

Cambridge CADASIL meeting 2018

Monday 11th June 2018

Q&A session

Diagnosis

Is it possible that more people than we know have CADASIL but have gone symptom-free and undetected into old age (when we no longer question strokes and dementia)?

Yes definitely. Looking at Dr Saskia Lesnik Oberstein's research from the Netherlands shows us that CADASIL is likely to be more common than previously thought. Therefore, it is very possible that there are people who have a CADASIL mutation but go symptom-free for most or even all of their lives.

What are the pros and cons of gaining a diagnosis when you have a family history of the disease?

Pros: If you don't have the mutation, then it will put your mind at rest as you then know that you definitely do not have the disease. If you do have the mutation, then you can then begin to make sure that you're looking after your cardiovascular risk factors (such as blood pressure, quitting smoking etc.) to ensure that you slow the disease progression down as much as possible. It also means that other members of your family can look into testing, which is particularly important if they are thinking about having children, as prenatal testing can then be used to ensure that future generations do not have the CADASIL mutation.

Cons: Some people would rather not know if they have the disease.

Symptoms

How common is anxiety in CADASIL? Can anything be done to alleviate this?

Anxiety can occur in CADASIL for many reasons. Often can be due to worry about the diagnosis or the symptoms of the disease. It is possible that the CADASIL itself cause brain changes that can also increase anxiety. It can often be treated by counselling and treatments such as cognitive behavioural therapy or helped by drugs. If you have anxiety symptoms which are worrying you your doctor could advise on the best way to treat them.

What is the range of outcomes that can occur with CADASIL? Is there a pattern to the symptoms? Can you put a timeline to it?

The range of outcomes that can occur is huge, and it is very difficult to put a pattern to this as it is very different for individuals. There has been some research done by Dr Saskia Lesnik Oberstein's team in the Netherlands, which has shown that some mutations are associated with worse outcomes. However, it is still incredibly variable and within families with the same mutation, some people can have much better outcomes whilst others are worse. Our research has shown that common risk factors such as smoking and high blood pressure make stroke occur earlier in patients with CADASIL, but this does not account for all differences seen. Other unknown factors also contribute. The CADASIL research database that we are currently collecting here in Cambridge is hoping to help us answer this question better in the future.

What are the signs that you have started to develop vascular dementia?

Cognitive problems due to CADASIL occur due to damage to the deeper parts of the brain. This results in signals passing through circuits which involve the white matter of the brain (deep part of the brain) more slowly. The most common symptoms are slowing in the speed of processing information, and difficulty in multitasking and attention. Memory disturbances are not so common early on in CADASIL.

It can be difficult to tell whether minor cognitive changes are due to psychological causes such as anxiety and depression or due to early signs of dementia. If you are uncertain then it can be helpful to have cognitive tests which can be arranged by a doctor. We also call these neuropsychological tests.

Are epileptic fits a common symptom of CADASIL?

Seizures can occur in CADASIL but they are rare. They can also occur as part of a CADASIL encephalopathy or coma, and if they occur in this setting, they do not usually recur when the encephalopathy has recovered.

Does the menstrual cycle affect CADASIL migraines? Can menopause affect CADASIL symptoms?

Oestrogen hormones can affect common migraine, and they can also have a similar effect on migraine in CADASIL. For example, in some people migraines can occur regularly at a certain point in the menstrual cycle. As the menopause occurs and oestrogen levels reduce this can be accompanied by a reduction in migraines.

Treatments

What is recommended regarding lifetime blood thinning medication i.e. Rivaroxaban/Warfarin in CADASIL?

Anticoagulants such as warfarin, or the new anticoagulants such as Rivaroxaban, can cause bleeding into the brain in patients with CADASIL. The risk is low but we would recommend not using these drugs unless there is a clear indication. There are some instances where they are still beneficial, such as atrial fibrillation or deep venous thrombosis. However unless there is a clear indication such as this we would recommend these drugs being avoided.

Are any supplements worth taking?

