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Case report

Adolescent Kawasaki Disease patient with coronary calcifications, severe 4-vessel stenosis, and a normal stress MRI

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Abstract: Kawasaki Disease is associated with early and late coronary abnormalities. Coronary calcifications have been noted on long-term follow ups in the region of the initial abnormalities. We present the first case of an asymptomatic adolescent with Kawasaki Disease and normal stress testing in whom the coronary calcium was associated with severe four vessel narrowing.

Keywords: Kawasaki; calcification; MRI; CT; giant aneurysm

1. Introduction

Kawasaki Disease (KD) is the most common cause of acquired heart disease in children within developed countries [1]. An acute vasculitis of childhood leads to coronary aneurysms in approximately 25% of the untreated cases. Even with treatment, 20% will develop a transient coronary dilation, while 1% will develop either large or giant aneurysms (>8 mm, Z-score ≥ +10). Large or giant aneurysms are at risk for rupture, and a myocardial infarction can occur from an acute or progressive thrombosis or stenosis [1]. Patients with a history of coronary artery aneurysms are at risk of late morbidity and mortality [2], and coronary aneurysms are associated with late calcifications [3]. Coronary artery calcifications (CAC) have been associated with stenosis in the area of calcifications [4]. Clinical criteria are used to diagnose Kawasaki Disease. Classic Kawasaki Disease is diagnosed in the presence of at least 5 days of fever together with 4 of the 5 following principle clinical features: (1) erythema and cracking of the lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa; (2) bilateral bulbar conjunctival injection without exudate; (3) rash:

maculopapular, diffuse erythroderma, or erythema multiforme-like; (4) erythema and edema of the hands and feet in the acute phase and/or periungual desquamation in the subacute phase; and (5) a cervical lymphadenopathy (≥1.5 cm diameter), which is usually unilateral. Incomplete Kawasaki Disease can be diagnosed with 2 or 3 clinical criteria and either certain laboratory criteria or coronary artery abnormalities (dilation/aneurysms) [1].

2. Case report

We present the first case of an adolescent with a history of KD and giant coronary aneurysms with significant CACs and a normal cardiac stress magnetic resonance imaging (MRI). He was diagnosed with Kawasaki's disease at 6 months of age and received an appropriate therapy with intravenous immunoglobulin and aspirin. Throughout his life, he had no cardiac symptoms except for one episode of syncope at 8 years of age while standing in the hot sun, which was attributed to dehydration. However, he did not perform any significant vigorous physical activities as an adolescent. He had a progressive increase in his body mass index (BMI) throughout his life. A chronologic history/evaluation is shown in Table 1.

Table 1. Patient history.

Age	Modality	LMCA Z-score	LAD Z-score	Circumflex	RCA Z-score	Other findings	BMI
6.5M	Echo	+3.5	+5.0	NWV	+6.5		20.0
6.6M	Echo	> +10	> +10	Giant	> +10		20.0
6.6M	Begun on Enoxaparin/aspirin						20.0
1.2Y	Cath	+6.6	+12.1	Giant	+12.2	-No stenosis	19.0
4.9Y	Echo	+5.0	+2.1	Normal	+4.5	-Possible proximal LAD stenosis	18.9
5.1Y	Cath	+1.6	+2.9	Normal	+4.4	-Probable mild stenosis distal to LAD aneurysm -Mild distal RCA stenosis	18.3
6.6Y	MRI	+2.6	NWV		+3.4	-Mild mid RCA narrowing (not felt to be significant)	22.3
6.7Y	Echo	+2.6	−0.3	NWV	+3.6		22.3
6.7Y	With no significant narrowing on MRI/no giant aneurysms placed on aspirin only						22.3
7.2–11.1Y	Echo × 4	+0.4–+3.3	−0.2–+3.1	NWV	+0.9–+2.7		23.0–31.0
11.6Y	Stress test	Normal					34.7
12.4Y	Echo	+1.3	−0.6	NWV	−0.8		34.8
12.9Y	Stress MRI	Normal left ventricular size/function, normal regadenoson stress perfusion with no fixed or reversible ischemia, normal delayed enhancement imaging with no evidence of myocardial ischemia, fibrosis, or infiltrative disease.					34.8
13.3Y	Echo	+2.3	NWV	NVW	+2.3		36.8
		Left ventricular diastolic dimension 56.1 mm, left ventricular systolic dimension 32.4 mm (fractional shortening 42%). Modified Simpsons ejection fraction 68%. MV E/A ratio 2.37, TDI Medial E/e' 8.39, TDI Lateral E/e' 5.99. Strain analysis not performed.					

