C3 glomerulopathy

Description

C3 glomerulopathy is a group of related conditions that cause the kidneys to malfunction. The major features of C3 glomerulopathy include high levels of protein in the urine (proteinuria), blood in the urine (hematuria), reduced amounts of urine, low levels of protein in the blood, and swelling in many areas of the body. Affected individuals may have particularly low levels of a protein called complement component 3 (or C3) in the blood.

The kidney problems associated with C3 glomerulopathy tend to worsen over time. About half of affected individuals develop end-stage renal disease (ESRD) within 10 years after their diagnosis. ESRD is a life-threatening condition that prevents the kidneys from filtering fluids and waste products from the body effectively.

Researchers have identified two major forms of C3 glomerulopathy: dense deposit disease and C3 glomerulonephritis. Although the two disorders cause similar kidney problems, the features of dense deposit disease tend to appear earlier than those of C3 glomerulonephritis, usually in adolescence. However, the signs and symptoms of either disease may not begin until adulthood.

One of the two forms of C3 glomerulopathy, dense deposit disease, can also be associated with other conditions unrelated to kidney function. For example, people with dense deposit disease may have acquired partial lipodystrophy, a condition characterized by a lack of fatty (adipose) tissue under the skin in the upper part of the body. Additionally, some people with dense deposit disease develop a buildup of yellowish deposits called drusen in the light-sensitive tissue at the back of the eye (the retina). These deposits usually appear in childhood or adolescence and can cause vision problems later in life.

Frequency

C3 glomerulopathy is very rare, affecting 1 to 2 per million people worldwide. It is equally common in men and women.

Causes

C3 glomerulopathy is associated with changes in many genes. Most of these genes provide instructions for making proteins that help regulate a part of the body's immune

response known as the complement system. This system is a group of proteins that work together to destroy foreign invaders (such as bacteria and viruses), trigger inflammation, and remove debris from cells and tissues. The complement system must be carefully regulated so it targets only unwanted materials and does not damage the body's healthy cells.

A specific mutation in one of the complement system-related genes, *CFHR5*, has been found to cause C3 glomerulopathy in people from the Mediterranean island of Cyprus. Mutation in the *C3* and *CFH* genes, as well as other complement system-related genes, have been found to cause the condition in other populations. The known mutations account for only a small percentage of all cases of C3 glomerulopathy. In most cases, the cause of the condition is unknown.

Several normal variants (polymorphisms) in complement system-related genes are associated with an increased likelihood of developing C3 glomerulopathy. In some cases, the increased risk is related to a group of specific variants in several genes, a combination known as a C3 glomerulopathy at-risk haplotype. While these polymorphisms increase the risk of C3 glomerulopathy, many people who inherit these genetic changes will never develop the condition.

The genetic changes related to C3 glomerulopathy "turn up," or increase the activation of, the complement system. The overactive system damages structures called glomeruli in the kidneys. These structures are clusters of tiny blood vessels that help filter waste products from the blood. Damage to glomeruli prevents the kidneys from filtering waste products normally and can lead to ESRD. Studies suggest that uncontrolled activation of the complement system also causes the other health problems that can occur with dense deposit disease, including acquired partial lipodystrophy and a buildup of drusen in the retina. Researchers are working to determine how these associated health problems are related to overactivity of the complement system.

Studies suggest that C3 glomerulopathy can also result from the presence of specialized proteins called autoantibodies. Autoantibodies cause the condition by altering the activity of proteins involved in regulating the complement system.

Learn more about the genes associated with C3 glomerulopathy

- C3
- C8A
- CFH
- CFHR5
- CFI

Additional Information from NCBI Gene:

- ADAM19
- C3AR1

- CD46
- CFB
- CFD
- CFHR1
- CFHR2
- CFHR3
- CR1

Inheritance

Most cases of C3 glomerulopathy are sporadic, which means they occur in people with no history of the disorder in their family. Only a few reported families have had more than one family member with C3 glomerulopathy. However, many affected people have had close relatives with autoimmune diseases, which occur when the immune system malfunctions and attacks the body's tissues and organs. The connection between C3 glomerulopathy and autoimmune diseases is not fully understood.

Other Names for This Condition

- C3 glomerulonephritis
- C3G
- DDD
- DDD/MPGNII
- Dense deposit disease
- Membranoproliferative glomerulonephritis type II

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: C3 Glomerulonephritis (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4055342/)
- Genetic Testing Registry: CFHR5 deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3553720/)
- Genetic Testing Registry: CFHR5-Related Dense Deposit Disease / Membranoproliferative Glomerulonephritis Type II (https://www.ncbi.nlm.nih.gov/gtr/conditions/CN120381/)
- Genetic Testing Registry: Factor H deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0398777/)
- Genetic Testing Registry: Mesangiocapillary glomerulonephritis, type II (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268743/)

Genetic and Rare Diseases Information Center

- Dense deposit disease (https://rarediseases.info.nih.gov/diseases/8555/index)
- Glomerulonephritis (https://rarediseases.info.nih.gov/diseases/6516/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22C3 glomerulopathy%22)

Catalog of Genes and Diseases from OMIM

- COMPLEMENT FACTOR H DEFICIENCY; CFHD (https://omim.org/entry/609814)
- C3 GLOMERULOPATHY 3; C3G3 (https://omim.org/entry/614809)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28c3+glomerulopathy%5BTIAB%5D%29+OR+%28c3+glomuleronephritis%5BTIAB%5D%29%29+OR+%28dense+deposit+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

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