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Blau's Disease / Juvenile Sarcoidosis

Version of 2016

2. DIAGNOSIS AND THERAPY

2.1 How is it diagnosed?

Generally, the following approach is followed for the diagnosis of Blau syndrome:
Clinical suspicion: It is relevant to consider Blau syndrome when a child presents a combination of symptoms (joint, skin, eye) out of the typical clinical triad. A detailed investigation into the family history should be considered, because this disease is very rare and inherited in an autosomal dominant manner. Demonstration of granulomas: to make the diagnosis of Blau syndrome/EOS, the presence of typical granulomas in affected tissue is essential. Granulomas can be seen on a biopsy of a skin lesion or of an inflamed joint. Other causes of granulomatous inflammation (such as tuberculosis, immune deficiency or other inflammatory diseases such as some vasculitides) need to be excluded by thorough clinical examination and blood tests, imaging and other tests. Genetic analysis: in the last couple of years, it has been possible to perform a genetic analysis of patients to ascertain the presence of mutations that are thought to be responsible for the development of Blau syndrome/EOS.

2.2 What is the importance of tests?

Skin biopsy: a skin biopsy involves the removal of a tiny piece of tissue from the skin and it is very easy to perform. If the skin biopsy shows granulomas, the diagnosis of Blau syndrome is made after exclusion of all other diseases that are associated with granuloma formation. Blood test: blood tests are important to exclude other diseases that can be associated with granulomatous inflammation (such as immune deficiency or Crohn’s disease). They are also important to see the

extent of inflammation and to evaluate the involvement of other organs (such as the kidney or liver). Genetic test: the only test that unambiguously confirms the diagnosis of Blau syndrome is a genetic test that shows the presence of a mutation in the NOD2 gene.

2.3 Can it be treated or cured?

It cannot be cured but it can be treated with drugs that control inflammation in the joints, the eyes and any involved organ. The drug treatment aims to control symptoms and halt the progression of the disease.

2.4 What are the treatments?

At present, there is no evidence concerning the optimal treatment for Blau syndrome/EOS. Joint problems can often be treated with anti-inflammatory non-steroidal drugs and methotrexate. Methotrexate is known for its capacity to control arthritis in many children with juvenile idiopathic arthritis; its effectiveness in Blau syndrome may be less marked. Uveitis is very difficult to control; local therapies (steroid eye drops or local steroid injection) may not be sufficient for many patients. The efficacy of methotrexate to control uveitis is not always sufficient and patients may need to take oral corticosteroids in order to control severe eye inflammation.
In patients with difficult-to-control inflammation of the eyes and/or joints and in patients with involvement of internal organs, the use of cytokine-inhibitors such as TNF-α inhibitors (infliximab, adalimumab) may be effective.

2.5 What are the side effects of drug therapy?

The most frequent adverse effects seen with methotrexate are nausea and abdominal distress on the day of intake. Blood tests are needed to monitor liver function and the number of white blood cells.
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 can cause suppression of growth, osteoporosis, high blood pressure and diabetes.
TNF-α inhibitors are recent drugs; they can be associated with an increased risk of infection, activation of tuberculosis and possible development of neurological or other immune diseases. A potential risk

of development of malignancies has been discussed; at present, there are no statistical data proving an increased risk of malignancies with these drugs.

2.6 How long should treatment last?

There are no data at present that support an optimal duration of treatment. It is essential to control inflammation in order to prevent joint damage, visual loss or damage to other organs.

2.7 What about unconventional or complementary therapies?

There is no evidence concerning this type of therapy for Blau syndrome/EOS.

2.8 What kind of periodic check-ups are necessary?

Children should be seen regularly (at least 3 times yearly) by their paediatric rheumatologist to monitor the control of the disease and adjust the medical treatment. It is also important to have regular visits with the ophthalmologist, at a frequency depending on the severity and evolution of eye inflammation. Children being treated should have blood and urine tests at least twice yearly.

2.9 How long will the disease last?

It is a life-long disease. 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 available data concerning the prognosis in the long-term is limited. Some children have been followed for more than 20 years and have attained almost normal growth, normal psychomotor development and a good quality of life with well-adjusted medical treatment.

2.11 Is it possible to recover completely?

No, because it is a genetic disease. However, appropriate medical follow-up and treatment will give the majority of patients a good quality of life. There are differences in the severity and progression of the disease among patients with Blau syndrome; at present, it is impossible to predict the disease course for the individual patient.