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BEHÇET'S DISEASE

What is it?

Behçet's syndrome (BS), or Behçet's disease, is a systemic vasculitis (inflammation of blood vessels) of unknown cause. The main symptoms are recurrent oral and genital ulcers, eye, joint, skin, blood vessel, and nervous system involvement. BS was named after a Turkish doctor, Prof. Dr. Hulusi Behçet, who described it in 1937.

How common is it?

BS is more common in some parts of the world. The geographical distribution of BS coincides with the historical 'silk route'. It is mainly observed in countries of the Far East, Middle East and Mediterranean basin, like Japan, Korea, China, Iran, Turkey, Tunisia, and Morocco. The prevalence rate among the adult population is 1/10,000 in Japan and 1-3/1,000 in Turkey. The prevalence is about 1/300,000 in Northern Europe. Few cases are reported from the United State and Australia. BS in children is rare, even in high risk populations. The diagnostic criteria are fulfilled, before the age of 16, in approximately 3% of all BS patients. Overall, the age of disease onset is 20-35. It is equally distributed amongst both sexes, but males have a more severe disease.

What are the causes of the disease?

The cause of the disease is unknown. Genetic susceptibility may have some role in the development of BS. There is no known specific trigger.

Research into the cause and treatment are being carried out in several centres.

Is it inherited?

There is no consistent pattern of inheritance in BS, however some genetic susceptibility is suspected. The syndrome is associated with a genetic predisposition (HLA-B5), especially in patients originating from the Mediterranean and the Far East. There have been reports of cases of families suffering from this disease.

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

The cause of the disease is unknown. BS cannot be prevented.

Is it contagious?

No, it is not.

What are the main symptoms?

1) Oral ulcers: These lesions are almost always present. Oral ulcers are the initial sign in about two-thirds of patients. The majority of children develop multiple, minor ulcers, indistinguishable from those seen in recurrent ulcers, which are common in childhood. Large ulcers are more rare, but can be very difficult to treat.

2) Genital ulcers: In boys the ulcers are located mainly on the scrotum and, less frequently, on the penis. In adult male patients, these almost always leave a scar. The external genitalia are, mainly, affected in girls. These ulcers resemble the oral ulcers. Children before puberty have less genital ulcers.

Boys may have recurrent orchitis.(testicular inflammation)

3) Skin involvement: There are different skin lesions. Acne-like lesions are present only after puberty. Erythema nodosum are red, painful, nodular lesions, usually located on the lower legs. These lesions are more frequent among prepubescent children.

Pathergy reaction is the reactivity of the skin of BS patients to a needle prick. This is used as a diagnostic test in BS. After a skin puncture with a sterile needle on the forearm, a papule, or pustule forms in 24 to 48 hours.

4) Eye involvement: This is one of the most serious manifestations of the disease. While the overall prevalence is approximately 50%, it increases to 70% in boys. Girls are affected less frequently. Disease is bilateral in the majority of patients. Eyes are involved usually within the first three years after the disease starts.

The course of the eye disease is chronic, with occasional flares. After each flare some structural damage occurs, causing gradual vision loss.

5) Joint involvement: Joints are involved in about 30-50% of the children with BS. Usually ankles, knees, wrists and elbows are affected and less than four joints are involved. This inflammation usually last a few weeks and resolves on its own. It is very rare for arthritis of BS to cause joint damage.

6) Neurological involvement: Rarely, children with BS can develop neurological problems. Seizures, increased intracranial pressure with associated headaches and cerebral symptoms are characteristic. The most severe forms are seen in males. Some patients may develop psychiatric problems.

7) Vascular involvement is seen in about 12-30% of juvenile BS patients and can signal a poor outcome.

Usually the large blood vessels are involved. Commonly effected are the vessels of the calves, resulting in them becoming swollen and painful.

8) Gastrointestinal involvement: This is especially common in patients from the Far East. Examination of the bowel reveals ulcers.

