Kawasaki disease is an acute infection of unknown etiology of the small to medium-sized blood vessels that exclusively affect children younger than 5 years. Kawasaki Syndrome is a rare disease that affects the blood vessels of children. Kawasaki disease is not contagious, and is most common in children aged from 1-2 years old; the incidence decreasing significantly above 8 years of age. The main cause or etiology of the disease remains unknown until today; however, there are several factors that are believed to play a role in the etiology of the condition.

Background of Kawasaki Syndrome

Kawasaki syndrome or disease is a febrile vasculitic syndrome that comes as an acute illness and appears in early childhood. It is also known as infantile periarteritis nodosa.
and mucocutaneous lymph node syndrome. The disorder was first reported in 1967 in Japan by Dr. Tomisaku Kawasaki.

Initially, Kawasaki disease was thought to be self-limited and benign; however, later reports showed that about 2% of patients died from the illness.

Pathophysiology of Kawasaki Syndrome

Even though the obvious and prominent features of the disorder are mucocutaneous. The syndrome is best recognized as a generalized vasculitis involving small to medium arteries. It affects mainly the coronary vessels; however, it may also affect any other artery, vein or capillary.

In the early stages of the disorder, the vascular media, as well as the endothelial cells, become edematous; however, the internal elastic lamina will remain intact at this stage.

An influx of neutrophils will occur after 7–9 days from the onset of the fever, which will be followed by a proliferation of IgA-producing plasma cells and cytotoxic lymphocytes.

Multiple cytokines are secreted by the inflammatory cells including monocyte chemotactic and activating factor, vascular endothelial growth factor, and tumor necrosis factor. The inflammatory cells also secrete matrix metalloproteinases and interleukins targeting the endothelial cells, which will result in vascular damage.

The active inflammatory cells are replaced by monocytes and fibroblasts over the next few weeks to months. At this stage, fibrous connective tissue begins to develop within the wall of the vessel and intima thickens and proliferates, which will eventually result in the narrowing of the vessel or the formation of a thrombus.

Etiology of Kawasaki Syndrome

According to most of the immunologic and epidemiological evidence, Kawasaki syndrome is most likely caused by an infection; however, the exact etiology remains unknown. Genetic predisposition, as well as autoimmune reactions, have also been suggested as possible etiologic factors for the disease.

Environmental factors

- It is estimated that a virus (such as adenovirus, cytomegalovirus, rotavirus, etc.), bacteria and mycoplasma might trigger the autoimmune reactions in the body resulting in Kawasaki disease.

Genetic factors

- The siblings of affected patients may develop the disease 10-20 times greater than normal people due to HR & RR alleles, predominately causing polymorphism in plasma-activating factor acetylhydrolase in resistance to immunoglobulins.

Epidemiology of Kawasaki Syndrome
United States

- Approximately 3,000 children are hospitalized in the United States every year because of Kawasaki syndrome.
- Epidemics of the disease occur primarily during spring and late winter at an interval of 2-3 years.
- Americans of Pacific Island and Asian descent, especially those of Japanese descent, are highly susceptible to the disease.

International

Japan was reported to have the highest incidence of the disorder, with a frequency of the diseases 20 times higher than in Western countries.

Other countries that show a high incidence of the disease are Korea and Taiwan.

Presentation of Kawasaki Syndrome

History

The history of prolonged fever more than 5 days is the diagnostic feature of the disease.

Other nonspecific symptoms may precede the onset of the fever, which include:

- Vomiting
- Cough
- Diarrhea
- Weakness
- Rhinorrhea
- Joint pain
- Abdominal pain
- Irritability
- Decreased oral intake

CRASH and Burn

“Burn”: At least 5 days of fever

“CRASH”

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Physical Examination

The American Heart Association (AHA) established a set of diagnostic criteria, which includes fever for more than five days, plus 4 of these 5 main clinical features:

1. Polymorphous rash: It is usually generalized; however, it could be limited to the lower extremities or the groin.
2. **Painless, nonexudative, bilateral bulbar conjunctival injection.**

3. **Changes in the pharynx and oral cavity:** Fissuring, erythema, strawberry tongue, crusting of the lips, and diffuse oropharyngeal mucosal injection.

4. Acute cervical non-purulent lymphadenopathy with a diameter of lymph nodes more than 1.5 cm. This **lymphadenopathy** is usually unilateral.

5. **Peripheral extremities changes:** Edema or reddening of the soles and palms, which may be followed by Beau lines (transverse grooves across the toenails and fingernails) as well as membranous desquamation of the tips of toes and fingers.

**Differential Diagnosis of Kawasaki Syndrome**

It is important to diagnose Kawasaki diseases in the early stages because any delay in the diagnosis may result in devastating cardiac complications such as coronary artery aneurysms.

Numerous focal infections may mimic Kawasaki disease, including:

- Orbital cellulitis
- Retropharyngeal phlegmon
- Deep neck infection
- Preseptal cellulitis
- Cervical lymphadenitis
- Peritonsillar abscess
- Retropharyngeal cellulitis or abscess

**Other differential diagnoses** include:

- Measles
- Leptospirosis
- Toxic epidermal necrolysis
- Juvenile idiopathic arthritis
- Lyme disease
- Pediatric rocky mountain spotted fever
- Infantile polyarteritis nodosa
- Juvenile idiopathic arthritis

**Diagnosis and Workup of Kawasaki Syndrome**

The diagnosis of Kawasaki diseases depends mainly on the symptoms. In the initial phases of the condition, almost all patients suffer from increased levels of acute-phase reactants:

- C-reactive protein
- Alpha1-antitrypsin
- Erythrocyte sedimentation rate

Recently, two urine proteins are being used as biomarkers of Kawasaki syndrome, as they are diagnostically superior to CRP and ESR. These two urine proteins are filming C and merino A.
Treatment of Kawasaki Syndrome

The main goal of management is to **relieve the symptoms** and **prevent the formation of coronary artery disease**. The principal step of treatment is the usage of full doses of intravenous immunoglobulin. Aspirin can also be used in the treatment of the condition.

Other **medications** that can be used in the management of the syndrome include:

- **Cyclophosphamide or methotrexate**: This is usually used in cases that are resistant to intravenous immunoglobulin treatment.
- **Clopidogrel, dipyridamole and other anti-platelet drugs**: This is mainly used in patients with significant involvement of the coronary arteries and a high risk for thrombus formation.
- **Low-molecular-weight heparin, Warfarin, and other anticoagulants**: Used in patients with a high risk of thrombus formation, especially patients with large aneurysms.
- **Infliximab** can be used in patients suffering from refractory cases with coronary aneurysms.
- **Corticosteroids** are used in patients who do not respond to standard treatments and therapies.
- A new therapy involving **ulinastatin (UTI)**, a neutrophil elastase inhibitor, is used to treat patients suffering from circulatory shock or pancreatitis; however, it is under clinical trials.

References


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