JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 9, NO. 7, 2016

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2016.02.036

EDITORIAL COMMENT

Intervention in Adults After Kawasaki Disease*

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Kawasaki disease (KD) in children was not always recognized worldwide in the 1960s and 1970s, and coronary artery lesions (CAL) caused by KD have persisted long into adulthood after the acute illness in childhood. Because the diagnosis of KD is clinical and depends on recognizing the major characteristic clinical features of the acute phase, there are undoubtedly many asymptomatic adult patients with CAL caused by KD who remain undiagnosed, forming a hidden cohort with this disease. CAL caused by KD is not always familiar to internists, and the affected population is a small group among ischemic heart disease in adults. In this issue of *JACC: Cardiovascular Interventions*, the paper by Gordon et al. (1) focuses on acute coronary syndrome (ACS) in this population of non-Japanese patients.

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The true adult population with CAL caused by KD is difficult to estimate. The history of the disease in childhood as remembered by adult patients and their parents may be incomplete, because the episode occurred long ago. On the other hand, the incidence of ectasia is <5% in the general adult population. Although ectasia is most commonly due to atherosclerosis, coronary artery disease of unknown etiology, which has never been reported before, may exist. Actually, we have on rare occasions experienced dilated coronary disease in adults. For example, it is questionable whether the ectasia of patient #17 in this article has been caused by KD (1). The findings in the coronary angiograms may resemble coronary artery aneurysms (CAA) in the acute phase despite the passage of 30 years or more after the acute KD. Did the patient have acute KD in adult? It seems that it is not typical CAL caused by KD in adults many years after acute KD in children. Recognizing "change in addition to aging" or "change over a long-term period" in these angiograms is difficult. Practically, the differential diagnosis of CAL caused by KD versus atherosclerosis with aging may be difficult in some adult patients. Therefore, in discussing the treatment and outcome of CAL caused by KD, the cohort of "KD-like" induced lesions should be distinguished from the cohort of KD (1).

The morphological changes of CAA seen after KD are caused by intimal thickening or thrombus formation in the convalescent stage after damage of the vessel wall due to acute vasculitis. The late period change of CAA after KD depends on the diameters of CAA, which reflect the degree of acute vasculitis. Usually, the internal diameter of a large CAA decreases over the years due to intimal thickening of the vessel wall, except for the extremely rare patient with an expanding aneurysm or new aneurysm. Even if CAA exceed 6 mm diameter in the acute phase, they often disappear. It is referred to as "regression "or "apparently angiographic normal coronary artery" in the late period after KD. Further, localized stenosis can appear in the regressed lesions. Large CAA do not always exist in the late period when localized stenosis appears, although large CAA in the acute phase can lead to stenotic lesions. Consequently, even small- to moderate-sized aneurysms that "normalize" by echocardiography in childhood can lead to stenosis and thrombosis decades after the acute illness such as mentioned in this article (1,2). In almost all patients, the morphologies of CAA after many years usually differ from those in the acute phase. In considering

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

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KD, it is very important to recognize the change of CAA over the long term.

The coronary artery wall, which is affected by severe vasculitis during acute KD, becomes thickened and firm and calcified after many years. Ringed calcification along large CAA in the proximal portion of the major coronary arteries on chest x-ray is typical and one of the characteristics in CAL caused by KD. CAA exceeding 6-mm diameter in the acute phase are frequently calcified after more than 10 years, thus in the late period, calcification can be considered as a marker of CAL caused by KD. Even when the CAA have regressed in coronary angiograms, calcification indicates involvement of the coronary artery wall after severe acute vasculitis. Further, the degree of coronary artery calcification can affect the device selection for percutaneous coronary intervention (PCI).

