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SPECIAL ISSUE - KAWASAKI DISEASE

History of the worldwide emergence of Kawasaki disease

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Abstract

Dr. Kawasaki saw his first case of the disease that would come to bear his name in 1961. His meticulous description of the clinical syndrome persists as the case definition to the present day. This review chronicles the emergence and recognition of Kawasaki disease in Asia and Western countries and articulates the old disease/new disease controversy.

Key words: Kawasaki disease, coronary artery aneurysm, history.

Tomisaku Kawasaki saw his first case of the pediatric vasculitis that would come to bear his name in January 1961, but the realization that he was seeing a new and unique clinical entity would await the examination of a second patient who was referred to him at the Red Cross Hospital from an outlying clinic in January of 1962. The wonderful narration by Kawasaki of his 'aha' moment can be viewed with a voice-over English translation at https://www.youtube.com/Kawasakidisease 'The Race for an Answer'. Over the next 5 years, Kawasaki gathered a total of 50 patients suffering from 'acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes' and published his series in the Japanese language in 1967.[1,2] It is remarkable that to this day, the case definition proposed by Kawasaki has stood the test of time and is used, essentially unchanged, by pediatricians around the world. His meticulous description of the 50 cases remains one of the great pieces of clinical descriptive exposition from the last century.

Kawasaki was not the only one seeing cases in Japan and other published descriptions of the disease that we now know as Kawasaki disease (KD) can be found dating back to the early 1950s.[3,4] The first Japanese case may have been a boy living in a fishing village near Yamaguchi, Japan, who at the age of 4 years in 1946 suffered 'measles' twice. After the War, he relocated to San Diego, California, where he was an aikido master until at the age of 48 years when he suffered a massive myocardial infarction due to thrombosis of a giant aneurysm.[5] In 2005, the patient met Drs. Kawasaki and Yanagawa, the chief epidemiologist for KD in Japan, who agreed that this gentleman was likely the first known Japanese KD patient (Kawasaki and Yanagawa, personal communication). Investigation of detailed hospital records between 1940 and 1965 by the team at Tokyo University Hospital revealed no pediatric cases consistent with KD prior to 1950.[6]

After the initial description of the syndrome in 1967, there ensued a significant controversy in Japan as to whether the sign/symptom complex described by Kawasaki was related to subsequent cardiac complications. Initially, Kawasaki maintained that his self-limited illness was a benign condition. The pathologist at the Red Cross Hospital, Noburo Tanaka, performed an autopsy on a case previously diagnosed as KD who subsequently died from a myocardial infarction. Tanaka voiced concern that a potentially fatal coronary artery vasculitis could be related to KD. This controversy was finally resolved in 1970 when the first Japanese nationwide survey documented 10 autopsy cases of sudden cardiac death following KD.[3] By the time of Kawasaki's first English language publication in 1974, the link between KD and coronary artery vasculitis was already well-established.[7]

KD was independently recognized as a newly emerging clinical entity in the early 1970s by pediatricians Marian Melish and Raquel Hicks and pathologist

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Eunice Larson at the University of Hawaii.[8,9] Melish, a pediatric infectious disease specialist, and Hicks, a pediatric rheumatologist, kept meeting at the bedside of young Asian children on whom they were both consulted. These patients were suffering from fever with mucocutaneous signs in a pattern that neither junior physician recognized as a named syndrome. However, the patients reminded Melish of two cases she had seen during her training in Rochester, New York, who suffered from a similar constellation of clinical findings (Melish, personal communication). In 1973, a visiting pediatrician from Japan showed Melish and Hicks photographs of Japanese patients with KD and the two immediately recognized the similarities to their cases. Melish wrote to Kawasaki and shared the excitement that cases of KD were also being seen in Japanese-American children in Hawaii. Melish presented an abstract of the Hawaiian cases in 1974 at the Society for Pediatric Research. They called the disease 'mucocutaneous lymph node syndrome', following the lead of the Japanese. Fatal cases were also being described in Hawaii and in 1973, Larson and her former mentor, Dr. Benjamin Landing, retrospectively diagnosed KD in a child who had died of acute myocardial infarction following resolution of the clinical illness.[9]

Although KD was emerging as a new clinical entity in Japan after World War II, case reports from all over the Western world in the early part of the 20th century clearly described a fatal condition of infants termed infantile periarteritis nodosa (IPN).[10,11] This uniformly fatal vasculitis was deemed pathologically indistinguishable from fatal KD by Landing and Larson in their landmark review of KD and IPN autopsies.[12] If one accepts the concept that IPN is simply the fatal form of KD, then case reports and series were reported throughout Western Europe and North and South America beginning in the 1930s.[13] A famous heart with coronary artery aneurysms from an autopsy reported in 1871 from St. Bartholomew's Hospital in London is purported to be the earliest record of a case of KD in the West, although the claim is disputed by others who failed to find any cases of IPN until the 1930s.[13,14]

So, is there consensus that KD/IPN was old in the West and new in Asia? As part of a project entitled 'Kawasaki disease: A Living History' funded by the National Library of Medicine through the KD Foundation in Boston, interviews were conducted in Japan, the Philippines, and India in an attempt to pinpoint the 'first case' of KD in those countries (interviews available at http://www.emory.edu/histmed/kd_main.html). Surprisingly, in the Philippines there was largely consensus among pediatrician and cardiologist interviewees that Dr. Luis Mobilangan diagnosed the first case in the Philippines in 1982.[15] In India, there was lively debate as to whether KD was a new disease versus an old disease hidden among the myriad of rash/fever illnesses including measles and rheumatic fever.[16,17] However, in interviews with senior pediatricians in India, there was consensus that the clinical features of KD were distinct from other pediatric illnesses and even physicians who had been in practice for over half a century recalled their first case of KD (https://www.youtube.com/Kawasakidisease 'The Eyes Cannot See What the Mind Does Not Know'). There was largely agreement that the first diagnosed case in India was in 1977 by Tenaja and Saxena.[18] Thus, in Japan, the Philippines and India there was strong support for the idea that KD was a new clinical entity first appearing in the decades after World War II.

By the 1980s, there were cases of KD reported on every continent. What remains unknown is the reason for simultaneous occurrence of KD around the world in the 1960s and 1970s. Had KD simply been masquerading as other diseases such as scarlet fever in the pre-antibiotic era? It is possible that improvements in health care, and especially the use of antimicrobials to treat infections and vaccines to prevent them, reduced the burden of rash/fever illnesses and allowed KD to be recognized as a distinct clinical entity. One approach to historical investigation might be to probe autopsy records and review cases of coronary artery aneurysms occurring in young adults. In a literature review seeking reports of young adults with KD-compatible coronary artery lesions, cases were discovered whose onset predated the original description of KD by Dr. Kawasaki by over a decade.[19] The new disease/old disease debate will only be finally settled when the inciting agent(s) is/are characterized. Until then, the mystery of the emergence of KD in countries around the world will remain unsolved.

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CONFLICTS OF INTEREST

None.

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