

How is DRPLA diagnosed?

Diagnosis can be confirmed by a genetic test. This involves taking a blood sample from the individual which is then analysed in order to identify the presence of the abnormal gene.

How common is DRPLA?

Previously, DRPLA was thought to primarily affect Japanese people, and was considered rare in Europe and the USA. However, more recent data has suggested that it may be an important genetic cause of late onset cerebellar ataxia in Caucasian patients, and the prevalence has been shown to be high in some regions of the UK, such as South Wales.

There is currently little information on the prevalence of cerebellar ataxias in the UK. However, a recent study of families in South Wales showed that DRPLA was the underlying genetic cause of 11.4% of families with dominant ataxia, compared to 0.4% in previously reported European series. This suggests that it is more common in the UK than previously thought, and likely to be under reported. [Wardle *et al.* JNNP 2007]

Management of DRPLA

Once a diagnosis has been confirmed, management of DRPLA is similar to that for all cerebellar ataxias. Physiotherapy may be helpful to help improve and maintain mobility. Speech and Language assessment and therapy may also be required. Occupational therapists can help determine any adaptations that need to be made in the home.

At present there are no disease modifying therapies available for any of the inherited ataxias, including DRPLA. However, there are a number of strategies that are useful in dealing with the effects of the disease. For example, fits (epilepsy) and involuntary movements (myoclonus, chorea) can be controlled with medications. In patients where there is a deterioration in intellectual function (dementia), support from a psychiatrist may be helpful in dealing with the effects on personality and memory.

In all cases it is important that each patient is seen regularly by a neurologist who can monitor their condition. Counselling, information, help and support are available to both the patient and their family from charities such as Ataxia UK (www.ataxia.org.uk)

Research on DRPLA in the UK

Dr Fanto's lab at King's College London studies the basic mechanisms that lead to loss of nerve cells in DRPLA using simple fly models of DRPLA. The lab is also engaged in research using more complex models, such as mouse models, which recapitulate more closely the human pathology as well as in samples from patients. This research is partly supported by Ataxia UK. (See more about this research at: https://www.ataxia.org.uk/international-research-conference). Clinical research on the distribution and frequency of DRPLA in the UK is undertaken by Dr Wardle and Professor Robertson at Cardiff University.

This information leaflet was written by Ataxia UK in collaboration with Dr Mark Wardle, Consultant Neurologist at the School of Medicine Cardiff University, and with Dr Olga Baron, Mr David Mazoud and Dr Manolis Fanto at King's College London.

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