Is the disease the same in every child?

No, it is not. Some may have mild disease with oral ulcers and some skin lesions, others may develop eye or nervous system involvement. There are also some differences between girls and boys. Boys usually have a more severe disease course, with more eye and vascular involvement than girls.

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

BS is rare in children compared to adults. There are some differences with reference to puberty. The disease in post-pubescent children is more like the adult disease. There are more familial cases among children with BS than adults. In general, in spite of some variations, BS in children does resembles the adult disease.

How is it diagnosed?

The diagnosis is mainly clinical. It may take one to five years before a child fulfills the international criteria described for BS. The diagnosis is usually delayed for an average of three years.

There are no specific laboratory findings for BS. Approximately half of the children carry HLA-B5 and this is linked to the more severe forms of the disease.

As previously described, a pathergy skin test is positive in about 60% 70 of the patients.

To diagnose vascular and nervous system involvement, specific imaging of the vessels and the brain may be needed.

Because BS is a multi-system disease, specialists in the treatment of eyes (ophthalmologist), skin (dermatologist), and the nervous system (neurologist) are co-operatively involved in the treatment of these patients.

What is the importance of tests?

1) A pathergy skin test is important for diagnosis. It is included in the International Study Group classification criteria for Behçet's Disease. Three to five skin punctures are applied on the inner surface of the forearm with a sterile needle. It hurts very little and the reaction is evaluated 24 to 48 h later.

This hyperreactivity can also be seen at sites where blood is drawn, or after surgery, therefore, patients with BS should not undergo unnecessary interventions.

2) Some blood tests are done for differential diagnosis, but there is no specific laboratory test for BS. Tests that show inflammation in general, are mildly elevated. A moderate anemia and an increase in white blood cell count may be detected. There is no need to repeat these tests, unless the patient is being monitored for disease activity and drug side effects.

3) Several Imaging techniques are applied to children with vascular and neurological involvement.

Can it be treated or cured?

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

What are the treatments?

There is no specific treatment, because the cause of BS is unknown. Different organ involvement requires different treatment regimes. At one end of the spectrum are patients with BS who do not need any therapy. On the other hand, patients with eye, central nervous system and vascular disease may require a combination of treatments.

Almost all the data available on the treatment of BS come from adult studies. The main drugs are listed below:

a) Colchicine: Previously, this drug has been used for almost every manifestation of BS but in a recent study it was shown to be more effective in the treatment of joint problems and erythema nodosum.

b) Corticosteroids: They are very effective in controlling inflammation. Steroids are mainly administered to children with eye, central nervous system and vascular disease, usually in large oral doses (1-2 mg/kg/day). When needed, they can be also given intravenously in higher doses (30 mg/kg/day administered as three doses on alternate

days), to achieve an immediate response. Topical (locally administered) steroids are used to treat oral ulcers, and eye disease in the form of eye drops.

c) Immunosuppressive drugs: This group of drugs are administered to children with severe disease, especially for eye and major organ involvement. They include Azathioprin, Cyclosporin-A and Cyclophosphamide.

d) Anti-aggregant and anti-coagulant therapy: used in selected cases with vascular involvement. In the majority of the patients aspirin is probably sufficient for this purpose.

e) Local treatments for oral and genital ulcers.

f) Anti-TNF therapy: this new group of drugs is being evaluated in selected centres.

g) Thalidomide is used to treat major oral ulcers in some centres.

The treatment and follow-up of BS patients requires a team approach. Besides a paediatric rheumatologist, an ophthalmologist, and a haematologist should be included in the team. The family and patient should always be in touch with the physician, or the centre responsible for treatment.

What are the side effects of drug therapy?

1) Diarrhea is the most common side-effect of colchicine. In rare cases, it may cause a drop in the number of white blood cells or platelets. Azospermia (a decrease in spermatozoon counts) has been mentioned, but this is not a major problem in therapeutic doses.

