Journal of Medical Ultrasonics (2019) 46:1–2
https://doi.org/10.1007/s10396-018-0922-x

EDITORIAL

Ultrasonic assessment of vascular function in Kawasaki disease

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Vascular lesions in Kawasaki disease

Kawasaki disease is a syndrome first reported by Dr. Kawasaki in 1967 [1]. It is a self-limited acute febrile condition that more commonly affects infants; it affects 12,000–14,000 children in Japan annually. The cause is unknown, but it is thought to essentially be systemic vasculitis. Inflammation, which appears more commonly in medium-sized muscular arteries, is particularly pronounced in the coronary arteries, and despite advances in treatment in the acute phase, 3% of diagnosed infants still suffer from late coronary artery aneurysms. In the acute phase, infiltration by inflammatory cells such as activated monocytes and macrophages occurs, which interact with vascular endothelial cells to secrete various adhesive molecules and cytokines, damaging the internal elastic membrane, medial smooth muscle, and intercellular matrix, which are important for maintaining the arterial structure, and leading to coronary artery lesions such as coronary artery aneurysms.

These coronary artery lesions are known to cause various changes in the long term. Histopathologically, fibrous tissue with hyalinization is found in the aneurysmal wall, and calcification is widely observed. Intimal hyperplasia is seen in the aneurysmal lumen, as well as regressed lesions with an "angiographically normalized" lumen, lumen narrowing and occlusion due to cellular tissue neointimal thickening and thrombus formation in the vicinity of the aneurysm, and recanalization. On the other hand, pathologic findings suggestive of vasculitic scarring are also observed in coronary arteries free of coronary artery aneurysms.

Observations by intravascular ultrasound (IVUS) have also revealed intimal hyperplasia and calcified lesions in residual aneurysms and regressed aneurysms, which is consistent with the histopathological findings. In recent years, optical coherence tomography (OCT) has allowed more detailed observations, leading to reports of findings such as white thrombi, disappearance of the media, and macrophage accumulation in coronary artery lesions.

These coronary artery lesions may be a state of post-inflammatory arteriosclerosis.

However, it is not yet clear whether suffering from Kawasaki disease in infancy is a risk factor for atherosclerotic lesions in adolescence and adulthood.

Ultrasonography for noninvasive assessment of vascular function in patients with Kawasaki disease

In the earliest stage of arteriosclerosis, infiltration of macrophages into vascular endothelial cells causes deposited foam cells to form, which become fatty streaks. As the fatty deposition progresses, atheroma and fibrous plaque form, and vascular stiffness begins to increase. Rupture of the plaque ultimately causes serious cardiovascular lesions.

The vascular endothelium is the innermost cell layer of blood vessels. Vascular endothelial cells produce and secrete various vasodilators and vasoconstrictors to regulate vascular tone and maintain the vascular structure by balancing them. Among them, nitric oxide (NO) is known as one of the most potent vasodilators secreted by vascular endothelial cells. Vascular endothelial dysfunction is a vascular disorder that occurs in the earliest stage of arteriosclerosis.

Vascular endothelial function is noninvasively assessed using flow-mediated dilation (FMD) by assessing the increased vascular flow in a forearm artery, as represented by the percent change in vascular diameter, after inflation and then deflation of a cuff. A rapid increase in vascular flow increases vessel wall shear stress in the brachial artery, NO in vascular endothelial cells is released into the vessel, and the brachial artery dilates, but the vessel does not dilate sufficiently in the presence of vascular endothelial dysfunction.

FMD is lower in patients in the late phase of Kawasaki disease, and there have been many reports indicating that

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this tendency is more pronounced in cases with coexisting coronary artery lesions, in particular. However, there have also been reports of no decrease in vascular endothelial function. With respect to vascular endothelial dysfunction in patients with no coronary artery lesion involvement, in particular, a consensus has not been reached.

Carotid intima–media thickness (IMT) is widely used as an indicator of atherosclerosis in adults. There are several reports of measurement of IMT in patients with Kawasaki disease in the literature. While there are reports of IMT thickening in Kawasaki disease patients with coronary artery lesion involvement, there are also reports of no significant difference versus a normal population. All of the reports were investigations with a small sample size, and, therefore, a consensus has not been reached.

Acute coronary syndrome in adult Kawasaki disease patients

The number of cases of acute coronary syndrome in adult patients in the late phase of Kawasaki disease has increased, and catheter intervention is being performed in these patients. Follow-up results for elective catheter intervention in Kawasaki disease patients with coronary artery lesion involvement have been good, but outcomes for catheter intervention in Kawasaki disease patients who have undergone emergency catheter intervention for acute coronary syndrome have been reported to be worse than those in atherosclerosis patients with acute coronary syndrome.

Intravenous gamma-globulin therapy, the current standard treatment for Kawasaki disease in the acute phase, was established in 1984 [2]. In addition, echocardiographic diagnosis, which is essential for the assessment of coronary artery lesions in the acute phase, was introduced in the latter half of the 1970s, with a systematic echocardiographic assessment method being established in 1984 [3].

Consequently, patients who contracted Kawasaki disease in the 1970s and early 1980s were unable to receive effective acute treatment, and they did not undergo accurate assessment of coronary artery lesions in the acute phase. These patients are now approaching the age (40–50 years) at which arteriosclerotic lesions commonly occur, and this problem is expected to gain more and more attention in the coming years.

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