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Age	Modality	LMCA Z-score	LAD Z-score	Circumflex	RCA Z-score	Other findings	BMI
14.3Y	CT	Focal CAC of distal LMCA prior to bifurcation (Figure 1A), severe branching CAC from the distal LMCA to the LAD and Circ (Figure 1B). The RCA demonstrated ectasia at its origin with focal CAC that corresponded to the saccular aneurysms noted on previous cardiac catheterizations (Figure 2). No evidence of collateral development. The study was performed primarily for angiographic assessment utilizing contrast enhancement and a CAC score was not able to be calculated.					
14.3y	Cath	80% distal LMCA stenosis continuing into the proximal LAD and Circ (90% stenosis of each), the LAD stenosis continues proximal to the first diagonal with an aneurysm of the proximal first diagonal (Figure 3A). 90% stenosis of the Circ is seen in Figure 3B, the stenotic LAD is again demonstrated. A 90% stenosis of the proximal RCA adjacent to the origin of the acute marginal (Figure 4). No evidence of collateral development.					
14.3	Exam	Blood pressure 123/67 mmHg. Normal S1 and S2, no S3 or S4, no clicks/rubs, 2/6 low-frequency, vibratory murmur at left lower sternal border (diminished with Valsalva maneuver and moving from supine to sitting). Diastole quiet. No brachial-femoral delay.					40.2
14.9Y	Surgery	4 vessel bypass grafting. Unremarkable post-operative course					

Note: (1) All studies showed a normal biventricular size and function with no evidence of a wall motion abnormality. All electrocardiograms were normal. (2) He was evaluated for syncope at 8.3 years without cardiac symptoms when he was out in the sun, which was attributed to dehydration. There was no other history of signs or symptoms referable to the cardiovascular system. The patient did not perform any significant vigorous physical activities. Legend: LMCA: Left main coronary artery; LAD: Left anterior descending coronary artery; Circ: circumflex coronary artery; RCA: Right coronary artery; BMI: Body mass index; M: Months; Y: Years; Echo: echocardiogram; Cath: Cardiac catheterization; CT: Computed tomography; CAC: Coronary artery calcium; MRI: Magnetic resonance imaging; NVW: Not well visualized; Exam: Physical examination.

