RETINA australia

Choroideremia

Choroideremia (also spelt Choroideraemia) is a genetic condition that causes progressive vision loss mostly in men and is due to a degeneration of the specialised light-sensing photoreceptor cells that line the back of the eye. The vision loss due to choroideremia gets worse over time, but the rate of progression can vary between two individuals. Choroideremia is likely to be underdiagnosed as its symptoms are quite similar to a number of other retinal conditions such as retinitis pigmentosa. The distinctive appearances at the back of the eye and X-linked inheritance pattern help eye doctors to make the diagnosis.

What are the symptoms of Choroideremia?

Choroideremia causes damage to the network of blood vessels behind the retina that are known as the choroid. The choroid supplies oxygen and nutrients to support and nourish the retinal pigment epithelial (RPE) cells and the photoreceptor (rod and cone) cells. One of the earliest symptoms of the condition is difficulty seeing at nighttime, due to rod cell death because of a lack of nourishment from the choroid. Over time, the visual field narrows and progresses to tunnel vision and blindness commonly occurs in late adulthood.

What is the cause of Choroideremia and how is it inherited?

Unlike some other retinal degenerations, such as RP, cases of choroideremia are due to mutations in just one gene, known as CHM. This gene makes an essential protein called REP-1, which is involved in escorting essential nutrients between cells in the back of the eye. However, about 20% of patients with a clinical diagnosis of Choroideremia have been found not to have a mutation in the CHM gene.

Choroideremia is genetically passed through families by an X-linked pattern of inheritance. The CHM gene is located on the X chromosome. Females have two X chromosomes, but generally only one of the chromosomes will carry a faulty copy of the gene and the other functioning copy will compensate. Therefore, females are carriers of the condition, but do not generally display the severe symptoms of the disease. In women, one or other of the two X chromosomes is randomly inactivated in every cell. Usually, in female carriers of X-linked disease genes, including CHM, this results in 50% of the retinal cells working on the altered CHM gene and the other 50% working on the normal copy of the CHM gene. These women will have very subtle, if any, symptoms of the disease.

Inactivation, however, in some women may be skewed in favour of either the normal or the altered CHM gene copy. If more than 50% of the normal CHM copy is inactivated, the carrier female will have more symptoms. In rare, extreme cases of skewed inactivation the carrier female might be almost as severely affected as a male. Males only have one X chromosome and will become affected by the condition if he receives a faulty copy of the gene. Affected males cannot pass on the disease to their sons, because they pass on

their Y chromosome. Men with choroideremia must pass on the disease gene to all of their daughters, who then become carriers of the gene. If a family member is diagnosed with choroideremia, it is strongly advised that other members of the family also have an eye exam by an eye doctor (ophthalmologist) who is specially trained to detect retinal diseases.

What treatments are available?

Maximising the remaining vision that an individual has is a crucial first step to take, and there are many new low vision aids including telescopic and magnifying lenses. The wide range of assistive technologies for people with visual impairments provides plenty of choice for users at all stages of sight loss, and this technology has also removed many barriers to education and employment. At this time there are no treatments available for choroideremia although in recent years there have been momentous leaps made in clinical research and development.

Over the past twenty years, researchers have identified the causative CHM gene, explored gene therapy in mouse models of disease and performed necessary safety tests of the treatment. This has culminated in the authorisation of a small number of gene therapy clinical trials. In these gene therapy trials, the researchers engineer a small, safe virus to deliver the correct version of the CHM gene into the light-sensing photoreceptor cells in the retina. The patient's retina is first detached and then the virus is injected underneath using a very fine needle.

Early results from this trial have been positive, no safety issues have been reported and, in some cases, gains in vision have been observed. The safety and effectiveness of this treatment is being monitored as a priority and there is great hope that a treatment will emerge in the future.

Aside from the above trial, a large study of the natural history of about 300 participants is being undertaken in the U.S.A. and some other countries. Completion of the study is expected late in 2019.