https://www.printo.it/pediatric-rheumatology/IE/intro

Kawasaki Disease

Version of 2016

1. WHAT IS KAWASAKI

1.1 What is it?

This disease was first reported in English medical literature in 1967 by a Japanese paediatrician named Tomisaku Kawasaki (the disease has been named after him); he identified a group of children with fever, skin rash, conjunctivitis (red eyes), enanthem (redness of the throat and mouth), swelling of the hands and feet and enlarged lymph nodes in the neck. Initially, the disease was called "mucocutaneous lymph node syndrome". A few years later, heart complications, such as aneurysms of the coronary arteries (large dilatation of these blood vessels) were reported.
Kawasaki disease (KD) is an acute systemic vasculitis, meaning that there is inflammation of the wall of blood vessels that can evolve to dilatations (aneurysms) of any medium-sized artery in the body, primarily the coronary arteries. However, the majority of children will show only the acute symptoms without cardiac complications.

1.2 How common is it?

KD is a rare disease, but one of the most common vasculitis disorders of childhood, along with Henoch-Schoenlein purpura. Kawasaki disease is described all over the world, although it is much more frequent in Japan. It is almost exclusively an illness of young children. Approximately 85% of children with KD are younger than 5 years, with peak age of incidence at 18–24 months; patients aged less than 3 months or more than 5 years are encountered less commonly, but are at increased risk of coronary artery aneurysms (CAA). It is more common in boys than in

girls. Although cases of KD can be diagnosed any time during the year, some seasonal clustering is known to occur, with an increased number in late winter and spring.

1.3 What are the causes of the disease?

The cause of KD remains unclear, although an infectious origin is suspected to be a triggering event. Hypersensitivity or a disordered immune response, probably triggered by an infectious agent (certain viruses or bacteria), may turn on an inflammatory process leading to inflammation and damage of the blood vessels in certain genetically predisposed individuals.

1.4 Is it inherited? Why does my child have this disease? Can it be prevented? Is it infectious?

KD is not a hereditary disease, although a genetic predisposition is suspected. It is very rare to have more than one member of a family with this disease. It is not infectious and it does not spread from one child to another. At present, there is no known prevention. It is possible, but very rare, to have a second episode of this disease in the same patient.

1.5 What are the main symptoms?

The illness presents with unexplained high fever. The child is usually very irritable. The fever can be accompanied or followed by conjunctival infection (redness of both eyes), without pus or secretions. The child can present different types of skin rash, such as measles or scarlet fever rash, urticaria (hives), papules, etc. The skin rash involves mainly the trunk and the extremities and often the diaper area as well, leading to redness and peeling of skin.

Mouth changes might include bright red cracked lips, red tongue (commonly called "strawberry" tongue) and pharyngeal redness. Hands and feet may also be involved with swelling and redness of the palms and soles. The fingers and toes may appear puffy and swollen. These features are followed by a characteristic peeling of skin around the tip of the fingers and toes (around the second to the third week). More than half of patients will present enlarged lymph nodes in the neck; it is

often a single lymph node of at least 1.5 cm.
Sometimes, other symptoms such as joint pain and/or swollen joints, abdominal pain, diarrhoea, irritability or headaches may be seen. In countries where the BCG vaccine (protection from tuberculosis) is given, younger children may show reddening of the BCG scar area.
The heart involvement is the most serious manifestation of KD, due to the possibility of long-term complications. Heart murmurs, rhythm disturbances, and ultrasound abnormalities may be detected. All the different layers of the heart may show some degree of inflammation, meaning that pericarditis (inflammation of the membrane surrounding the heart), myocarditis (inflammation of the cardiac muscle) and also valve involvement may occur. However, the main feature of this disease is the development of coronary artery aneurysms (CAA).

1.6 Is the disease the same in every child?

The severity of the disease varies from child to child. Not every child has every clinical manifestation and most patients will not develop heart involvement. Aneurysms are seen in only 2 to 6 of 100 children who receive treatment. Some children (especially those younger than 1 year) often show incomplete forms of the disease, meaning that they do not present all the characteristic clinical manifestations, making the diagnosis more difficult. Some of these young children may develop aneurysms. They are diagnosed as atypical KD.

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

This is a disease of childhood, although there are rare reports of KD in adulthood.

2. DIAGNOSIS AND THERAPY

2.1 How is it diagnosed?

KD is a clinical or bedside diagnosis. This means that the diagnosis is made only on the basis of a clinical evaluation by a doctor. A definite diagnosis can be made if unexplained high fever lasting for 5 or more days is present along with 4 of the 5 following features: bilateral

conjunctivitis (i.e. inflammation of the membrane covering the eyeball), enlarged lymph nodes, skin rash, mouth and tongue involvement and extremities changes. The doctor must verify that there is no evidence of any other disease that could explain the same symptoms. Some children show incomplete forms of the disease, meaning that they present with fewer clinical criteria, making the diagnosis more difficult. Such cases are called incomplete KD.

2.2 How long will the disease last?

KD is an illness with three phases: acute, which includes the first 2 weeks when the fever and the other symptoms are present; sub-acute, from the second to the fourth week, a period in which the platelet count begins to rise and aneurysms can appear; and the recovery phase, from the first to the third month, when all the altered lab tests return to normal and some of the blood vessels abnormalities (such as CAA) are resolved or diminished in size.
If untreated, the disease may run a self-limiting course over about 2 weeks leaving the coronaries damaged all the same.