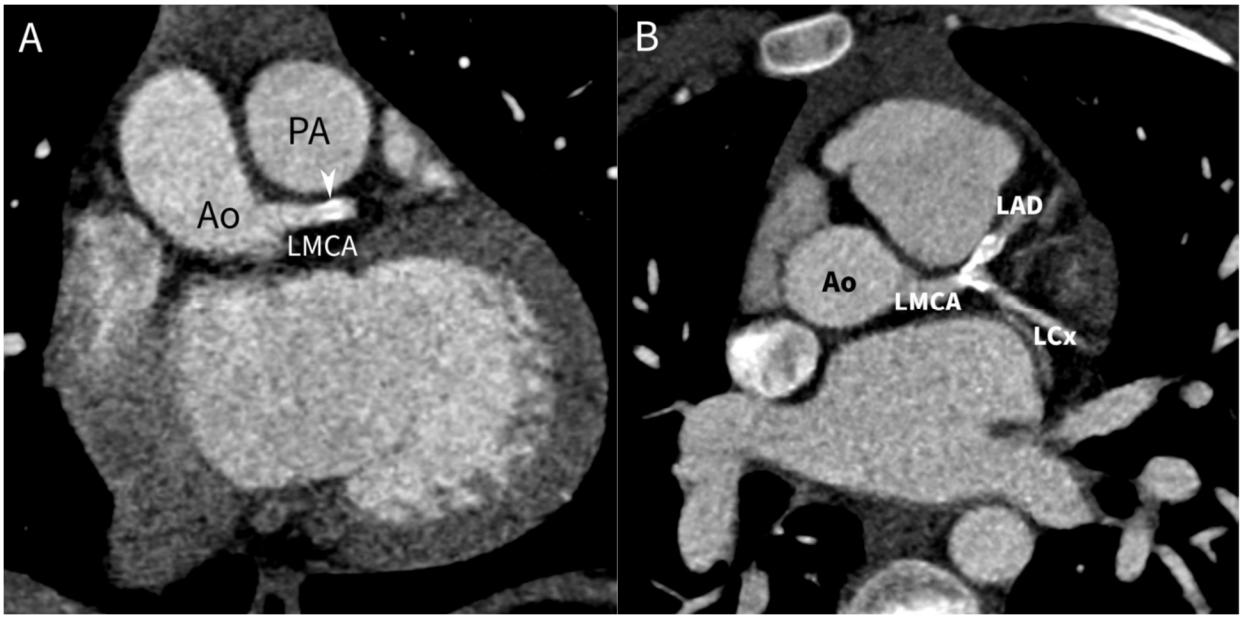

Figure 1. A: Coronal oblique view through root of the aorta (Ao) showing the origin of the left main coronary artery (LMCA) from the left sinus of Valsalva. A focal CAC is seen in the distal aspect of the LMCA prior to its bifurcation alongside a partially seen pulmonary artery (PA). B: Axial oblique view through the root of the aorta (Ao), showing severe branching CAC extending from the distal left main coronary artery (LMCA) to the left anterior descending artery (LAD) and the left circumflex artery (LCx).

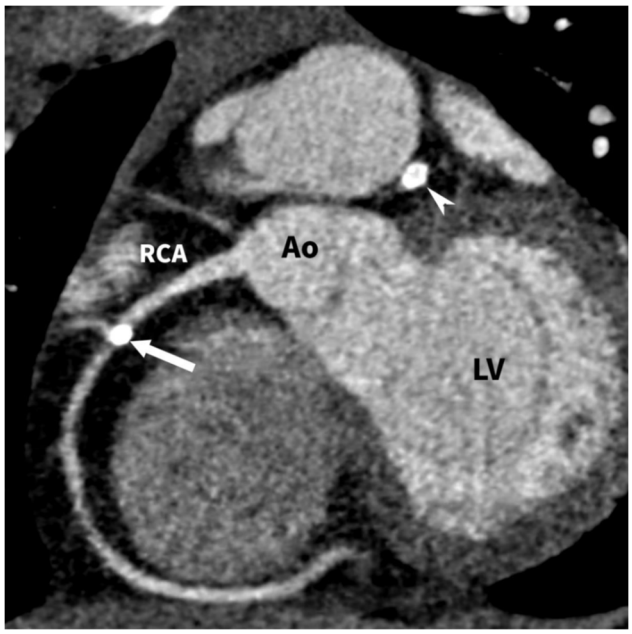

Figure 2. Coronal oblique view through the left ventricle (LV) and aortic root (Ao) shows the right coronary artery (RCA) originating from the right sinus of Valsalva and a normal course through the right atrioventricular groove. Mild ectasia is noted at the origin. A focal CAC corresponding to the location of a prior saccular aneurysm is indicated by the arrow. Additionally, we note the partially seen CAC of the left coronary artery, which is depicted in detail in Figure 1.

