



NALP-12 related recurrent fever

What is it?

NALP-12 related recurrent fever is a genetic disease. The responsible gene is called NALP-12, which has a role in inflammatory signalling pathways. Patients suffer from recurrent bouts of fever accompanied by a variety of symptoms as headache, joint pain or joint swelling and skin rash. Symptoms probably are triggered by cold exposure. Untreated, the disease could be very invalidating, but not life threatening.

How common is it?

The disease is very rare. Currently, less than 10 patients have been identified worldwide.

What are the causes of the disease?

NALP-12 related recurrent fever is a genetic disease. The responsible gene is called NALP-12. The genetically modified gene is responsible for a disturbance of the inflammatory response of the body. The exact mechanism of this disturbance is still under investigation.

Is it inherited?

NALP-12 related recurrent fever is inherited as an autosomal dominant disease. This means that to have NALP-12 related recurrent fever one needs to have one of the parents affected. Sometimes, there is no other member of the family suffering of recurrent fever: either the gene has been damaged at the child's conception (called a de novo mutation) or the parent who carries the mutation may not exhibit the clinical symptoms or exhibit only a very mild form of the disease (variable penetrance).

Why has my child got this disease? Can it be prevented?

The child has the disease because it has inherited his disease from one of his parents that carries a NALP-12 gene mutation unless a de novo mutation has occurred. The person who carries the mutation may, or may not, exhibit the clinical symptoms of NALP-12 related recurrent fever. The disease cannot currently be prevented.

Is it contagious?

NALP-12 related recurrent fever is not an infectious disease. Only genetically affected subjects develop the disease.

What are the main symptoms?

The main symptom is fever. Fever lasts about 5-10 days and recurs at irregular intervals (weeks to months). The bouts of fever are accompanied by a variety of symptoms. These may include headache, joint pain and joint swelling, urticarial rash and myalgia. Fever bouts are probably triggered by cold exposure. In one family sensorineural hearing loss was observed, but not retrieved in other patients.

Is the disease the same in every child?

The disease is not the same in every child: the disease varies between a mild and a more severe form. Moreover, the type, duration and severity of attacks may be different each time, even in the same child.

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

As patients grow up, the fever attacks seem to become fewer and milder. However, some disease activity will remain in most if not all affected individuals.

How is it diagnosed?

An expert physician will suspect on the basis of clinical symptoms identified during a physical examination and from taking a family medical history.

Several blood analyses are useful to detect inflammation during the attacks. The diagnosis is ascertained only by genetic analysis providing evidence of mutations. Differential diagnoses are other conditions presenting with recurrent fever especially cryopyrin associated periodic syndromes.

What is the importance of tests?

The laboratory tests, as mentioned before, are important in diagnosing NALP-12 related recurrent fever. Tests like CRP, serum Amyloid-A-protein (SAA) and whole blood count are ordered during an attack to see the extent of inflammation. These are repeated after the child becomes symptom-free, to observe if the results are back to normal, or near normal. A small amount of blood is also needed for the genetic analysis.

Can it be treated or cured?

NALP-12 related recurrent fever cannot be cured. There is no effective preventive treatment for attacks. Treating the symptoms can reduce inflammation and pain. Some new drugs to control inflammatory symptoms are currently under investigation.

What are the treatments?

The treatments for NALP-12 related recurrent fever include non steroidal anti-inflammatory drugs such as indomethacin, corticosteroids, such as prednisolone and possibly biologicals, such as anakinra (Kineret®). None of these drugs appears to be uniformly effective, but all of them appear to help in some patients. Proof of their efficacy and safety in NALP-12 related recurrent fever is still lacking.

What are the side effects of drug therapy?

This depends on the drug that is used. NSAID's can give rise to headaches, stomach ulcers and kidney damage, corticosteroids and biologicals increase susceptibility to infections. In addition, corticosteroids may cause a wide variety of side effects.

How long should treatment last for?

There are no hard data to support life-long therapy. Given the normal tendency to improvement as patients grow up, it is probably wise to attempt drug withdrawal in patients whose disease appears to be quiescent.

What about unconventional or complementary therapies?

There are no published reports of effective complementary remedies

What kind of periodic check-ups are necessary?

Children being affected with NALP-12 related recurrent fever should have blood and urine tests for at least twice a year.

How long will the disease last for?

It is a life-long disease, although with age, symptoms may get milder.

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

NALP-12 related recurrent fever is a life-long disease, although with age, symptoms may get milder. But as the disease is very rare, the exact long term prognosis is still unknown.