2.3 What is the importance of tests?

Currently, there is no laboratory test that can help to conclusively diagnose the disease. A cluster of tests, such as elevated ESR (erythrocyte sedimentation rate), high CRP level, leukocytosis (increased number of white blood cells), anaemia (low count of red blood cells), low serum albumin and raised liver enzymes, may help in making the diagnosis. The number of platelets (the cells involved in blood clotting) is generally normal in the first weeks of the disease but begins to rise in the second week, reaching very high counts.
Children should undergo periodic examinations and assessment of blood tests until the platelet counts and ESR return to normal.
An initial electrocardiogram (ECG) and echocardiogram should be performed. The echocardiogram can detect dilatation (widening) or aneurysms by evaluating the shape and size of the coronary arteries. In the case of a child with coronary abnormalities, follow-up echocardiograms and additional studies and evaluations will be needed.

2.4 Can it be treated/cured?

The majority of children with KD can be cured; however, some patients develop heart complications, despite the use of proper treatment. The disease cannot be prevented but the best way to decrease coronary complications is to make an early diagnosis and to start treatment as early as possible.

2.5 What are the treatments?

A child with definite or suspected KD should be admitted to the hospital for observation and monitoring and should be evaluated for possible heart involvement.

To diminish the frequency of heart complications, treatment should be started as soon as the diagnosis is made.

Treatment consists of a single high dose of intravenous immunoglobulin (IVIG) and aspirin. This treatment will diminish the inflammation, dramatically relieving the acute symptoms. High dose IVIG is the essential part of treatment since it is able to reduce the occurrence of coronary abnormalities in a high proportion of patients. Though very expensive, for now it remains the most effective form of treatment. In patients with special risk factors, simultaneous corticosteroids may be given. Patients who do not respond to one or two doses of IVIG have other therapeutic alternatives, including high dose intravenous corticosteroids and biologic drug therapy.

2.6 Do all children respond to intravenous immunoglobulin?

Fortunately, most children will need just a single dose. Those who do not respond may need a second dose, or doses of corticosteroids. In rare cases, new molecules called biological drugs may be given.

2.7 What are the side effects of drug therapy?

IVIG therapy is usually safe and well-tolerated. Rarely, inflammation of the meninges (aseptic meningitis) can occur.

Following IVIG therapy, live attenuated vaccinations should be postponed. (Discuss each vaccine with your paediatrician). Aspirin at high dose can cause nausea or stomach upset.

2.8 What treatment is recommended after immunoglobulin and high dose aspirin? How long should treatment last?

After the fever settles down (usually in 24-48 hours), the dose of aspirin will be tapered down. The low dose of aspirin is maintained due to its effect on the platelets; this means that the platelets will not stick together. This treatment is useful to prevent formation of thrombi (blood clots) inside the aneurysms or the inner linings of inflamed blood vessels, since thrombus formation inside an aneurysm or blood vessel may lead to cutting off of the blood supply to the areas supplied by the blood vessels (cardiac infarction, the most dangerous complication of KD). Low dose aspirin is continued until normalisation of inflammatory markers and a normal follow-up echo. Children with persistent aneurysms should receive aspirin or other anti-clotting drugs under a doctor's supervision for longer periods.

2.9 My religion does not allow me to use blood and blood products. What about unconventional/complementary therapies?

There is no place for unconventional treatments for this disease. IVIG is the proven treatment of choice. Corticosteroids might be effective in case IVIG cannot be used.

2.10 Who is involved in the medical care of the child?

The paediatrician, the paediatric cardiologist and the paediatric rheumatologist may take care of the acute stage and follow-up of children with KD. In places where a paediatric rheumatologist is not available, the paediatrician along with the cardiologist should monitor patients, especially the ones who have had heart involvement.

2.11 What is the long-term evolution (prognosis) of the disease?

For the majority of patients, the prognosis is excellent, as they will develop a normal life, with normal growth and development.
The prognosis of patients with persistent coronary arteries abnormalities depends mainly on the development of vascular narrowing (stenosis) and obstructions (occlusions). They may be prone to heart symptoms in early life and may need to stay under the care of

a cardiologist experienced in the long-term care of children with KD.

3. EVERYDAY LIFE

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

If the disease does not involve the heart, the child and family usually lead a normal life. Although most children with Kawasaki disease recover completely, it may be a little while before your child stops feeling tired and irritable.

3.2 What about school?

Once the disease is well-controlled, as is generally the case using the currently available medications, and the acute phase is over, the child should have no problem participating in all the same activities as their healthy peers. School for children is what work is for adults: a place where they learn how to become independent and productive individuals. Parents and teachers should do whatever they can to allow the child to 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.

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. Therefore, children who did not develop heart involvement will not have any restriction in sports or any other daily life activity. However, children with coronary aneurysms should consult a paediatric cardiologist regarding participation in competitive activities, especially during adolescence.

3.4 What about diet?

There is no evidence that diet can influence the disease. In general, the child should observe a balanced, normal diet for his/her age. A healthy,

well-balanced diet with sufficient proteins, calcium and vitamins is recommended for a growing child. Overeating should be avoided in patients taking corticosteroids because these drugs may increase appetite.

3.5 Can the child be vaccinated?

Following IVIG therapy, live attenuated vaccinations should be postponed.

The physician should decide which vaccines the child can receive on a case by case basis. Overall, vaccinations do not seem to increase the disease activity and do not cause severe adverse events in KD patients. Non-live composite vaccines appear to be safe in KD patients, even those on immunosuppressive drugs, although most studies are unable to fully assess rare vaccination-induced harm.

Patients on high dose immunosuppressive drugs should be advised by their physician to measure pathogen-specific antibody concentrations after vaccination.