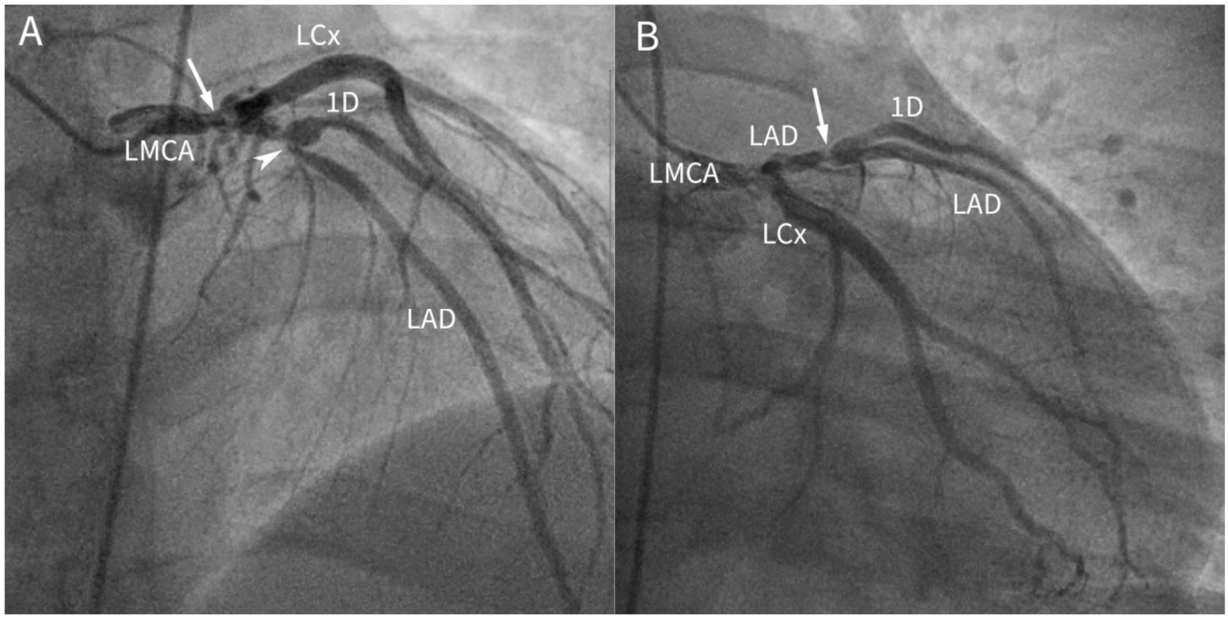

Figure 3. A: Cardiac catheterization showing the left main coronary artery (LMCA), the left circumflex coronary artery (LCx), the left anterior descending coronary artery (LAD), and the first diagonal branch (1D). The arrow points to the stenosis of the LMCA leading to a complex bifurcation. An aneurysm (arrowhead) is seen at the origin of the first diagonal branch adjacent to a focal area with a significant stenosis of the left anterior descending coronary artery (LAD). B: Cardiac catheterization showing the left main coronary artery (LMCA), the left anterior descending coronary artery (LAD), and the left circumflex coronary artery (LCx). The arrow points to a high-grade stenosis of the proximal LAD adjacent to the takeoff of the first diagonal branch (1D).

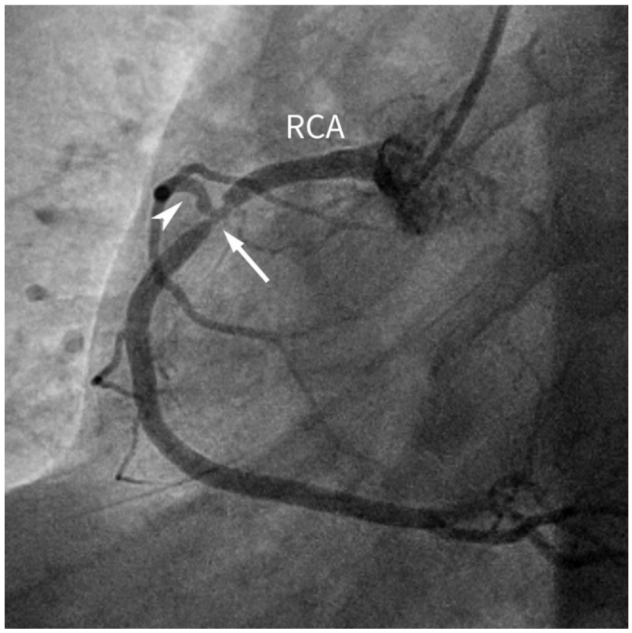

Figure 4. Cardiac catheterization showing the right coronary artery (RCA). A high-grade stenosis (arrow) is seen adjacent to the origin of the acute marginal branch (arrowhead).

3. Discussion and conclusions

KD is considered a "rare" disease, and the etiology remains speculative. Coronary abnormalities are the primary long-term complications, and echocardiography is considered the gold standard for a routine evaluation in the pediatric population. This case describes an adolescent KD patient with a normal stress MRI, and whose severe multivessel coronary narrowing was diagnosed after a cardiac CT identified CAC. While a cardiac CT is not recommended in the acute phase, it can be useful for the evaluation of distal coronary artery aneurysms, which are not well visualized echocardiographically [5]. The best long term follow-up approach remains under debate.