2) Corticosteroids are the most effective anti-inflammatory drugs, but their use is limited, because their long-term use is associated with serious side effects, like diabetes mellitus, hypertension, osteoporosis, cataract formation and retardation in growth. Children who have to be treated with steroids should receive it once a day as a morning dose. For prolonged administration, calcium preparations should be added to the treatment list.

3) Immunosuppressive drugs: Azathioprin 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 kidneys, but can cause hypertension. It can also cause 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 under these treatments have to be followed closely and should have blood and urine tests done every one or two months.

How long should treatment last for?

There is no standard answer to this question. Generally, the immunosuppressive therapy is stopped after a minimum of two years, or when the patient has been in remission for two years.

However, children with vascular and eye disease, where complete remission is not easy to achieve, the therapy may be life-long. In such instances, the medication and doses are modified according to clinical manifestations.

What about unconventional or complementary therapies?

There is no such therapy for BS.

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, who is experienced in treating uveitis, should examine the eyes. The frequency of check-ups depends on the activity of disease and the type of medication used.

How long will the disease last for?

Usually the course of the disease includes periods of remissions and exacerbations. The overall activity, generally, decreases with time.

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

There is no sufficient data on the long-term follow-up of patients with childhood BS. From the data available, we know that there are many patients with BS who do not need any treatment.

However, children with eye, nervous system, and vascular involvement require special treatment and follow-up.

BS can be fatal in rare cases, mainly because of vascular involvement (rupture of pulmonary arterial or other peripheral aneurysms), severe central nervous system involvement and intestinal ulcerations and perforations, seen especially among some ethnic groups of patients (Japanese).

The main cause of morbidity is eye disease, which can be very severe.

The child's growth may be retarded, mainly secondary to steroid therapy.

Is it possible to recover completely?

Children with milder disease may recover, but the majority may have long periods of remission, followed by flares of the disease.

How could the disease affect the child and family's daily life?

Like any other chronic disease, BS does affect the child and the family's daily life. If the disease is mild, without eye and other major organ involvements, usually the family may lead a normal life.

The most common problem with this group is the recurrent oral ulcers, which may be troublesome in many children. These lesions may be painful and can interfere with eating and drinking. Eye involvement may also be a serious problem for the family.

What about school?

It is essential to continue education in children with chronic diseases. In BS, unless there is eye or other major organ involvement, the children with BS can attend school regularly. Visual impairment may necessitate special educational programmes.

What about sports?

The child can attend sports activities if there is only skin and mucosa involvement. During attacks of joint inflammation, sports should be avoided. Arthritis in BS is short-lived and resolves completely. The patient may restart sports after the inflammation is gone.

However children with eye and vascular problems have to limit their activities. Prolonged standing should be discouraged in patients with vascular involvement of the lower extremities.

What about diet?

There is no restriction with regard to food intake.

Can climate influence the course of the disease?

No there is no known effect of climate on the expression of BS.

Can the child be vaccinated?

The physician should decide about which vaccines the child can receive. If a patient is being treated with an immunosuppressive drug (steroids, azathioprin, cyclosporine-A, cyclophosphamide, anti-TNF etc.) vaccination with live, attenuated viruses (such as anti-rubella, anti-measles, anti-parotitis, anti-polio Sabin) have to be postponed.

Vaccines that do not contain living viruses, but only infectious proteins (anti tetanus, anti diphtheria, anti polio Salk, anti hepatitis B, anti pertussis, pneumococcus, haemophilus, meningococcus), can be performed.

What about sexual life, pregnancy, birth controls?

One of the major problems with sexual life is the development of genital ulcers. They can be recurrent and painful and interfere with sexual intercourse. Females with BS have mild disease, they will have a normal pregnancy.

Birth control should be considered if the patient is on immunosuppressive drugs. Patients are advised to consult their physician about birth control and pregnancy.