However, CAA also complicate atherosclerosis, and furthermore, coronary artery calcification increases with aging; clinically, the location of coronary artery calcification and aneurysms helps to differentiate KD and atherosclerosis etiologies. In KD, calcification is usually limited to the site of pre-existing CAA, whereas in atherosclerosis, it does not colocate with aneurysms. Lesions due to atherosclerosis are diffuse, whereas they are usually localized in KD because they reflect the degree of acute vasculitis. This article reports computed tomography calcium scores in patients (1). However, it is unclear whether the computed tomography score is useful or not in managing this population. Further investigations are needed.

Symptoms are rare in this population until the onset of ACS; consequently, the presence of coronary artery disease was unsuspected in many adult patients until the sudden attack, and preventive antithrombotic therapy was not considered. Therefore, the prevalence of ACS in follow-up patients from childhood would be different from that in adult patients with a suspected KD history. For coronary revascularization, an elective coronary revascularization is considered for most patients in the follow-up group whereas emergency coronary revascularization would be needed in suspected KD adult patients presenting with ACS.

The treatment for ACS has improved remarkably over the last 4 decades, thanks to improved PCI. Giant calcified aneurysms involving the proximal portion of the major branches were the most common culprit lesions, and in most cases, thrombus formation within the aneurysm precipitated the ACS. Most adult KD patients with ACS have giant CAA >8 mm. Early revascularization after acute myocardial infarction minimizes the infarct area, and it was applied to some ACS in this population, but simple aspiration or thrombolytic therapy was not always successful because of the large volume of thrombus in the giant aneurysm. Further, percutaneous coronary balloon angioplasty would be needed in addition to aspiration. Re-occlusion of the culprit lesion sometimes can occur a short time after a successful procedure, because of reformation of thrombus.

It is difficult to evaluate the precise diameter of culprit lesions because of massive thrombus. Some stent malpositions were reported because of underestimation of the diameter or the morphological characteristics. The new aneurysm and stent malposition after drug-eluting stent for so-called “segmental stenosis” was reported (3). Segmental stenosis means recanalization in the aneurysm by small new vessels, which often cause early occlusion after acute KD. It must be recognized that they differ from total occlusion due to atherosclerosis, which has recently developed in its treatment. It seems that PCI for segmental stenosis isn’t always necessary if collateral arteries are well developed. The long-term outcome of stent implantation in this population is unknown. If the patient is younger, it may be better to avoid emergency stent implantation except in life-threatening situations requiring rescue.

Percutaneous transluminal coronary rotational atherectomy (PTCRA) is generally selected as the best intervention for severe localized stenosis with calcification. In a target vessel in which a burr larger than 2.15 mm of the diameter can be used, good patency of the vessel can be maintained by close follow-up and re-PTCRA. A new aneurysm may develop after high-pressure balloon angioplasty in addition to PTCRA (4). Restenosis within the first year after PTCRA often develops because of reactive intimal thickening after procedure, and the patient should be carefully followed (5).

Coronary artery bypass grafting and PCI as coronary artery revascularization procedures are often needed in patients with multivessel disease to ensure long-term life, because the time of appearance of localized stenosis varies, ranging from several months to more than 10 years after the onset of KD in a given patient. Once good flow in the internal thoracic artery graft 1 year after surgery is confirmed, graft patency will persist for more than 20 years. On the other hand, one should be careful that saphenous vein graft in the late period after grafting can cause acute myocardial infarction due to thrombus formation in the graft. The post-coronary artery bypass grafting left ventricular ejection fraction is related to the outcome in this population. A coronary revascularization to the left anterior descending artery can be

important in these patients to preserve the left ventricular ejection fraction (6).

Systemic artery aneurysms that are found in patients with severe acute KD vasculitis <1 year old are very rare. Although intervention for these lesions is debatable, collateral arteries in most cases will be well developed during continued antithrombotic therapy. More needs to be learned about the characteristics of lesions caused by KD in this uncommon but life-threatening condition.

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KEY WORDS coronary artery aneurysm, coronary artery calcification, coronary artery lesions, coronary artery revascularization, Kawasaki disease, percutaneous coronary intervention