In any patient with concerns for coronary narrowing, some form of functional assessment is necessary. Per the 2017 American Heart Association Diagnosis, Treatment and Long-Term Management of Kawasaki Disease Guidelines, for giant aneurysms that regressed to small aneurysms, it is reasonable to assess for inducible myocardial ischemia every 1–2 years (Class IIa, level of evidence B) [1]. However, pediatric patients are not typically able to fully participate in stress testing until around 10 years of age. Additionally, radionuclide stress imaging in pediatric institutions is typically not available. Additionally, radionuclide stress imaging would expose pediatric patients to repetitive radiation-based procedures throughout their lifetimes. A stress MRI is a relatively new modality in pediatrics with increasing availability that does not require radiation. A stress MRI in adults is felt to "accurately assess myocardial ischemia, myocardial viability, and cardiac function without exposure to ionizing radiation" [6], and can repetitively assess a patient for regional wall abnormalities and myocardial perfusion without radiation. Therefore, this patient underwent a stress MRI for a functional assessment, which was normal. A stress MRI is limited by its inability to be combined with exercise and several patient related factors: claustrophobia, obesity, the possible need for sedation, and any patient with a ferromagnetic device may not be an ideal candidate [6]. Additionally, a stress MRI is a relatively new modality and professional experience with its interpretation may be limited (particularly in pediatric institutions). A possible explanation for the normal results of the stress MRI could be a balanced myocardial ischemia, which is a condition where the blood flow is equally reduced to the myocardium during stress. Additionally, there was a 16-month interval between the stress MRI and the cardiac CT, which could have been a progressive coronary artery stenosis. Myocardial scintigraphy could be used to further map the myocardial blood flow. However, myocardial scintigraphy and other cardiac radionuclide-based testing are not available in most pediatric institutions and were not able to be performed.

Moreover, patients with coronary narrowing require some form of anatomic/angiographic assessment. Per the 2017 American Heart Association Diagnosis, Treatment and Long-Term Management of Kawasaki Disease Guidelines, further imaging with angiography (i.e., CT, MRI, invasive) may be considered for periodic surveillance every 2–5 years (Class IIb, level of evidence C) [1]. In order to reduce frequent invasive cardiac catheterizations, a contrast enhanced CT is often the modality of choice, which this patient subsequently underwent. This revealed multiple areas of severe CAC. Since the degree of stenosis cannot be seen within a severe calcification, the patient underwent cardiac catheterization, which revealed his severe 4 vessel disease.

CAC is a feature that may increase the long-term risk of myocardial ischemia in KD patients [1]. The exact etiology of CAC remains unknown. Yokouchi (2022) histologically studied 24 KD patients with coronary aneurysms who died within 3 years of their diagnosis [7]. The autopsies revealed 14 out of the 24 patients had CAC. This was seen in the organized portion of the thrombus (n = 12) and in the

thickened tunica of the intima (n = 3). It was noted that as the duration after diagnosis of KD increased, the calcified lesion increased in size. Additionally, the calcified area tended to increase as the diameter of the aneurysm increased. It was concluded that coronary artery aneurysm calcification starts early in the remote phase of KD, and it is closely related to the organization of the thrombi.

Ino (1990) studied 116 KD patients by angiography (average ~7.2 years after diagnosis), where 9.1% of those with an angiographic coronary abnormality demonstrated CAC [8]. Chakraborty (2020) evaluated 21 KD patients >10 years after an initial diagnosis via a cardiac CT [9]. None of the patients with initially normal coronaries demonstrated any abnormality. However, 2 out of the 4 patients with initial echocardiographic coronary abnormalities had persistent CT abnormalities and 1 had CAC (25% of those with an initial abnormality and 5% of total). It was speculated that CAC was likely to be dystrophic rather than atherosclerotic. Kahn (2017) reviewed 166 patients with a history of KD (median interval from KD to CT 15.1 years) [10]. Coronary arteries classified as either normal, persistently dilated, or with a remodeled aneurysm had no CACs. 19 out of the 24 patients (79%) with coronary aneurysms had CAC (median volume 542 mm^3). For subjects imaged ≥9 years after their acute KD (n = 144), the presence of CAC had a sensitivity of 95% and a specificity of 100% for detecting coronary artery abnormalities (defined as coronary artery aneurysm and/or stenosis). They concluded that CAC scanning may be a useful tool to screen patients with either a remote history of KD or suspected KD and unknown coronary artery status [10].

