Is Kawasaki Disease a New Disease?
– A Pathological Perspective –

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Is Kawasaki disease (KD) a new disease? The article by Takahashi et al in this issue of the Journal may give us some suggestions.¹ They reviewed 380 autopsy cases of pediatric systemic vasculitis syndrome from the last 50 years from the Annual of Pathological Autopsy Cases in Japan. The first diagnosed autopsy case of KD occurred in 1969. This was 2 years after Kawasaki’s first description of this disease in 1967.² A small number of cases, however, were pathologically diagnosed as infantile polyarteritis or periarteritis nodosa before 1969. At the present time, infantile polyarteritis is thought to be identical to fatal KD pathologically,³ and now KD is known as a systemic vasculitis syndrome that occurs in infants and young children, with a wide spectrum of clinical symptoms and disease severity including fatal cases. In the old clinical literature before Kawasaki’s first description there are some case reports consistent with KD. Those clinical diagnoses consisted of polyarteritis nodosa,⁴ Stevens-Johnson syndrome⁵ and scarlet fever,⁶ which resemble KD in clinical presentation. In Japan, patients with prospectively suspected KD were seen after the 1950s and they were diagnosed as having Izumi fever, Stevens-Johnson syndrome or scarlet fever.⁷ This means that KD certainly existed before Kawasaki’s first description. It is suspected, however, that those cases were very few in number and occurred seldom. Thus KD is not a new disease but newly recognized as a clinical entity by Dr Kawasaki’s piercing observation of the patients.

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Why has KD so rapidly increased from the 1960s and is still increasing now, particularly in Japan? This mystery may depend mainly on the etiology of this disease. Many hypotheses on the etiology and pathogenesis of KD have been proposed, but the etiology remains uncertain at present. KD is widely scattered in the community, is self-limited, has multiorgan involvement, can recur, and has a tendency toward small epidemics in winter–spring. This may suggest some common infectious agent(s).⁸ Also, epidemiological studies suggest a genetic predisposition to this disease. Recently a genome-wide linkage analysis identified a polymorphism in the gene ITPKC as being KD susceptible.⁹ It is highly likely that multiple genes are involved in KD susceptibility. These findings suggest that this disease may be caused in some susceptible children by a common infectious agent(s). The question remains, however, as to why KD has rapidly increased in incidence in Japan. Some additional environmental factors may be involved. It is critical to elucidate the etiology of KD at the present time.

Almost 45 years have passed since the first description by Kawasaki, and the patients from the early era have already grown into middle age. A certain number of KD patients with coronary artery sequelae may have developed adult coronary artery disease.¹⁰ The issues for KD in adulthood include the lack of diagnosis of KD in the early era or before Kawasaki’s first description, although the patients had the coronary artery disease due to KD, or the lack of evaluation of the coronary lesions during childhood KD; the presence of persistent coronary artery sequelae due to KD in adult patients, some of whom may need bypass surgery or percutaneous coronary intervention;¹¹ the development of premature atherosclerosis in adult patients with coronary artery involvement or regressed coronary aneurysms after KD, due to the presence of intimal thickening and endothelial dysfunction.¹² Education for prevention of atherosclerosis in school children may be necessary to avoid other coronary risk factors, such as smoking or diet. The natural history of KD with coronary artery lesions from childhood to adolescence is distinctive,¹³ but long-term consequences are still uncertain, and need to be clarified via collaboration between pediatric cardiologists and adult cardiologists. The coronary artery lesions may change or progress to ischemic heart disease, accelerated by aging with hypertension or atherosclerosis. KD coronary artery sequelae may be an important cause of ischemic heart disease in young adults under 40 years of age, particularly in Japan. Adult cardiologists should be aware of this condition and include KD sequelae in the differential diagnosis of early onset coronary artery disease in adults.

References

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Circulation Journal Vol.76, April 2012


