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Coronary artery aneurysm after Kawasaki disease

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Abstract. The complication of coronary artery aneurysm development after Kawasaki disease is currently not common after introducing human immunoglobulin therapy. Still, it is a life-threatening complication requiring consistent life-long follow-up to avoid acute coronary syndrome. We present a case report of a Kawasaki disease patient with initial large coronary artery aneurysm regressing to medium size coronary artery aneurysm. Based on the recent recommendation from the American Heart Association for Kawasaki disease management, an adequate thromboprophylaxis was set in this patient. Fig. 3, Tab. 4, Ref. 17, on-line full text (Free, PDF) www.cardiologyletters.sk

Key words: Kawasaki disease – coronary artery aneurysm – thromboprophylaxis – long-term follow-up

Kawasaki disease (KD) is an acute vasculitis of middle arteries with an unknown etiology, typical for children to the age 5, with a wide spectrum of symptoms (1, 2, 3). In most cases it has a very good prognosis with low mortality rate (4, 5, 6). The essential factor affecting the survival rate of patients with KD is inflammation of the coronary arteries, potentially causing formation of a coronary artery aneurysm (CAA) (5, 6). Currently, after introducing intravenous immunoglobulin therapy in the acute phase of the disease, the risk for CAA development dropsed significantly from 25% to 3-4% (7, 8, 9, 10). Potential development of coronary artery stenoses in patients with CAA can lead to myocardial infarction. This is why patients with CAA need life-long follow-up with adequate prevention of myocardial ischemia either by antiplatelet or anticoagulation therapy, if indicated (4).

The vast majority of CAA cases regress with diameter normalisation mostly within 2 years (11, 12). It is important to stress that the regression can be only relative compared to the increasing body surface area during the fast growth of children in infancy and early childhood. The relative regression of coronary artery growth can appear also after the first decade, at the time of the second growth spurt during puberty (11, 13). Post mortem examination of CAA with light and transmission electron microscopy has found a pathological vessel wall architecture proving the thrombogenic risk to be still higher after CAA relative regression (14).

Coronary artery (CA) stenoses can develop especially in giant CAA in the long-term follow-up. The risk of CA stenoses development in patients with CAA is 3%, 10%, 20% per 1 year, 2 years, and 10 years respectively (11).

Patients with damaged CAs are usually set on antiplatelet therapy due to the increased risk of acute coronary syndrome (ACS) in the long-term follow-up (4, 11). As patients with giant aneurysm present with ACS more commonly, anticoagulation therapy is indicated in this group of patients (15, 16). Recent AHA recommenda-

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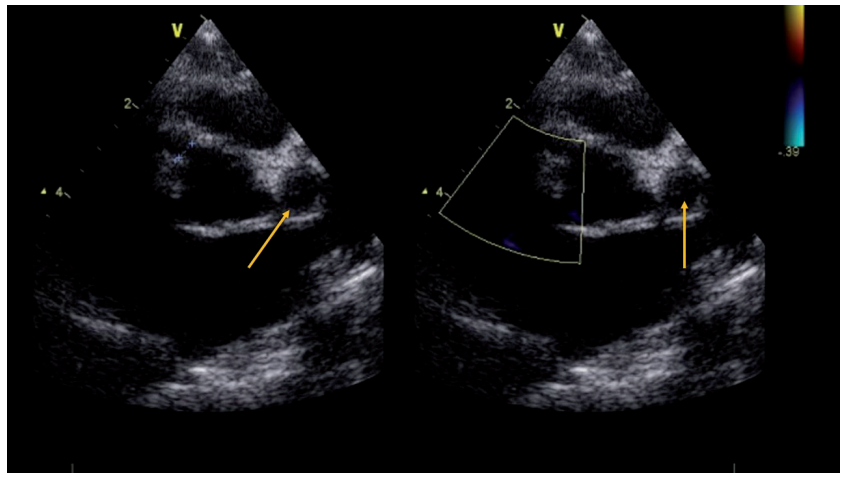

Figure 1 Echocardiography (short-axis view) with coronary artery aneurysm, yellow arrow pointing at coronary artery aneurysm (left anterior descending artery diameter of 10 mm). NÚSCH, a. s., DKC

tions summarize the follow-up and treatment of patients with KD (4).