Additionally, there is data correlating the initial size of a coronary artery aneurysm with the development of a stenotic lesion. Tsuda (2018) showed the cutoff points of the coronary artery diameter within the first 100 days after the onset of KD, which led to a stenotic lesion in the late period, with a diameter of ≥6.1 mm (BSA of <0.50 m^2) and ≥8.0 mm (BSA of ≥0.50 m^2) [11]. Those cutoff points would have corresponded with a Z-score of at least +10.0 on 2-dimensional echocardiography. A similar study by Tsujii (2017) in 65 patient (median interval from diagnosis to cardiac CT 16 years) had similar results and concluded that an acute coronary dilation that exceeds ~5 mm can lead to late abnormalities of the coronary wall and that CAC increases with age [12]. Kaichi (2008) demonstrated that the coronary arterial diameters of all branches that eventually calcified in 79 KD patients were 6 mm or greater. The incidence of CAC in branches measuring 6 mm or greater on the initial coronary angiogram were 12% at 5 years, 44% at 10 years, and 94% at 20 years (n = 141) [3].

Nikolaou (2011) described a CT as indicated for CAC scoring (or coronary vessel wall imaging in general), MRI for stress, cine MRI, stress perfusion MRI, and both CT and MRI for non-invasive coronary angiography and myocardial viability imaging [13]. Similarly, Dietz (2015) described CAC as being easily identified by a cardiac CT and a cardiac MRI as the most useful methods for functional imaging [14]. This was supported by Stijn (2021), who compared 54 KD patients who underwent both a cardiac CT and a cardiac MRI, and concluded the CT was more sensitive than the MRI for the diagnosis of coronary artery aneurysms [15]. There are numerous modalities to assess CAC. However, CAC cannot be detected by a cardiac MRA, because the signal for calcium drops and a coronary artery stenosis with calcification is seen as a coronary narrowing with signal drop [16]. Angiography is felt to have a high detection specificity for CAC, but with moderate to low detection sensitivity [17]; moreover, it is invasive. A cardiac CT is felt to have both a high specificity and sensitivity for CAC detection and is noninvasive [17]. This makes it a common choice to evaluate CAC. Both modalities involve radiation exposure. Although there is no role for CAC scoring in the acute phase of KD, some studies suggest that CAC can be used to screen those with a questionable history of KD with an unknown coronary involvement [10]. For long term KD, a follow-up cardiac CT is a technique that

can identify CAC without the need of an intravenous contrast [18]. While the 2017 American Heart Association Diagnosis, Treatment and Long-Term Management of Kawasaki Disease Guidelines do not have specific recommendations for CAC scoring, they do state "low-dose, non-contrast CT calcium scoring also has been demonstrated to be useful in KD patients to guide selection for further evaluation with coronary angiography." [1].

In this case, the patient had two normal stress tests (one routine and one cardiac stress MRI). He was asymptomatic, and the degree of his coronary pathology was diagnosed only after the cardiac CT revealed the CAC. This study highlights the need to evaluate all chronic KD patients with a history of giant coronary aneurysms with a combination of some form of functional testing and anatomic testing (i.e., a cardiac CT that will not only to assess coronary anatomy, but is also able to assess for a CAC). Additionally, there is data to suggest a cardiac CT is a useful screening tool in patients with suspected remote KD and an unknown coronary artery status [10].

Author contributions

All authors participated to varied degrees in the prepartion of this manuscript and consented to the published version of the manuscript.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Ethics approval of research and informed consent

This case report was approved by the Phoenix Childrens IRB: # IRB-24-184. The Phoenix Children's IRB does not require patient's parents' consent for a case report.

Conflict of interest

The authors declare no conflict of interest.

