www.printo.it/pediatric-rheumatology/ZA_GB/intro

Familial Mediterranean Fever

Version of 2016

1. WHAT IS FMF

1.1 What is it?

Familial Mediterranean Fever (FMF) is a genetically transmitted disease. Patients suffer from recurrent bouts of fever, accompanied by abdominal or chest pain, joint pains and swelling. The disease generally affects people of Mediterranean and Middle Eastern descent, in particular Jews, Turks, Arabs and Armenians.

1.2 How common is it?

The frequency of the disease in high-risk populations is about 1-3 in 1000. It is rare in other ethnic groups. However, since the discovery of the associated gene, it is being diagnosed more frequently, even among populations where it was thought to be very rare, such as Italians, Greek and Americans.
FMF attacks start before 20 years of age in approximately 90% of patients. In more than half of patients, the disease appears in the first decade of life.

1.3 What are the causes of the disease?

FMF is a genetic disease. The responsible gene is called the MEFV gene and it affects a protein that plays a role in the natural resolution of inflammation. If this gene carries a mutation, as it does in FMF, this regulation cannot function properly and patients experience attacks of fever.

1.4 Is it inherited?

It is mostly inherited as an autosomal recessive disease, which means that parents usually do not show symptoms of the disease. This type of transmission means that to have FMF, both copies of the MEFV gene in an individual (one from the mother and the other from the father) are mutated; hence, both parents are carriers (a carrier has only one mutated copy but not the disease). If the disease is present in the extended family, it is likely to be in a sibling, a cousin, an uncle or a distant relative. However, as seen in a small proportion of cases, if one parent has FMF and the other is a carrier, there is a 50% chance that their child will get the disease. In a minority of patients, one or even both copies of the gene appear to be normal.

1.5 Why does my child have this disease? Can it be prevented?

Your child has the disease because they have a fault (mutation) in the gene that causes FMF.

1.6 Is it infectious?

No, it is not.

1.7 What are the main symptoms?

The main symptoms of the disease are recurrent fever accompanied by abdominal, chest or joint pain. Abdominal attacks are the most common, seen in about 90% of patients. Attacks with chest pain occur in 20-40%, and joint pain occurs in 50-60% of patients.
Usually, children complain of a particular attack type, such as recurrent abdominal pain and fever. Some patients experience different attack types, one at a time or in combination.
These attacks are self-limited (meaning that they resolve without treatment) and last between one and four days. Patients recover fully at the end of an attack and feel well in between these bouts. Some of the attacks may be so painful that the patient or family seeks medical help. Severe abdominal attacks may mimic acute appendicitis and therefore some patients may undergo unnecessary abdominal surgery, such as an appendectomy.

However, some attacks, even in the same patient, may be mild enough to be confused with other common causes of abdominal pain affecting children, such as constipation, or gastroeneteritis. This is one of the reasons why it is hard to recognize FMF patients. During abdominal pain, the child is usually constipated but as the pain gets better, softer stools appear.
The child can have very high fever during one attack, and a milder increase in temperature in another. The chest pain usually only affects one side, and it may be so severe that the patient cannot breathe deeply enough. It resolves within days.
Usually, only one joint is affected at a time (monoarthritis). It is commonly an ankle or a knee. It may be so swollen and painful that the child cannot walk. In about one-third of patients, there is a red skin rash over the involved joint. Joint attacks may last somewhat longer than the other forms of attacks and it can take from four days to two weeks before the pain resolves completely. In some children, the sole finding of the disease may be recurrent joint pain and swelling, which is misdiagnosed as acute rheumatic fever or juvenile idiopathic arthritis. In about 5-10% of cases, joint involvement becomes chronic and may cause damage to the joint.
In some cases, there is a characteristic rash (skin eruption) of FMF called "erysipelas-like erythema", usually observed over the lower extremities and joints. Some children may complain of leg pains.
Rarer forms of attack present with recurrent pericarditis (inflammation of the outer layer of the heart), myositis (muscle inflammation), meningitis (inflammation of the membrane surrounding the brain and spinal cord) and periorchitis (inflammation surrounding the testicle).

1.8 What are the possible complications?

Some other diseases that are characterised by blood vessel inflammation (vasculitis) are seen more frequently among children with FMF, such as Henoch-Schönlein purpura and polyarteritis nodosa. The most severe complication of FMF in untreated cases is the development of amyloidosis. Amyloid is a special protein that deposits in certain organs, such as the kidneys, gut, skin and heart and causes gradual loss of function, especially of the kidneys. It is not specific for FMF and it may complicate other chronic inflammatory diseases that are not properly treated. Protein in the urine may be a clue to the diagnosis.

Finding amyloid in the gut or kidney (by biopsy) will confirm the diagnosis. Children who are receiving a proper dose of colchicine (see drug therapy) are safe from the risk of developing this life-threatening complication.

1.9 Is the disease the same in every child?

It is not the same in every child. Moreover, the type, duration and severity of attacks may be different each time, even in the same child.

1.10 Is the disease in children different from the disease in adults?

In general, FMF in children resembles that seen in adults. However, some features of the disease, such arthritis (joint inflammation) and myositis, are more common in childhood. The frequency of attacks usually decreases as the patient gets older. Periorchitis is detected more often in young boys than adult males. The risk of amyloidosis is higher among untreated patients with early disease onset.