This article presents a case report of a patient with Kawasaki disease with developed CAA, emphasizing the importance of the implementation of the actual recommendations for management of patients with this severe complication.

Case report

Complete clinical signs of Kawasaki disease (KD) presented in a 2-year-old boy. Despite administration of a full dose of intravenous immunoglobulins (2 g/kg), echocardiography delineated a coronary artery aneurysm (CAA) of 10.5 mm diameter on the left anterior descending artery (LAD) on day 18 of the disease (**Figure 1**). The patient was initially treated with subcutaneous dalteparin (150 IU/kg) and peroral acetylsalicylic acid (ASA) (5 mg/kg). 6 months later, catheterizational coronarography imaged a 6 mm diameter of the CAA. Consequently, the therapy was switched to warfarin monotherapy. Periodical echocardiograms for CAA diameter assessment were performed in the next 4 years of follow-up. 7.5 years after the onset of KD the patient underwent cardiac MRI with the aim to detect potential myocardial ischemia. The negative result of late gadolinium enhancement ruled out any ischemic myocardial changes (**Figure 2**). Due to no optimal echocardiographic acoustic window, CTA was performed to objectify the current size of CAA (**Figure 3, 4**). The CTA did not confirm mild progression of CAA diameter to 7.3 mm measured on the cardiac MRI. The diameter of CAA measured by the CTA was without any significant change in comparison to its size 6 months after the onset of the disease. The size of CAA measured by the cardiac MRI was overestimated due to moving image artefacts. The diameter of CAA 6.0 mm measured on the CTA was expressed in Z-score for the first time in the pa-

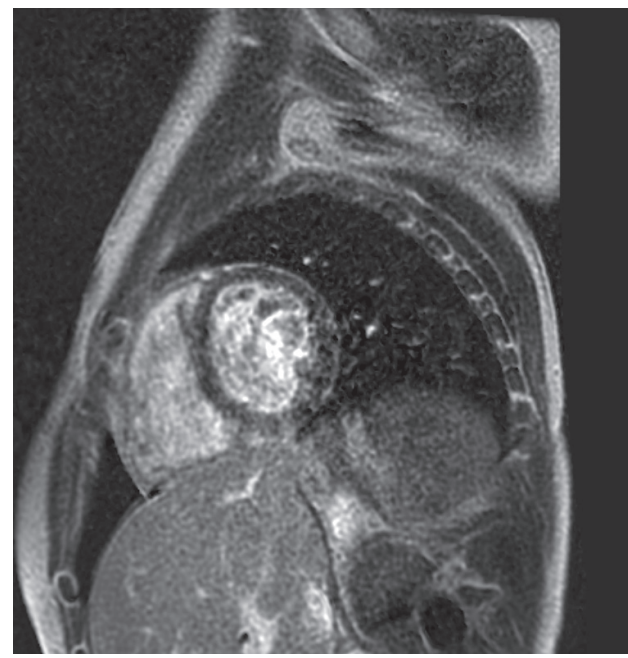

Figure 2 Cardiac MRI (short-axis) with negative finding of late gadolinium enhancement in left ventricular myocardium. NÚSCH, a. s., DKC

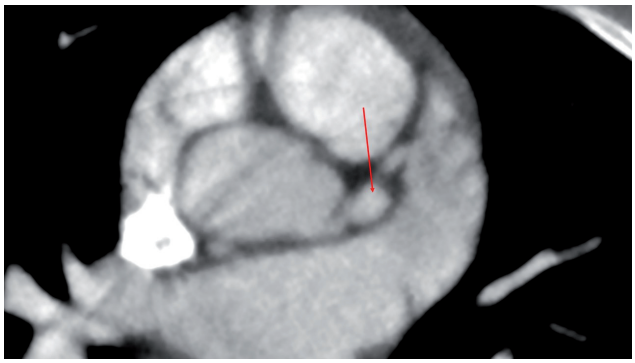

Figure 3 CTAG (axial view) with coronary artery aneurysm, red arrow pointing at coronary artery aneurysm (left anterior descending artery) of 6 mm diameter. NÚSCH, a. s., DKC

