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Behcet’s Disease

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2. DIAGNOSIS AND THERAPY

2.1 How is it diagnosed?

The diagnosis is primarily clinical (based on a collection of symptoms and signs). It may take one to five years before a child fulfils the international criteria described for BD. These criteria require the presence of oral ulcers plus 2 of the following characteristics: genital ulcers, typical skin lesions, a positive pathergy test or eye involvement. The diagnosis is usually delayed for an average of three years.
There are no specific laboratory findings for BD. Approximately half of children with BD carry the genetic marker HLA-B5 and this is linked to the more severe forms of the disease.
As described above, a pathergy skin test is positive in about 60-70% of patients. However, the frequency is lower in some ethnic groups. To diagnose vascular and nervous system involvement, specific imaging of the vessels and the brain may be needed.
As BD is a multi-system disease (it can affect many parts of the body), specialists in the treatment of eyes (ophthalmologist), skin (dermatologist) and the nervous system (neurologist) co-operate in treatment.

2.2 What is the importance of tests?

A pathergy skin test may help in diagnosis. It is included in the International Study Group classification criteria for Behçet’s Disease. Three skin punctures are applied on the inner surface of the forearm with a sterile needle. It hurts very little and the reaction (raised lump in the skin) is evaluated 24 to 48 hours later. Increased hyper-reactivity of

the skin can also be seen at sites where blood is taken or after surgery. Therefore, patients with BD should not undergo unnecessary interventions.
Some blood tests are done to rule out other conditions that can mimic BD, but there is no specific laboratory test for BD. In general, tests show that inflammation is mildly elevated. Moderate anaemia and an increase in white blood cell count may be detected. These tests only need repeating when your doctor thinks this may be helpful to monitor the disease or medication side-effects.
Several imaging techniques are used in children with blood vessel and nervous system involvement.

2.3 Can it be treated or cured?

The disease can go into remission, but may have flare-ups. It can be controlled, but not cured.

2.4 What are the treatments?

There is no specific treatment, because the cause of BD is unknown. Different organ involvement requires different treatment approaches. At one end of the spectrum there are patients with BD who do not need any therapy. On the other end, patients with eye, central nervous system and blood vessel disease may require a combination of treatments. Almost all available data on the treatment of BD comes from adult studies. The main drugs are listed below:

Colchicine: This drug used to be prescribed for almost every symptom of BD, but in a recent study it was shown to be more effective in the treatment of joint problems and erythema nodosum (painful lumps on shins) and mouth ulcers.

Corticosteroids: Corticosteroids are very effective in controlling inflammation. Corticosteroids are primarily administered to children with eye, central nervous system and blood vessel disease, usually in large doses by mouth (1-2 mg/kg/day). When needed, they can be also given intravenously (into a vein) at higher doses (30 mg/kg/day, to be administered in three doses on alternate days) to achieve an immediate response. Topical (locally administered) corticosteroids are used to treat mouth ulcers and eye disease (in the form of eye drops for the latter).

Immunosuppressive drugs: This group of drugs is administered to children with severe disease, especially for eye and major organ or blood vessel involvement. They include azathioprine, cyclosporine-A and cyclophosphamide.

Antiaggregant and anticoagulant therapy: Both options are used occasionally in children with blood vessel involvement. In the majority of patients, aspirin is probably sufficient for this purpose.

Anti-TNF therapy: This new group of drugs is useful for certain features of the disease.

Thalidomide: This drug is used at some centres to treat major mouth ulcers.

Local treatment for oral and genital ulcers is very important. The treatment and follow-up of BD patients requires a team approach. In addition to a paediatric rheumatologist, an ophthalmologist and a haematologist should be included in the team. The family and the patient should always be in touch with the physician or the centre responsible for treatment.

2.5 What are the side effects of drug therapy?

Diarrhoea is the most common side effect of colchicine. In rare cases, this drug may cause a drop in the number of white blood cells or platelets. Azospermia (a decrease in sperm counts) has been reported but is not a major problem with the therapeutic doses used for this disease; sperm counts return to normal when the dose is lowered or the treatment is stopped.

Corticosteroids are the most effective anti-inflammatory drugs, but their use is limited, because in the long-term they are associated with serious side effects, like diabetes mellitus, high blood pressure, osteoporosis (brittle bones), cataract formation and reduced growth. Children who have to be treated with corticosteroids should receive it once a day, in the morning. For prolonged administration, calcium preparations should be added to the treatment.

Of the immunosuppressive drugs, azathioprine may be toxic to the liver, may cause a decrease in the number of blood cells and increase susceptibility to infections. Cyclosporin-A is mainly toxic to the kidneys, but it may also cause high blood pressure, or an increase in body hair and problems with the gums. The side effects of cyclophosphamide are mainly depression of bone marrow and bladder problems. Long-term

administration interferes with the menstrual cycle and may cause infertility. Patients being treated with immunosuppressive drugs must be followed closely and should have blood and urine tests every one or two months.
Anti-TNF drugs and other biologic agents are also being increasingly used in children who do not respond to first line treatments. Anti-TNF and other biologics increase the frequency of infections.

2.6 How long should treatment last?

There is no standard answer to this question. Generally, immunosuppressive therapy is stopped after a minimum of two years or once the patient has been in remission for two years. However, in children with blood vessel and eye disease, where complete remission is not easy to achieve, the therapy may last much longer. In such instances, the medication and doses are modified according to new or on-going symptoms.

2.7 What about unconventional or complementary therapies?

There are many complementary and alternative therapies available and this can be confusing for patients and their families. Think carefully about the risks and benefits of trying these therapies as there is little proven benefit and they can be costly in terms of time, burden to the child and money. If you are interested in seeking complementary and alternative therapies, please discuss these options with your paediatric rheumatologist. Some therapies can interact with conventional medications. Most doctors will not be opposed to you seeking other options, provided you follow medical advice. It is very important not to stop taking your prescribed medications. When medications are needed to keep the disease under control, it can be very dangerous to stop taking them if the disease is still active. Please discuss medication concerns with your child’s doctor.

2.8 What kind of periodic check-ups are necessary?

Periodic check-ups are necessary to monitor disease activity and treatment and are especially important for children with eye inflammation. An eye specialist experienced in treating uveitis

(inflammatory eye disease) should examine the eyes. The frequency of check-ups depends on the disease activity and on the type of medication being used.

2.9 How long will the disease last?

Typically, the course of the disease includes periods of remission and episodes of flares. The overall activity generally decreases with time.

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

There is very limited data on the long-term outcome of patients with childhood BD. From the data available, we know that many patients with BD do not need any treatment. However, children with eye, nervous system and blood vessel involvement require special treatment and follow-up. BD can be fatal, but only in rare cases. This is mainly because of a consequence of blood vessel involvement (rupture of pulmonary arteries or other peripheral aneurysms - balloon like dilations of blood vessels), severe central nervous system involvement and intestinal ulcerations and perforations, seen especially among certain ethnic groups of patients (e.g. Japanese). The main cause of morbidity (poor outcome) is eye disease, which can be very severe. The child’s growth may be retarded, mainly as a secondary consequence of steroid therapy.

2.11 Is it possible to recover completely?

Children with milder disease may recover, but the majority of paediatric patients have long periods of remission followed by flare-ups of the disease.