COL4A1-Related Brain Small-Vessel Disease

Subjects: Genetics & Heredity

Contributor: Catherine Yang

COL4A1-related brain small-vessel disease is part of a group of conditions called the *COL4A1*-related disorders. The conditions in this group have a range of signs and symptoms that involve fragile blood vessels. *COL4A1*-related brain small-vessel disease is characterized by weakening of the blood vessels in the brain. Stroke is often the first symptom of this condition, typically occurring in mid-adulthood. In affected individuals, stroke is usually caused by bleeding in the brain (hemorrhagic stroke) rather than a lack of blood flow in the brain (ischemic stroke), although either type can occur. Individuals with this condition are at increased risk of having more than one stroke in their lifetime. People with *COL4A1*-related brain small vessel disease also have leukoencephalopathy, which is a change in a type of brain tissue called white matter that can be seen with magnetic resonance imaging (MRI). Affected individuals may also experience seizures and migraine headaches accompanied by visual sensations known as auras.

genetic conditions

1. Introduction

Some people with *COL4A1*-related brain small-vessel disease have an eye abnormality called Axenfeld-Rieger anomaly. Axenfeld-Rieger anomaly involves underdevelopment and eventual tearing of the colored part of the eye (iris) and a pupil that is not in the center of the eye. Other eye problems experienced by people with *COL4A1*-related brain small-vessel disease include clouding of the lens of the eye (cataract) and the presence of arteries that twist and turn abnormally within the light-sensitive tissue at the back of the eye (arterial retinal tortuosity). Axenfeld-Rieger anomaly and cataract can cause impaired vision. Arterial retinal tortuosity can cause episodes of bleeding within the eye following any minor trauma to the eye, leading to temporary vision loss.

The severity of the condition varies greatly among affected individuals. Some individuals with *COL4A1*-related brain small-vessel disease do not have any signs or symptoms of the condition.

2. Frequency

COL4A1-related brain small-vessel disease is a rare condition, although the exact prevalence is unknown. At least 50 individuals with this condition have been described in the scientific literature.

3. Causes

As the name suggests, mutations in the *COL4A1* gene cause *COL4A1*-related brain small vessel disease. The *COL4A1* gene provides instructions for making one component of a protein called type IV collagen. Type IV collagen molecules attach to each other to form complex protein networks. These protein networks are the main components of basement membranes, which are thin sheet-like structures that separate and support cells in many tissues. Type IV collagen networks play an important role in the basement membranes in virtually all tissues throughout the body, particularly the basement membranes surrounding the body's blood vessels (vasculature).

The *COL4A1* gene mutations that cause *COL4A1*-related brain small-vessel disease result in the production of a protein that disrupts the structure of type IV collagen. As a result, type IV collagen molecules cannot attach to each other to form the protein networks in basement membranes. Basement membranes without these networks are unstable, leading to weakening of the tissues that they surround. In people with *COL4A1*-related brain small-vessel disease, the vasculature in the brain weakens, which can lead to blood vessel breakage and stroke. Similar blood vessel weakness and breakage occurs in the eyes of some affected individuals.

3.1. The Gene Associated with COL4A1-Related Brain Small-Vessel Disease

- COL4A1

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition. Rarely, new mutations in the gene occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- brain small-vessel disease with hemorrhage

References

1. Lanfranconi S, Markus HS. COL4A1 mutations as a monogenic cause of cerebralsmall vessel disease: a systematic review. Stroke. 2010 Aug;41(8):e513-8. doi:10.1161/STROKEAHA.110.581918.
2. Sibon I, Coupry I, Menegon P, Bouchet JP, Gorry P, Burgelin I, Calvas P,Orignac I, Dousset V, Lacombe D, Orgogozo JM, Arveiler B, Goizet C. COL4A1mutation in Axenfeld-Rieger anomaly with leukoencephalopathy and stroke. AnnNeurol. 2007 Aug;62(2):177-84.
3. Vahedi K, Alamowitch S. Clinical spectrum of type IV collagen (COL4A1)mutations: a novel genetic multisystem disease. Curr Opin Neurol. 2011Feb;24(1):63-8. doi: 10.1097/WCO.0b013e32834232c6. Review.

4. Volonghi I, Pezzini A, Del Zotto E, Giossi A, Costa P, Ferrari D, Padovani A. Role of COL4A1 in basement-membrane integrity and cerebral small-vessel disease. The COL4A1 stroke syndrome. Curr Med Chem. 2010;17(13):1317-24. Review.

Retrieved from https://encyclopedia.pub/entry/history/show/11201