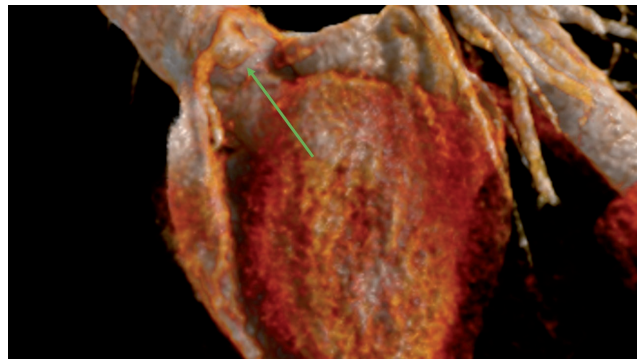

Figure 4 CTAG (left lateral view): 3D virtual reconstruction, green arrow pointing at coronary artery aneurysm (left anterior descending artery) of 6 mm diameter. NÚSCH, a. s., DKC

Table 1 Risk classification of CAA (4)

1.	**No changes all time (Z-score always < +2)**
2.	**Dilatation (Z-score: +2 to < +2,5)**
3.	**Small aneurysm (Z-score: +2 to < +5)**
3.1.	Persistent
3.2.	Regression to dilatation or normal luminal diameter
4.	**Medium aneurysm (Z-score: +5 to < +10, diameter < 8 mm)**
4.1.	Persistent
4.2.	Regression to small aneurysm
4.3.	Regression to dilatation or normal luminal diameter
5.	**Large (giant) aneurysm (Z-score: > +10, or diameter > 8 mm)**
5.1.	Persistent
5.2.	Regression to medium aneurysm
5.3.	Regression to small aneurysm
5.4.	Regression to dilatation or normal luminal diameter

tient's follow-up. The Dallaire et al. Z-score system was applied. Z-score 6.9 value of the latest CAA diameter was re-evaluated according to the recent AHA recommendations for the diagnosis treatment and long-term management of Kawasaki disease (1). Based on this, the aneurysm was categorized as a large or giant aneurysm regressed to a medium aneurysm (Z-score ≥10, or absolute dimension ≥8 mm, regressed to Z-score: +5 to < +10, diameter < 8 mm) (**Table 1**).

Afterwards, according to the long-term prophylaxis recommendation (**Table 2**), the therapy was updated from the unnecessary anticoagulation therapy to dual antiplatelet therapy (ASA + clopidogrel), which improved the quality of the patient's life. Based on long-term

Table 2 Long-term Thromboprophylaxis (4)

Risk classification	Low-dose ASA	Anticoagulation (Warfarin or LMWH)	Dual antiplatelet therapy (ASA+clopidogrel)
1.	4-6 wk. then discontinuite	Not indicated	Not indicated
2.	Indicated until regression to normal	Not indicated	Not indicated
3.1.	Indicated	Not indicated	Not indicated
3.2.	May be considered	Not indicated	Not indicated
4.1.	Indicated	Not indicated	May be considered
4.2.	Indicated	Not indicated	May be considered
4.3.	Reasonably indicated	Not indicated	Not recommended except in the presence of inducible myocardial ischemia
5.1.	Indicated	Reasonably indicated	May be considered in addition to anticoagulation*
5.2.	Indicated	Not indicated	Reasonably indicated
5.3.	Indicated	Not indicated	Not indicated
5.4.	Reasonably indicated	Not indicated	Not indicated

Green: Class I recommendation (should be performed), Yellow: Class IIa recommendation (it is reasonable to perform), Orange: Class IIb recommendation (may be considered), Red: Class III recommendation (should not be performed.)
*May be considered in addition to anticoagulation in the setting of very extensive or distal CAA, or in history of coronary artery thrombosis

follow-up recommendation (**Table 3**), a regular yearly interval of cardiology assessment including physical examination, echocardiography and electrocardiography was determined, because the patient still stays at a higher risk of ACS. In addition, assessment for inducible myocardial ischemia by stress echocardiography, stress electrocardiography, stress with magnetic resonance perfusion imaging, and stress with nuclear medicine perfusion imaging should be performed yearly as well (**Table 3**). The frequency of additional cardiology assessment by CTA, MRI or catheterizational coronarography may be reconsidered every 2 – 5 years in this case (**Table 3**).