There is no evidence from clinical trials that any supplements benefit patients with CADASIL. However there have not been any good studies examining this question. It has been suggested that L-Arginine might improve CADASIL but there is no evidence for this. However it is unlikely to do any harm. There has been a suggestion that high levels of homocysteine might make CADASIL worse. This is a naturally occurring chemical which can have raised levels in the blood, particularly if there is a deficiency of folic acid. If homocysteine levels are very elevated we do sometimes suggest treating them with vitamins such as folic acid and B vitamins. More important than taking any supplements is to keep yourself generally healthy and ensure that you do not have untreated cardiovascular risk factors such as high blood pressure, do not smoke, keep a healthy weight, and exercise regularly.

Are statins of benefit to CADASIL patients?

Statins have been shown to reduce the risk of recurrent stroke in people with common stroke. The evidence that they work in stroke caused by disease of the small blood vessels in the brain is less strong. There is no evidence to show whether they do, or don't, help in CADASIL. Because of their benefit in common stroke we tend to recommend taking statins in CADASIL if the cholesterol is elevated although the evidence for this is not strong.

What medication should be avoided in CADASIL?

We would recommend avoiding warfarin and other anticoagulants unless there is a good indication for them (see other question). We would not recommend taking a combination of both aspirin and clopidogrel (Plavix) as this could increase the risk of bleeding into the brain.

Recent evidence suggests Triptan drugs such as Imigran seem to be safe in CADASIL and can help people with migraines.

We do not know whether thrombolysis is useful in people who have stroke with CADASIL. It does help patients with common stroke but whether it helps blockage of small blood vessels in patients with CADASIL is uncertain. However, if a CADASIL patient suffers a stroke with a significant deficit it is reasonable to give thrombolysis.

Considering the reported success of the use of HBOT in cases of stroke and other neurological disorders, what are your opinions of its potential for reducing the effects of CADASIL strokes and migraines?

Hyperbaric oxygen was suggested as a treatment for multiple sclerosis although it is not widely used for the condition. A few patients have used it in CADASIL. The rationale for this is that if there is a shortage of blood supply in the brain, increasing oxygen may help the amount of oxygen that gets to the brain tissue. There have been no trials to see whether it works in CADASIL. Some patients say it may have had a benefit while others report no benefit. It can be expensive and difficult to access.

Is it safe for people with CADASIL to take Actazolamide as it sounds like it could be of benefit?

Acetazolamide results in an increase in blood flow to the brain. It has been suggested that it might help treat migraine in patients with CADASIL. Some patients have reported an improvement in their migraine but in most cases it does not seem to have a major effect.

If a medicine is successfully developed will it help all CADASIL patients (exon 1 to ...) or will it only make a difference for people with the most common exons?

It is very likely that a medicine developed will help all CADASIL patients. However, this is completely dependent on the specific mechanism that the medicine would target. For example, some medicines are being investigated to target problems with the gene specifically, whereas some are trying to target other downstream effects to reduce the disease progression.

Care

Should our GP's be interested in looking after and monitoring our situation, if so, what should we expect from them?

Due to the rare nature of CADASIL, most GPs may not have heard of the disease before when you first approach them about it. It can be helpful to take a copy of the information leaflet which we give to patients attending the Cambridge clinic available from our website (www.cadasil.co.uk) to provide information for them.

How can you best access support when you are too young to qualify for most support services?

You should be able to access support services through your GP or Hospital Consultant, whatever your age. However, some charity support services for stroke and dementia are primarily targeted at older patients, because these conditions usually affect older people. It is worth asking your GP or Hospital Consultant whether there are any services available for younger patients with these conditions, as there sometimes are, although this varies widely by area in this country.

Lifestyle

I fly regularly; does this have any effect on CADASIL?

No, flying regularly has no effect on CADASIL.

What is the law regarding having CADASIL and Car Insurance – do we have to declare it and if yes what is the cost implication?

Car insurance is not specifically included in the law but should follow the same guidelines as for other insurance. This is that you don't need to share predictive genetic test results but you should answer truthfully about any symptoms that can compromise your ability to drive safely if you are asked for that.

Support group

I would like to be involved in raising awareness of CADASIL, among GPs and general population – what can I do to help?

Karen Carter, founder of the CADASIL Support UK charity and support group, is currently compiling a list of GPs and neurologists who are aware of CADASIL, to help give patients somewhere to turn to when they are diagnosed. She is also very interested in helping to raise awareness. Please get in touch with her by emailing info@cadasilsupportuk.co.uk or going to the website for more information www.cadasilsupportuk.co.uk