




Importance of blood pressure control in Kawasaki disease with expanded multiple giant coronary aneurysms with a 32 mm maximum diameter: a case report

Yuji Moritoh ^{1*}, Masahiro Kamada ¹, Shinsaku Matsumoto², and Koji Kido ²

¹Department of Pediatric Cardiology, Hiroshima Citizens Hospital, 7-33 Moto-machi, Hiroshima 730-8518, Japan; ²Department of Anesthesiology, Hiroshima Citizens Hospital, 7-33 Moto-machi, Hiroshima 730-8518, Japan

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Background

Ruptured coronary artery aneurysm is rare, but the most serious complications of an acute phase of Kawasaki disease (KD) with giant coronary artery aneurysm (GCAA). Progressive or super GCAA, which rapidly dilates and continue to increase over a diameter of 10 mm, are more susceptible to rupture.

Case summary

We report the case of a 6-year-old boy with KD who had multiple super GCAAs with a high risk of GCAA rupture. On admission to our hospital, he presented with fever, chest pain, and Stage II hypertension. Echocardiographic Z-scores adjusted for body surface area were used for measurements. The coronary artery diameter of segment 1 was 24.3 mm with a Z-score of 20.8; the diameter of segment 3 was 24.4 mm; the diameter of the left anterior descending branch was 32.6 mm with a Z-score of 20.1. The super GCAAs showed a tendency to expand compared to the latest echocardiography, and thrombus formation was observed in the super GCAA of segment 3. The patient was treated with anti-inflammatory therapy, antithrombotic therapy, and antihypertensive therapy with continuous arterial pressure monitoring with the goal of not exceeding the 5th percentile of the normal standard during the period when there was a risk of progressive coronary aneurysm expansion. He was discharged without any neurological complications.

Discussion

We speculated that the patient's hypertension was the cause of an expanding coronary artery aneurysm. In conclusion, KD patients with super GCAA may benefit from aggressive blood pressure control with continuous arterial pressure monitoring.

Keywords

Kawasaki disease • Coronary artery aneurysm • Blood pressure • Plasma exchange • Case report

* Corresponding author. Tel: +81 822 21 2291, Email: yuji6103031945@gmail.com

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Learning points

- In Kawasaki disease (KD), super giant coronary artery aneurysms (GCAAs), which rapidly dilate and can exceed 10 mm in diameter, carry a high risk of rupture.
- Strict control of blood pressure with continuous monitoring of arterial pressure under general anaesthesia can be useful in KD patients with super GCAA.

Introduction

Kawasaki disease (KD) is an acute systemic vasculitis of childhood that leads to coronary artery aneurysms (CAAs). In KD, the complication rate of giant CAAs (GCAAs)—those with a diameter >8 mm or Z-score of 10—is only 0.13%.^{1–3} However, the rupture risk is reportedly high in KD patients with a progressively expanding GCAA of at least 10 mm in diameter, which can be termed a ‘super GCAA’.^{4,5}

Here we report on the case of a boy with refractory KD and present the importance of managed treatment, especially with regard to blood pressure (BP) control. This is the first case of a paediatric patient in acute phase of KD with multiple GCAAs over 20 mm and left anterior descending branch (LAD) with a 32 mm maximum diameter who survived without neurological sequelae.

Timeline

Case presentation

A 6-year-old Japanese boy with history of autism spectrum disorder was admitted to a referral hospital on Day 4 of fever with conjunctival hyperaemia, redness of the lips, enlarged cervical lymph nodes, swollen hands and feet, and a polymorphous rash. Kawasaki disease was diagnosed, and high-dose intravenous immunoglobulin (IVIG; 4 g/kg total) administered. After 4 days, the serum C-reactive protein (CRP) level had increased to 22.0 mg/dL. Intravenous methylprednisolone (30 mg/kg) was therefore administered for 3 days, followed by oral prednisolone treatment. On Day 13 of the illness, echocardiography revealed dilatation of the right coronary artery (RCA) and LAD, respectively. Oral administration of warfarin was therefore initiated. On Day 38, echocardiography showed severe dilation of the maximum diameters of the RCA and LAD CAAs of 21.6 and 30.4 mm, respectively. On Day 41, he was admitted to our tertiary hospital with chest pain.