References

1. McCrindle BW, Rowley AH, Newburger JW, et al. (2017) Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation* 135: e927–e999. https://doi.org/10.1161/CIR.0000000000000484
2. Butt W (2020) Kawasaki disease: complex long-term issues for pediatric and adult cardiologists. *Can J Cardiol* 36: 1566–1568. https://doi.org/10.1016/j.cjca.2020.04.043
3. Kaichi S, Tsuda E, Fujita H, et al. (2008) Acute coronary artery dilation due to Kawasaki disease and subsequent late calcification as detected by electron beam computed tomography. *Pediatr Cardiol* 29: 568–573. https://doi.org/10.1007/s00246-007-9144-5

4. Lapierre C, Bitsch A, Guérin R, et al. (2010) Follow-up chest X-ray in patients with Kawasaki disease: the significance and clinical application of coronary artery macro-calcification. *Pediatr Cardiol* 31: 56–61. https://doi.org/10.1007/s00246-009-9548-5
5. Singhal M, Pilania RK, Jindal AK, et al. (2023) Distal coronary artery abnormalities in Kawasaki disease: experience on CT coronary angiography in 176 children. *Rheumatology* 62: 815–823. https://doi.org/10.1093/rheumatology/keac217
6. Patel AR, Salerno M, Kwong RY, et al. (2021) Stress cardiac magnetic resonance myocardial perfusion imaging: JACC review topic of the week. *J Am Coll Cardiol* 78: 1655–1668. https://doi.org/10.1016/j.jacc.2021.08.022
7. Yokouchi Y, Oharaseki T, Asakawa N, et al. (2022) Histological studies shed new light on the initiation and characteristics of calcification of coronary artery aneurysms in Kawasaki disease. *Cardiovasc Pathol* 61: 107456. https://doi.org/10.1016/j.carpath.2022.107456
8. Ino T, Shimazaki S, Akimoto K, et al. (1990) Coronary artery calcification in Kawasaki disease. *Pediatr Radiol* 20: 520–523. https://doi.org/10.1007/BF02011380
9. Chakraborty R, Singhal M, Pandiarajan V, et al. (2021) Coronary arterial abnormalities detected in children over 10 years following initial Kawasaki disease using cardiac computed tomography. *Cardiol Young* 31: 998–1002. https://doi.org/10.1017/S1047951121000020
10. Kahn AM, Budoff MJ, Daniels LB, et al. (2017) Usefulness of calcium scoring as a screening examination in patients with a history of Kawasaki disease. *Am J Cardiol* 119: 967–971. https://doi.org/10.1016/j.amjcard.2016.11.055
11. Tsuda E, Tsujii N, Hayama Y (2018) Stenotic lesions and the maximum diameter of coronary artery aneurysms in Kawasaki disease. *J Pediatr* 194: 165–170.e2. https://doi.org/10.1016/j.jpeds.2017.09.077
12. Tsujii N, Tsuda E, Kanzaki S, et al. (2017) Late wall thickening and calcification in patients after Kawasaki disease. *J Pediatr* 181: 167–171.e2. https://doi.org/10.1016/j.jpeds.2016.10.026
13. Nikolaou K, Alkadhi H, Bamberg F, et al. (2011) MRI and CT in the diagnosis of coronary artery disease: indications and applications. *Insights Imaging* 2: 9–24. https://doi.org/10.1007/s13244-010-0049-0
14. Dietz SM, Tacke CE, Kuipers IM, et al. (2015) Cardiovascular imaging in children and adults following Kawasaki disease. *Insights Imaging* 6: 697–705. https://doi.org/10.1007/s13244-015-0422-0
15. van Stijn D, Planken N, Kuipers I, et al. (2021) CT angiography or cardiac MRI for detection of coronary artery aneurysms in Kawasaki disease. *Front Pediatr* 9: 630462. https://doi.org/10.3389/fped.2021.630462
16. Tsuda E, Singhal M (2018) Role of imaging studies in Kawasaki disease. *Int J Rheum Dis* 21: 56–63. https://doi.org/10.1111/1756-185X.13210
17. Andrews J, Psaltis PJ, Di Bartolo BA, et al. (2018) Coronary arterial calcification: a review of mechanisms, promoters and imaging. *Trends Cardiovasc Med* 28: 491–501. https://doi.org/10.1016/j.tcm.2018.04.007

18. Kahn AM, Budoff MJ, Daniels LB, et al. (2012) Calcium scoring in patients with a history of Kawasaki disease. *JACC Cardiovasc Imaging* 5: 264–272. https://doi.org/10.1016/j.jcmg.2011.12.010