Familial Mediterranean fever

Description

Familial Mediterranean fever is an inherited condition characterized by recurrent episodes of painful inflammation in the abdomen, chest, or joints. These episodes are often accompanied by fever and sometimes a rash or headache. Occasionally inflammation may occur in other parts of the body, such as the heart; the membrane surrounding the brain and spinal cord; and in males, the testicles. In about half of affected individuals, attacks are preceded by mild signs and symptoms known as a prodrome. Prodromal symptoms include mildly uncomfortable sensations in the area that will later become inflamed, or more general feelings of discomfort.

The first episode of illness in familial Mediterranean fever usually occurs in childhood or the teenage years, but in some cases, the initial attack occurs much later in life. Typically, episodes last 12 to 72 hours and can vary in severity. Episodes generally occur once a month, and in affected women of reproductive age, attacks often correspond with menstruation or ovulation. However, the length of time between episodes can range from days to years. During these periods, affected individuals usually have no signs or symptoms related to the condition. However, without treatment to help prevent attacks and complications, a buildup of protein deposits (amyloidosis) in the body’s organs and tissues may occur, especially in the kidneys, which can lead to kidney failure.

Frequency

Familial Mediterranean fever primarily affects populations originating in the Mediterranean region, particularly people of Armenian, Arab, Turkish, or Jewish ancestry. The disorder affects 1 in 200 to 1,000 people in these populations. It is less common in other populations.

Causes

Familial Mediterranean fever is caused by variants (also known as mutations) in the MEFV gene. The MEFV gene provides instructions for making a protein called pyrin (also known as marenostrin), which is found in white blood cells. This protein is involved in the immune system, helping to regulate the process of inflammation. Inflammation occurs when the immune system sends signaling molecules and white blood cells to a site of injury or disease to fight microbial invaders and facilitate tissue repair. When this
process is complete, the body stops the inflammatory response to prevent damage to its own cells and tissues.

Variants in the \textit{MEFV} gene reduce the activity of the pyrin protein, which disrupts control of the inflammation process. An inappropriate or prolonged inflammatory response can result, leading to fever and pain in the abdomen, chest, or joints.

Normal variations in the \textit{SAA1} gene may modify the course of familial Mediterranean fever. Some evidence suggests that a particular version of the \textit{SAA1} gene (called the alpha variant) increases the risk of amyloidosis among people with familial Mediterranean fever.

Learn more about the genes associated with Familial Mediterranean fever

- MEFV
- SAA1

\textbf{Inheritance}

Familial Mediterranean fever is usually inherited in an autosomal recessive pattern, which means both copies of the \textit{MEFV} gene in each cell have variants. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition. Research shows that about one-third of people with familial Mediterranean fever have a single \textit{MEFV} gene variant, though most experts believe there is a second variant somewhere else in the gene that has not been detected by genetic testing.

In rare cases, this condition appears to be inherited in an autosomal dominant pattern. An autosomal dominant inheritance pattern describes cases in which one copy of the altered gene in each cell is sufficient to cause the disorder. In autosomal dominant inheritance, affected individuals often inherit the variant from one affected parent.

However, another mechanism is believed to account for some cases of familial Mediterranean fever that were originally thought to be inherited in an autosomal dominant pattern. A gene variant that occurs frequently in a population may result in a disorder with autosomal recessive inheritance appearing in multiple generations in a family, a pattern that mimics autosomal dominant inheritance. If one parent has familial Mediterranean fever (with variants in both copies of the \textit{MEFV} gene in each cell) and the other parent is an unaffected carrier (with a variant in one copy of the \textit{MEFV} gene in each cell), it may appear as if the affected child inherited the disorder only from the affected parent. This appearance of autosomal dominant inheritance when the pattern is actually autosomal recessive is called pseudodominance.
Other Names for This Condition

- Benign paroxysmal peritonitis
- Familial paroxysmal polyserositis
- FMF
- MEF
- Recurrent polyserositis
- Reimann periodic disease
- Siegal-Cattan-Mamou disease
- Wolff periodic disease

Additional Information & Resources

Genetic Testing Information


Genetic and Rare Diseases Information Center


Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (https://clinicaltrials.gov/ct2/results?cond=%22familial+mediterranean+fever%22)

Catalog of Genes and Diseases from OMIM

- FAMILIAL MEDITERRANEAN FEVER (https://omim.org/entry/249100)
- FAMILIAL MEDITERRANEAN FEVER, AUTOSOMAL DOMINANT (https://omim.org/entry/134610)
Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Familial+Mediterranean+Fever%5BMAJR%5D%29+AND+%28Mediterranean+fever%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D)

References