On admission, his temperature was 38.4°C, pulse 120 beats/min, and BP 128/75 mmHg. His heart rhythm was regular, with a systolic murmur of Levine II/VI due to mitral regurgitation. Serum CRP (2.1 mg/dL) and troponin T (0.18 ng/mL) values were elevated, with transient mild ST depression in the lateral leads ([Supplementary material online, Figure S1](#)). Echocardiography showed multiple GCAAs, particularly with marked RCA dilation, and the LAD appeared to be expanding. Furthermore, thrombus formation was observed in the super GCAA in segment 3 of the peripheral RCA, with the super GCAA in segment 6 of the LAD exerting slight pressure on the left ventricle (LV) ([Figure 1, Video 1–2](#)).⁶

Owing to the high risk of CAA rupture, the patient was immediately transferred to the intensive care unit (ICU) for endotracheal

Day 4 from fever onset	A typical Kawasaki disease (KD) case was diagnosed, and high-dose intravenous immunoglobulin was administered
Day 8–10	Intravenous methylprednisolone was administered
Day 11	Prednisolone was started and continued until the Day 41
Day 13	Echocardiography showed dilatation of up to 8.5 and 7.3 mm in the right coronary artery (RCA) and left anterior descending branch (LAD), respectively; therefore, oral administration of warfarin was started
Day 38	Serum C-reactive protein positivity persisted and echocardiography showed severe dilation of the maximum diameters of the RCA and LAD giant coronary artery aneurysms (GCAA) of 21.6 and 30.4 mm, respectively
Day 41	<ul style="list-style-type: none"> • The patient was admitted to our tertiary hospital due to chest pain • Echocardiography showed multiple super GCAAs and thrombus formation was observed in the super GCAA • The patient was treated with anti-inflammatory therapy, antithrombotic therapy, and aggressive antihypertensive therapy
Day 49	Echocardiography showed that the progressive expansion of the GCAAs had ceased, and the thrombus had almost disappeared
Day 67	Echocardiography showed a thrombus formation again in the GCAA
Day 91	<ul style="list-style-type: none"> • Echocardiography confirmed that the thrombus had disappeared • The patient was discharged without neurological sequelae
One year after the onset of KD	The patient is doing well as an outpatient

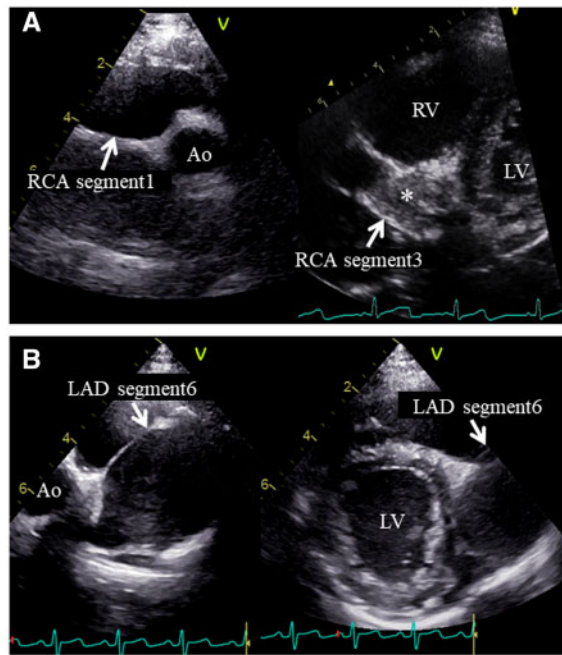


Figure 1 (A) Parasternal short-axis view (left) and modified apical four-chamber view (right) echocardiography upon admission to our hospital shows that the right coronary artery segments 1 and 3 maximum diameter (Z-score for body surface area) of the coronary arteries is 24.3 mm (+20.8) and 24.4 mm, respectively, and a thrombus (*) is found in the giant coronary artery aneurysm of the right coronary artery segment 3. (B) Parasternal short-axis view echocardiography at admission shows that the left anterior descending branch segment 6 maximum diameter (Z-score for body surface area) of the coronary arteries is 32.6 mm (+20.1) and the prominently dilated left anterior descending branch aneurysm mildly compresses the left ventricle from the left upper side during diastole. Ao, aorta; LAD, left anterior descending branch; LV, left ventricle; RCA, right coronary artery; RV, right ventricle.

