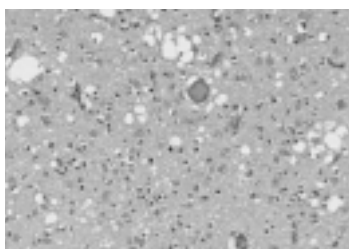


Familial CJD

Familial CJD is an inherited form of Creutzfeldt-Jakob disease, which belongs to a group of rare, and fatal, brain disorders called the prion diseases. These occur in both humans and animals, and include BSE.

Introduction to CJD



Microphotograph of spongiform change in brain tissue taken from someone with CJD

There are fewer than five new cases of familial CJD occurring in the UK each year. Like the other forms of CJD, familial CJD is characterised by dementia (mental decline with symptoms such as memory loss) and neurological problems such as unsteadiness. The brain of someone with familial CJD will also show the spongiform change which is the hallmark of all forms of the disease – the brain tissue has a spongy appearance when viewed under a microscope.

The underlying cause for all forms of prion disease is an abnormal form of a protein called PrP, found in its normal form in the brain and in other parts of the body. Once formed, the prion protein can convert normal PrP molecules into the abnormal form.

In familial CJD, there is a mutation in the PrP gene which seems to make the conversion into the abnormal form more likely. Several different mutations have now been identified. There are two other, even rarer, inherited brain diseases which resemble familial CJD. These are Gerstmann-Straussler-Scheinker disease (GSS) and fatal familial insomnia (FFI). Both are associated with PrP mutations.

Inheriting a risk of CJD

We all inherit two copies of the PrP gene – one from our mother and one from our father. Familial CJD, GSS and FFI are all inherited in an autosomal dominant fashion. That is, you need to possess just one mutated copy of the PrP gene to develop the disease. A person carrying the mutated gene has a 50 per cent chance of passing it on to each child. Since CJD does not usually strike until late in life, when people have usually had their children, the gene has persisted in the population. However, it is now possible to test for mutations in the PrP gene (see below).

How CJD can be transmitted

CJD is unique in that it can be both inherited and transmitted. However, it is not infectious in the usual way, as the causative agent is not a bacteria or a virus. The only way that the disease could be transmitted from someone with familial CJD is if infected tissue (mainly the brain) passed into the body of someone else. This has happened on a few occasions in the past when, unknowingly, contaminated surgical instruments were re-used, giving rise to so-called iatrogenic cases of CJD. And although there is no evidence that CJD can be transmitted through blood, people with a family history of CJD are asked not to give blood to minimise any potential risk.

Symptoms of familial CJD

The symptoms of the familial form of CJD vary, depending on the type of PrP mutation involved. There may even be great variation in the symptoms within affected members of the same family. Sometimes, the symptom pattern is similar to that found in sporadic CJD, namely:

- Initially, depression, memory lapses, maybe unusual fatigue. However, rapid progression to dementia and obvious neurological symptoms distinguish CJD from depression.
- Within weeks, unsteadiness and lack of co-ordination (sometimes, these symptoms are the first to appear).
- Sudden jerky movements, rigid limbs, maybe blindness and incontinence.

Eventually the person loses the ability to move or speak, and will need full-time nursing care.

Familial CJD often strikes at an earlier age than the sporadic form: the average age of onset is 52, compared to 65. The course of the disease is often longer, and the patient may survive for several years after the onset of symptoms.

Symptoms of GSS and FFI

GSS usually starts with clumsiness, unsteadiness, and shakiness, together with rigidity in the limbs. Dementia sets in later, and the patient may survive for several years. In FFI the main symptom is a progressive and untreatable form of insomnia. FFI differs from the other prion diseases in that brain damage is confined to the thalamus, the area which is involved in relaying information to and from the brain, and in controlling sleep-wake cycles. Eventually FFI leads to a complete breakdown of the brain's control of bodily functions, coma, and death.

Genetic testing and diagnosis

Mutations in the PrP gene can now be detected via a blood test. At risk family members who do not have symptoms therefore can opt to find out whether they carry the mutation. In most (but not all) cases a person is certain to develop the disease eventually if they carry one of the known mutations. Furthermore, it may also be possible to tell, from the form of the PrP gene carried, whether the person will have early or later onset disease.

Obviously, undergoing PrP gene testing is a serious matter and should be not be done without the full consent of the person involved, and full pre- and post-test support and counselling by specialist staff. The results will have an impact on other family members and they should also be involved in discussions.

Ante-natal testing where a foetus is at risk of carrying the mutation is also possible. This gives the couple a chance to opt for termination, and so avoids passing the disease on. However, this also involves difficult decision, for a child carrying a mutated PrP gene is likely to enjoy normal health for many years before the onset of disease.

For people with symptoms of familial CJD, the investigations are the same as for any other prion disease. However, in addition, a simple blood test should confirm the presence of a PrP gene mutation. EEG often but not always shows characteristic changes. Magnetic resonance imaging will be done to eliminate other conditions such as a tumour. Blood and other biochemical tests are likely to be normal. The only definite diagnosis comes, as with sporadic CJD, by examining the brain for spongiform change after death. However, in the case of inherited prion disease, the family history of neurological disease will be a very important pointer in the diagnosis.

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