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Familial Mediterranean Fever

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2. DIAGNOSIS AND TREATMENT

2.1 How is it diagnosed?

Generally the following approach is followed:

Clinical suspicion: It is possible to consider FMF only after the child experiences a minimum of three attacks. A detailed history of the ethnic background should be considered, as well as relatives with similar complaints, or renal insufficiency.
The parents should be asked to give a detailed description of previous attacks.

Follow-up: A child with suspected FMF should be monitored closely before a definite diagnosis is made. During this follow-up period, if possible, the patient should be seen during an attack for a thorough physical examination and for blood tests to assess the presence of inflammation. Generally, these tests become positive during an attack and return to normal or near normal after the attack subsides. Classification criteria have been designed to help recognize FMF. It is not always possible to see a child during an attack for various reasons. Therefore, the parents are asked to keep a diary and describe what happens. They can also use a local laboratory for blood tests.

Response to colchicine treatment: Children with clinical and laboratory findings that make the diagnosis of FMF highly probable are given colchicine for approximately six months and the symptoms are then re-evaluated. In case of FMF, attacks either stop completely or decrease in number, severity and duration.

Only after the above steps are completed can the patient be diagnosed as having FMF and prescribed life-long colchicine.
As FMF affects a number of different systems in the body, various specialists might be involved in the diagnosis and management of FMF. These include general paediatricians, paediatric or general rheumatologists, nephrologists (kidney specialists) and gastroenterologists (digestive system).

Genetic analysis: Recently, it has been possible to perform genetic analysis of patients to ascertain the presence of mutations that are thought to be responsible for the development of FMF.
The clinical diagnosis of FMF is confirmed if the patient carries 2 mutations, one from each parent. However, the mutations that have been described to date are found in about 70-80% of patients with FMF. That means there are FMF patients with one or even no mutation; therefore, the diagnosis of FMF still depends on clinical judgement. Genetic analysis may not be available in every treatment centre.
Fever and abdominal pain are very common complaints in childhood. Therefore, it is sometimes not easy to diagnose FMF, even in high-risk populations. It might take a couple of years before it can be recognized. This delay in diagnosis should be minimized because of the increased risk of amyloidosis in untreated patients.
There are a number of other diseases with recurrent bouts of fever, abdominal and joint pain. Some of these diseases are also genetic and share some common clinical features; however, each has its own distinguishing clinical and laboratory characteristics.

2.2 What is the importance of tests?

Laboratory tests are important in diagnosing and monitoring FMF. Tests such as erythrocyte sedimentation rate (ESR), CRP, full blood count are important during an attack (at least 24-48 hours after the start of the attack) to assess the extent of inflammation. These tests are repeated after the child becomes symptom-free to observe if the results are back to, or near-normal. In about one-third of patients, the tests return to normal levels. In the remaining two-thirds, the levels decrease significantly but remain above the upper limit of normal.
A small amount of blood is also required for the genetic analysis. Children who are on life-long colchicine treatment must provide blood

and urine samples twice a year for monitoring purposes.
A sample of urine is also tested for the presence of protein and red blood cells. There may be temporary changes during attacks but persistent elevated protein levels in an early morning urine sample may suggest amyloidosis. The physician may then perform a rectal or kidney biopsy. Rectal biopsy involves the removal of a very small piece of tissue from the rectum; it is very easy to perform. If the rectal biopsy fails to show amyloid, a kidney biopsy is necessary to confirm the diagnosis. For a kidney biopsy, the child must spend a night at the hospital. The tissues obtained from the biopsy are stained and then examined for deposits of amyloid.

2.3 Can it be treated or cured?

FMF cannot be cured but it can be treated with life-long use of colchicine. In this way, recurrent attacks can be prevented or decreased and amyloidosis can be prevented. If the patient stops taking the drug, the attacks and the risk of amyloidosis will recur.

2.4 What are the treatments?

The treatment for FMF is simple, inexpensive and does not involve any major drug side effects, as long as it is taken in the right dose.
Colchicine is the drug of choice for the treatment of FMF. After the diagnosis is made, the child must take the drug for the rest of his/her life. If taken properly (every day, at sufficient dose) the attacks: disappear in about 60% of patients; a partial response is obtained in 30%; and it is ineffective in 5-10% of patients.
This treatment not only controls the attacks but also eliminates the risk of amyloidosis. Therefore, it is crucial for the doctors to repeatedly explain to parents and the patient how vital it is to take this drug in the dose prescribed. Compliance is very important. If this is established, the child can live a normal life with a normal life expectancy. Parents should not modify the dose without consulting the physician.
The dose of colchicine should not be increased during an attack, as such an increase is ineffective. The important thing is to prevent attacks by taking colchicine regularly.
Biologic agents are used in some patients resistant to colchicine.

2.5 What are the side effects of drug therapy?

It is not easy to accept that a child must take pills forever. Parents are often worried about the potential side effects of colchicine. It is a safe drug with minor side effects that usually respond to dose reduction. The most frequent side effect is diarrhoea.

Some children cannot tolerate the given dose because of frequent watery stools. In such cases, the dose should be reduced until it is tolerated and then slowly, with small increments, increased back to the appropriate dose. Lactose in the diet can be reduced for about 3 weeks; gastrointestinal symptoms often disappear as a result.

Other side effects include nausea, vomiting and abdominal cramps. In rare cases, it may cause muscle weakness. The number of peripheral blood cells (white and red blood cells and platelets) may decrease occasionally, but recover with dose reduction.

2.6 How long should treatment last?

FMF requires life-long preventive treatment.

2.7 What about unconventional or complementary therapies?

No complementary therapy is known for FMF.

2.8 What kind of periodic check-ups are necessary?

Children being treated should have blood and urine tests at least twice a year.

2.9 How long will the disease last?

FMF is a life-long disease.

2.10 What is the long-term prognosis (predicted outcome and course) of the disease?

If treated properly with life-long colchicine, children with FMF live a normal life. If there is a delay in diagnosis or lack of compliance with treatment, the risk of developing amyloidosis increases, which results in

a poor prognosis. Children who develop amyloidosis may require a kidney transplant.
Growth retardation is not a major problem in FMF.

2.11 Is it possible to recover completely?

No, because it is a genetic disease. However, life-long therapy with colchicine gives the patient the opportunity to live a normal life, without restrictions and with no risk of developing amyloidosis.