International Journal of Rheumatic Diseases

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International Journal of Rheumatic Diseases

EDITORIAL

The Legacy of Dr. Tomisaku Kawasaki—A Tribute to the Legendary Japanese Pediatrician on His 100th Birth Anniversary: February 07, 2025

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Received: 3 January 2025 | **Accepted:** 6 January 2025

Keywords: acquired heart disease | coronary artery abnormalities | history | Kawasaki disease | Tomisaku Kawasaki

1 | Introduction

Dr. Tomisaku Kawasaki was born on February 7, 1925, in Tokyo, Japan. Growing up as the youngest of seven children in Tokyo's Asakusa district, he was passionate about plants, fruit and botany. However, he decided to pursue a career in medicine as desired by his mother. He graduated from Chiba Medical College in 1948, soon after the end of World War II. He went on to complete his specialization in Pediatrics from the same medical college. Subsequently, he joined the Japanese Red Cross Central Hospital located on the outskirts of Tokyo in the year 1950.

After 10 years into his pediatric practice, in January 1961, he came across a 4 year and 3-month-old boy, who had presented with fever for 2 weeks, bilateral conjunctival hyperemia, dried, red and cracked lips with erythema of the oral cavity, unilateral cervical adenopathy, erythematous skin rash, and red and indurated palms and soles. He also noticed that the patient had mild hemolytic anemia, jaundice, with neutrophilic leucocytosis, elevated erythrocyte sedimentation rate and a "strong positive" C-reactive protein. However, blood and throat swab cultures were negative. The boy did not respond to antimicrobials, but the fever subsided after 2 weeks [1–4].

Dr. Kawasaki was intrigued by the clinical presentation of this boy and was convinced that he appeared to have a condition that had never been described before. He discharged the patient as "diagnosis unknown". He presented this clinical case in a conference but his colleagues opined that this could be a milder variant of scarlet fever, or even Stevens-Johnson syndrome. Dr. Kawasaki, however, remained unconvinced [1–4]. At this time Dr. Kawasaki felt that this appeared to be a benign self-limiting condition and had no idea that this could affect coronary arteries.

A year later, he experienced the second case, whose face looked exactly like the boy who was undiagnosed a year ago. This intrigued Dr. Kawasaki and he was sure that he was dealing with a new disease that had hitherto not been described in any textbook before. In 1962, he had collated seven cases with similar clinical features and presented these at the Japan Pediatric Society Chiba Regional Meeting as "*Non-scarlet fever syndrome with desquamation from the fingertip*". By 1964, he had gathered 22 such patients and presented them as "Mucocutaneous lymph node syndrome (MCLS)." In 1965 Dr. Noboru Tanaka, a pathologist, performed an autopsy on a patient who had previously been diagnosed to have MCLS by Dr. Kawasaki and who suffered a sudden cardiac arrest [1, 3]. Dr. Tanaka noticed that the child had coronary artery thrombosis. This led to the suspicion that KD is not a benign disease but may be associated with a very serious cardiac complication. During this time academic pediatricians in Japan, however, remained unconvinced that what Dr. Kawasaki had described was indeed something unique. He continued to face much opposition, and even criticism, from the academia in Japan.

In 1967, Dr. Kawasaki published a series of 50 cases in a Japanese language journal "Arerugi," entitled "Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children" [5]. This article was a comprehensive clinical description over 44 pages and is a tribute to the clinical and observation skills of Dr. Kawasaki. This

article drew the attention of many Japanese pediatricians. Three years later, the significance of his findings gained international recognition when the Ministry of Health and Welfare in Japan established a Research Committee on "Mucocutaneous Lymph node Syndrome" (Kawasaki disease Research Committee). It comprised of pediatricians, epidemiologists, pathologists and microbiologists. The first nation-wide survey of Kawasaki disease was carried out in 1970. The first edition of "Diagnostic Guidelines of KD" was compiled by the Research Committee, and it was circulated amongst all hospitals in Japan having more than 100 beds and a separate pediatric department. The Research Committee began gathering information from across the country using a questionnaire [6].

In the late 1950s and 1960s another distinguished Japanese pediatrician, Dr. Takajiro Yamamoto, had also came across similar cases with fever and rash symptom complex. Some of these patients had also shown evidence of gallop rhythm. Later, in 1968, Dr. Yamamoto published a case series of 23 patients of which 11 had electrocardiographic abnormalities [7]. In 1974, Kawasaki published his experience in an English language journal (Pediatrics) for the first time [6]. This publication received widespread attention from pediatricians all over the world. By this time, it had become clear that KD was indeed associated with a risk of serious cardiac complications. However, confusion still persisted about whether KD and Infantile polyarteritis nodosa (IPN) were distinct entities [8]. In 1972, Tanaka et al. published an article that suggested a link between IPN and KD based on autopsy findings [9–11]. The Japanese Research Committee found that there were 20 sudden death cases reported in patients with MCLS and 4 amongst those had been autopsied. All 4 patients had coronary artery aneurysms with thrombosis. Based on multiple autopsy findings, Dr. Zenshiro Onouchi and his colleagues in Kyoto concluded that the fatal form of IPN is a spectrum of severe KD [12].

In the early 1970s, Dr. Marian Melish and Dr. Raquel Hicks in Hawaii, USA, noticed a similar presentation in a few children. They also noticed a peculiar association of this condition with children of Japanese ancestry [13]. The emergence of this new disease spectrum from the 1960s to 1970s in various parts of the world with special predilection for Japanese children lead to the hypothesis that the disease probably originated in Japan, and later spread to other parts of the world. Another hypothesis stated that in the preantibiotic era, this condition may have been confused with scarlet fever and had remained undiagnosed. After the widespread use of antimicrobials for treatment of scarlet fever in the 1960s and 1970s, it become clear that MCLS was indeed a distinct entity [4].

