

## Kawasaki Disease: The Debate Continues Till Date

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Tomisaku Kawasaki, a pediatrician saw a 4 years old child in 1961 with features of an unknown disease later known as Kawasaki disease (KD) in his honor. He presented his findings in a clinical conference at the Red Cross Hospital in Hiroo, Tokyo. A year later he came across yet another child with similar presentation. In the following years he happened to see about 50 more such patients. He published his findings in 1967 in a local medical journal in Japanese language [1]. The English version of the disease was published only in 1974 [2]. Despite the disease having been reported from almost all parts of the world ever since 1970s and the extensive advancement in the medical field, the debate on the etiology, clinical presentation, epidemiology and treatment of KD continues till date. KD is an acute febrile illness with multi organ vasculitis primarily affecting infants and young children under 5 years of age. It is also known as Mucocutaneous Lymph Node Syndrome (MLNS), infantile vasculitis, Kawasaki syndrome and immune vasculitis. Usually small to medium sized blood vessels are affected in KD. The male children are affected one and a half times more than female ones. The disease also sometimes affects children over 5 years of age and is rarely encountered in adults. Most of the patients are of Japanese and pacific islanders origin and is reported more often from developed world including USA in particular. The disease has now been increasingly reported from all over the world including the developing countries [3-8]. It may have some seasonal variations. Genetic constitution may be responsible for increased susceptibility in some patients. Clinical features and epidemiological findings suggest that KD may be caused by an infectious agent. Various agents like rug shampoo, bacteria, viruses, parasites, fungi and their super antigens have been incriminated in the pathogenesis of the disease. Recently a number of reports associate the streptococci with the KD [9-12]. A more recent report concludes that our knowledge of the infectious agent (s) involved and the genetic characteristics of susceptible children remain only partial [13].

The KD which is now regarded as a leading cause of acquired heart disease in the developed world starts abruptly with high grade fever lasting 5 days or more with at least four of the following other features i.e. bilateral non purulent conjunctivitis; mucosal inflammation including sore/cracked lips, inflamed pharynx or strawberry tongue; erythema of the palms and soles, desquamation of fingers and toes and peripheral non-pitting oedema; polymorphous rash; or cervical lymphadenopathy. The American and the Japanese criteria of KD definition may differ slightly. However, about 10% of children still do not meet the strict criteria. These cases may fall into sub acute, incomplete or atypical KD. The disease has a predilection for cardiac tissues in particular the coronary arteries. Although most of the patients recover from acute symptoms even if untreated, the risk of the cardiac complications may be high. Without treatment, 20 to 25% of patients develop cardiac complications [14]. The latter include coronary aneurysms, ischemic heart disease, myocarditis, coronary thrombus, myocardial infarction and sudden heart failure. It is also debatable if the KD predisposes the host to atherosclerosis. About 1 % patients especially with giant coronary aneurysms may die. However, long term mortality may be much higher. It is relevant to mention here that many of the coronary aneurysms detected in adults may be possibly attributed to KD acquired in their childhood. Depending upon various phases of

the disease some patients may even present with aseptic meningitis, hyperemic tympanic membrane, uveitis, diarrhoea, abdominal pain, pneumonitis, facial nerve palsy, seizures, ataxia, cerebral infarctions, gallbladder hydrops, arthritis, erythema and induration at the recent site of BCG vaccination, testicular swelling and peripheral gangrene. The disease should be carefully differentiated from scarlet fever, toxic shock syndrome, measles, glandular fever, Stevens –Johnson syndrome and viral meningitis.

Radiological investigations may be useful for cardiac assessment. Chest radiography, CT and MRI are not routinely done. Echocardiography especially 2-dimensional may have 100% sensitivity and about 90 % specificity in detecting coronary aneurysms. While CT may be more sensitive in detecting coronary calcification, MRI may be useful for long term cardiac follow up.

Patients with KD should be hospitalized as early as possible and standard treatment may be instituted within 24 hours or at least within 10 days of onset of fever which will help minimize complications. Intravenous gammaglobulin (IVIG) 2gm/kg as a single dose is the most effective remedy. This may be combined with high dose aspirin, though the role of aspirin has been debatable. Some clinicians do not advocate aspirin therapy lest the children should develop Reye's syndrome. If the fever does not respond to the first dose of IVIG within 24 hours, a second dose may be administered. The third dose of IVIG is rarely recommended. The cases refractory to IVIG may require steroids, infliximab, low dose methotrexate, cyclophosphamide or even plasma exchange. Etanercept therapy is also currently under consideration for such cases.

It appears that though a few pathogens may be capable of triggering immune vasculitis seen in KD, the overall pathogenesis of the disease is largely determined by the genetic constitution/susceptibility of the host. It is probably more pertinent and logical here to state that it is the soil (host) that counts more than the seed (infecting agent) in the genesis of the disease. Given the subtle and variable clinical presentation of the disease and subsequent serious cardiac complications, any parsimonious attitude especially in requesting for an echocardiogram may not be justifiable. While a pragmatic approach in near future may elucidate more facts about the etio pathogenesis of this disease, the general awareness particularly in the developing world may lead to effectively reduce both the immediate and late morbidity and mortality which may ensue months, years and even decades after the initial illness.

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