



<https://printo.it/pediatric-rheumatology/IE/intro>

## **Majeed Syndrome**

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### **1. WHAT IS MAJEED**

#### **1.1 What is it?**

Majeed syndrome is a rare genetic disease. Affected children suffer from Chronic Recurrent Multifocal Osteomyelitis (CRMO), Congenital Dyserythropoietic Anaemia (CDA) and inflammatory dermatosis.

#### **1.2 How common is it?**

The disease is very rare and described only families of Middle East origin (Jordan, Turkey). The actual prevalence is estimated at less than 1/1,000,000 children.

#### **1.3 What are the causes of the disease?**

The disease is caused by mutations in the LPIN2 gene on chromosome 18p that codes for a protein called lipin-2. Researchers believe that this protein may play a role in the processing of fats (lipid metabolism). However, no lipid abnormalities have been found with Majeed syndrome.

Lipin-2 also may be involved in controlling inflammation and in cell division.

Mutations in the LPIN2 gene alter the structure and function of lipin-2. It is unclear how these genetic changes lead to bone disease, anaemia and inflammation of the skin in people with Majeed syndrome.

#### **1.4 Is it inherited?**

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It is inherited as an autosomal recessive disease (which means that it is not linked to gender and that neither parent necessarily has symptoms of the disease). This type of transmission means that to have Majeed Syndrome, an individual needs two mutated genes, one from the mother and the other from the father. Hence, both parents are carriers (a carrier has only one mutated copy but not the disease) and not patients. Although carriers typically do not show signs and symptoms of the condition, some parents of children with Majeed syndrome have had an inflammatory skin disorder called psoriasis. Parents who have a child with Majeed syndrome have a 25% risk that another child will have the same disease. Antenatal diagnosis is possible.

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

The child has the disease because it was born with the mutated genes that cause Majeed Syndrome.

### **1.6 Is it infectious?**

No, it is not.

### **1.7 What are the main symptoms?**

Majeed Syndrome is characterised by chronic recurrent multifocal osteomyelitis (CRMO), congenital dyserythropoietic anaemia (CDA) and inflammatory dermatosis. The CRMO associated with this syndrome can be differentiated from isolated CRMO by an earlier age at onset (in infancy), more frequent episodes, shorter and less frequent remissions and the fact that it is probably life-long, leading to retarded growth and/or joint contractures. CDA is characterised by peripheral and bone marrow microcytosis. It can be variable in severity, ranging from mild, unnoticeable anaemia to a blood transfusion-dependent form. The inflammatory dermatosis is usually Sweet syndrome but can also be pustulosis.

### **1.8 What are the possible complications?**

CRMO can lead to complications such as slow growth and the development of joint deformities called contractures, which restrict the

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movement of certain joints; the anaemia may result in symptoms including tiredness (fatigue), weakness, pale skin, and shortness of breath. Complications of congenital dyserythropoietic anaemia can range from mild to severe.

### **1.9 Is the disease the same in every child?**

Due to the extreme rarity of this condition, little is known about the variability of the clinical manifestations. In any case, the severity of symptoms may vary among different children leading to a milder or more severe clinical picture.

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

Little is known about the natural history of the disease. In any case, adult patients present more disabilities related to the development of complications.

## **2. DIAGNOSIS AND THERAPY**

### **2.1 How is it diagnosed?**

The disease should be suspected on the basis of the clinical presentation. The definitive diagnosis must be confirmed by genetic analysis. The diagnosis is confirmed if the patient carries 2 mutations, one from each parent. Genetic analysis may not be available in every tertiary care centre.

### **2.2 What is the importance of tests?**

Blood tests such as erythrocyte sedimentation rate (ESR), CRP, whole blood count and fibrinogen are important during disease activity to assess the extent of inflammation and anaemia.

These tests are periodically repeated to evaluate if the results are back to or near normal. A small amount of blood is also needed for the genetic analysis.

### **2.3 Can it be treated or cured?**

Majeed syndrome can be treated (see below) but not cured since it is a

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genetic disease.

#### **2.4 What are the treatments?**

There is no standardised therapeutic regimen for Majeed syndrome. CRMO is usually treated, as a first line, with non-steroidal anti-inflammatory drugs (NSAIDs). Physical therapy is important to avoid disuse atrophy of muscles and contractures. If CRMO does not respond to NSAIDs, corticosteroids can be used to control CRMO and skin manifestations; however, the complications of long-term use of corticosteroids limit their use in children. Recently, good response to anti-IL1 drugs has been described in 2 related children. CDA is treated with red blood cell transfusion if indicated.

#### **2.5 What are the side effects of drug therapy?**

Corticosteroids are associated with possible side effects such as weight gain, swelling of the face and mood swings. If the steroids are prescribed for a prolonged period, they may cause suppression of growth, osteoporosis, high blood pressure and diabetes.

The most troublesome side effect of anakinra is the painful reaction at the site of injection, comparable to an insect sting. Especially in the first weeks of treatment, these may be quite painful. Infections have been observed among patients treated with anakinra or canakinumab for diseases other than Majeed Syndrome.

#### **2.6 How long should treatment last?**

Treatment is life-long.

#### **2.7 What about unconventional or complementary therapies?**

There are no known complementary therapies for this disease.

#### **2.8 What kind of periodic check-ups are necessary?**

Children should be seen regularly (at least 3 times yearly) by a paediatric rheumatologist to monitor the control of the disease and adjust the medical treatment. Periodic complete blood count (CBC) and

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acute phase reactants should be carried out to determine if red blood cell transfusion is necessary and to evaluate the control of inflammation.

### **2.9 How long will the disease last?**

This disease is life-long. However, the activity of the disease may fluctuate over time.

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

The long-term prognosis depends on the severity of clinical manifestations, particularly on the severity of dyserythropoietic anaemia and disease complications. If left untreated, the quality of life is poor as a result of recurrent pain, chronic anaemia and possible complications including contractures and disuse atrophy of the muscles.

### **2.11 Is it possible to recover completely?**

No, because it is a genetic disease.

## **3. EVERYDAY LIFE**

### **3.1 How might the disease affect the child and the family's daily life?**

The child and the family face major problems before the disease is diagnosed.

Some children must deal with bone deformities, which may seriously interfere with normal activities. Another problem may be the psychological burden of life-long treatment. Patient and parent education programmes can address this issue.

### **3.2 What about school?**

It is essential to continue education in children with chronic diseases. There are a few factors that may cause problems for school attendance and it is therefore important to explain the child's possible needs to

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teachers. Parents and teachers should do whatever they can to allow the child participate in school activities in a normal way, in order not only for the child to be successful academically but also to be accepted and appreciated by both peers and adults. Future integration in the professional world is essential for a young patient and is one of the aims of the global care of chronically ill patients.

### **3.3 What about sports?**

Playing sports is an essential aspect of the everyday life of any child. One of the aims of therapy is to allow children to conduct a normal life as much as possible and to consider themselves not different from their peers. All activities can therefore be performed as tolerated. However, restricted physical activity or rest may be necessary during the acute phase.

### **3.4 What about diet?**

There is no specific diet.

### **3.5 Can climate influence the course of the disease?**

No, it cannot.

### **3.6 Can the child be vaccinated?**

Yes, the child can be vaccinated. However, parents need to contact the treating physician for live attenuated vaccines.

### **3.7 What about sexual life, pregnancy, birth control?**

So far, no information on this aspect in adult patients is available in the literature. As a general rule, like for other autoinflammatory diseases, it is better to plan a pregnancy in order to adapt treatment in advance due to the possible side effect of biologic agents on a foetus.