In 1975, Dr. Hirohisa Kato published a landmark article, "Coronary aneurysms in infants and young children with acute febrile mucocutaneous lymph node syndrome" in which he documented coronary aneurysms in infants and young children with MCLS [14]. This was the first time that coronary aneurysms had been documented during life (Figure 1).

2 | KD Is Now the Most Common Cause of Acquired Heart disease in Children Worldwide

KD is now the most common cause of acquired heart disease in children worldwide. Epidemiological data from developed regions such as Japan, North America, and Europe indicate that KD has surpassed rheumatic fever in this role. Over the last three decades, the incidence of acute rheumatic fever has declined significantly and continues to decrease globally. On the other hand, the incidence of KD has shown a steady increase in several countries (e.g., Japan, Korea, Taiwan) [15]. Similar trends have been observed in low-middle-income countries such as India [16–18]. Whether this increased incidence represents a true increase in the occurrence of disease, or is secondary to increased ascertainment (as a result of increased awareness about KD amongst physicians) remains conjectural [16–18].

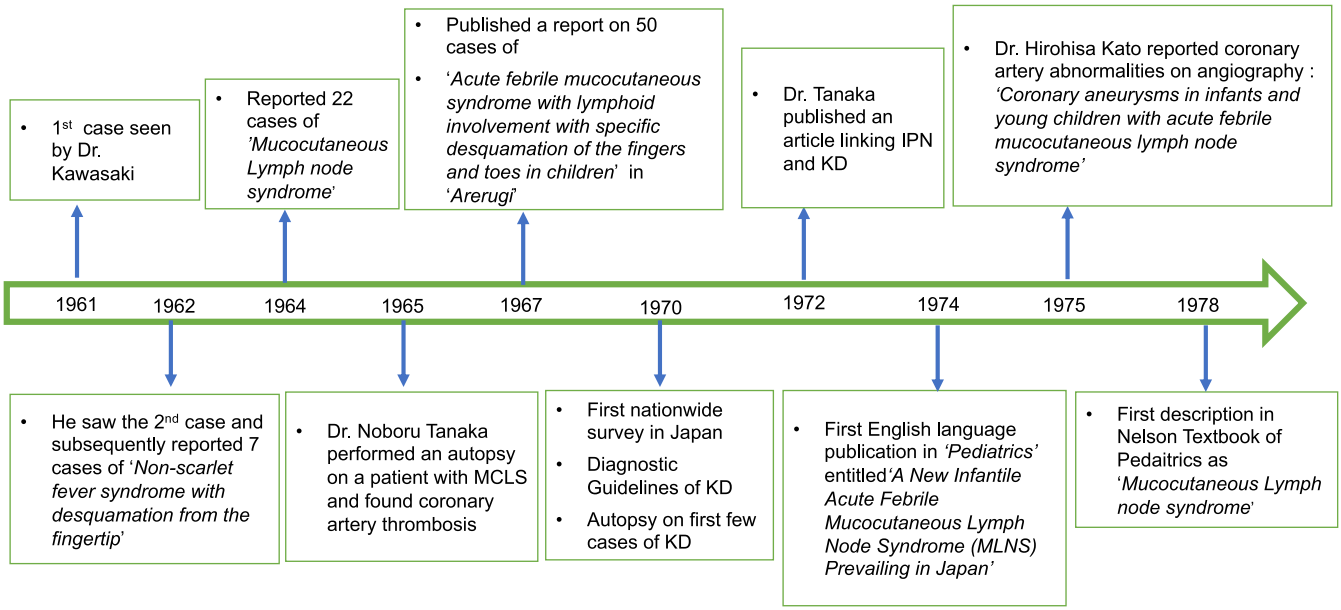

FIGURE 1 | Kawasaki disease: A timeline of events. IPN, infantile polyarteritis nodosa; KD, Kawasaki disease; MCLS, mucocutaneous lymph node syndrome.

Even 57 years after the initial description of KD, there are no specific diagnostic tests for the condition. The present guidelines for diagnosis of KD are in many ways similar to what Dr. Kawasaki had described way back in 1967. KD is diagnosed based on a constellation of clinical features and the diagnosis is still clinical [19, 20] There is, as yet, no confirmatory biomarker for the diagnosis of KD [19, 20]. As the etiology of KD is still not known, one cannot prevent the occurrence of KD. One must, however, ensure early diagnosis of KD as it is possible to prevent serious complications in the majority of patients if they are treated appropriately. Children with KD who remain undiagnosed, or are diagnosed late, are at risk of significant cardiac morbidity and, at times, even mortality.

3 | The Rich Legacy of Dr. Tomisaku Kawasaki (1925–2020)

After retiring from the Japanese Red Cross Hospital as Director in 1990, Dr. Kawasaki founded the Japan Kawasaki Disease Research Center, serving as its Director until 2019 and later as Honorary Chairman until 2020. Under his leadership, the center became a pivotal institution for research and education on Kawasaki disease. This centre has contributed significantly to increasing awareness about this condition all over the world.

Over the last few decades while the nomenclature of most vasculitic disorders has been changed, KD continues to retain its eponymous description. This is a tribute to the life and work of Dr. Tomisaku Kawasaki. He has been an inspiration for generations of pediatricians, internists, and cardiologists all over the world. Dr. Kawasaki breathed his last on June 05, 2020.

Author Contributions

A.T., R.K.P. writing – original draft, figures, writing – review and editing. A.T., R.K.P., H.H., S.S. Literature search, data collection, editing of the manuscript. R.K.P., S.S. conceptualisation, study design, overall supervision, critical editing of the manuscript at each step and final approval.

Acknowledgments

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Date Availability Statement

The data underlying this article are available in the manuscript.

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