Discussion

Nowadays, the long-term follow-up of patients with CAA after KD is necessary due to the higher risk of ACS. The first-line drug to prevent ACS is ASA (4). In patients with giant CAA, better survival was recorded in patients on anticoagulation therapy: low-molecular--weight-heparin (LMWH) or warfarin (15, 16, 17). Both of the latter therapies pose a challenge for the patients. Although the risk of bleeding or ACS on LMWH therapy is very low, regular traumatisation with subcutaneous injections increases the discomfort of these patients. On the other hand, the need for a warfarin specific diet and regular INR control can lead to worse patients´ compliance.

Currently, according to AHA recommendations from 2017, updated in 2019, the anticoagulation therapy is indicated only in patients with persistent giant CAA, due to the higher risk of ACS development (4). It is important to treat these patients according to these recommendations to avoid unnecessary over anticoagulation in patients with a medium-size or small-size aneurysm, as was proved by this case study.

Conclusions

The goal of this article is to emphasize the fact that the diameters of the coronary arteries in KD patients need to be indexed to the body surface area, as the use of these indexed values expressed in the Z-score system categorize each patient into the specific risk classification scale of CAA (**Table 1**) according to the recent AHA recommendations for diagnosis, treatment, and long-term management of Kawasaki disease (4). This AHA Scientific statement: Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease from 2019 offer a few Z-score systems for coronary arteries evaluation. The Z-score from Dallaire et al. seems to be the ideal one for evaluation of coronary artery diameters in children. In comparison to other Z-score systems it offers 2 basic advantages: the relatively high number of pediatric subjects and reference values for even distal parts of CAs. Applying risk classification of CAA helps to improve complex management of KD patients with residual coronary arteries dilatation or aneurysm. Not only can a long-term thromboprophylaxis be properly set, but also an optimal long-term follow-up protocol can be recommended.

Table 3 Long-term follow up recommendation (4)

Risk classification	Frequency of cardiology assessment	Assessment of inducible myocardial ischemia	Frequency of additional cardiology assessment
1.	discharge btw. 4 wk and 12 mo.	None	None
2.	if regress to normal, discharge btw. 4 wk. to 12 mo.; if persist, reassess every 2-5 y.	None	None
3.1.	Assess at 6 mo., then yearly	Assess every 2-3 y.	Every 3-5 y.
3.2.	Assess every 1-3 y. (may omit ECHO)	Assess every 3-5 y.	May be considered, if there is an inducible ischemia or ventricular dysfunction
4.1.	Assess at 3,6 and 12 mo., then every 6-12 mo.	Assess every 1-3 y.	every 2-5 y.
4.2.	Assess yearly	Assess every 2-3 y.	every 3-5 y.
4.3.	Assess every 1-2 y. (may omit ECHO)	Assess every 2-5 y.	May be considered, if there is an inducible ischemia or ventricular dysfunction
5.1.	Assess at 3, 6 ,9 12 mo., then every 3-6 mo.	Assess every 6-12 mo.	Baseline within first year; may be considered 1-5 y.
5.2.	Assess every 6-12 mo.	Assess yearly	every 2-5 y.
5.3.	Asses every 6-12 mo.	Assess every 1-2 y.	every 2-5 y.
5.4.	Assess every 1-2 y. (may omit ECHO)	Assess every 2-5 y.	every 2-5 y.

Black text: reasonably indicated to perform (Class IIa), Red text: may be considered (Class IIb)

The risk classification of coronary arteries diameter in the Z-score system and its application into current AHA recommendations for the diagnosis, treatment, and long--term management of Kawasaki disease led us to a radical change in the thromboprophylaxis therapy in the patient presented in this case. It also helped us to reset an optimal long-term follow-up protocol for the patient.

With the goal of reaching the best possible outcome for KD patients with residual coronary artery dilatation or aneurysm, we also emphasize the need to use these current recommendations by all paediatric cardiologists around Slovakia.

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