intubation and general anaesthesia. Various antihypertensive agents, including nicardipine hydrochloride, carperitide, and sodium nitroprusside hydrate, were administered to ensure strict BP control, that is, a systolic BP ≤ 80 mmHg under continuous arterial BP monitoring. Continuous heparin infusion was administered as antithrombotic therapy, and plasma exchange performed for 6 days as an anti-inflammatory therapy. After plasma exchange, infliximab (5 mg/kg) and additional IVIG (6 g/kg total) were administered. Echocardiography on Day 49 confirmed that the thrombus in the GCAA of the RCA had almost completely disappeared. The CAA failed to expand under strict BP control and plasma exchange; thus, the sedative was gradually discontinued, and the antihypertensive drug switched to an oral formulation. The patient was discharged from the ICU on hospital day 23 (Figure 2). Thereafter, he continued receiving continuous heparin infusion and a combination of oral aspirin (from Day 4, 5 mg/kg/day), warfarin (from Day 59, 0.15–0.25 mg/kg/day), and clopidogrel (from Day 64, 1 mg/kg/day) to prevent GCAA thrombus formation, as his prothrombin time and international normalized ratio (PT/INR)

had not reached the target of 2.5–3.0 s. However, echocardiography on Day 67 showed GCAA thrombus formation in segment 3 of the RCA. When intravenous alteplase (0.75 mg/kg) was administered and the warfarin dose increased to achieve a PT/INR of 3.0–3.5 s, the thrombus gradually shrank and disappeared (Figure 3). The patient was discharged on Day 91. Cardiac computed tomography (CT) and cardiac magnetic resonance imaging (CMR) performed 4 months after illness onset showed no change in CAA size (Figure 4), no thrombus formation in segment 3 of the RCA, and well-preserved cardiac function (Video 3), respectively. However, myocardial perfusion imaging by first-pass contrast-enhanced CMR showed hypoperfusion in the RCA perfusion region of the LV upon adenosine loading. Furthermore, late gadolinium enhancement (LGE) was observed in the same region at rest (Figure 5). One year has passed since the onset of KD, and he is doing well as an outpatient on triple antithrombotic therapy.

Discussion

Kawasaki disease-associated GCAA rupture occurs within the first few months of onset.⁴ Rupture is a life-threatening complication. We examined 14 cases of CAA rupture since 1990, when IVIG treatment was introduced worldwide.⁷ In nine of them for which echocardiographic findings were described, the maximum CAA diameter was 10–19 mm in six, maximum RCA diameter was 20 mm in one, and maximum RCA diameter was 30 mm in one (Supplementary material online, Table S1). Twelve patients died (86%). The neurological prognosis of the survivors was not specified.^{4,8} Including unruptured cases, there are no reports of paediatric patients in the acute phase of KD with multiple GCCAs over 20 mm or a LAD with a 32 mm maximum diameter.

Hypertension reportedly increases the risk of various cardiovascular lesions in adults.⁹ However, few reports have examined the relationship between BP and the acute phase of KD when the coronary artery may expand. In KD patients with CAA, the internal elastic lamina of the coronary artery wall, an important component of arterial architecture, becomes dissociated and is destroyed.¹⁰ We speculate that these patients are more vulnerable to elevated BP. Our patient had multiple super GCCAs and Stage II hypertension (>99th percentile of normal), probably due to the steroids.¹¹ He was subjected to actively administered antihypertensive therapy to prevent CAA expansion and rupture.

There are no specific guidelines for BP control in patients with KD. The 2017 American College of Cardiology/American Heart Association/etc. hypertension management guidelines do not consider diastolic BP in determining cardiovascular risk.⁹ We therefore placed emphasis on the systolic BP—which exerts the highest pressure on the coronary wall—in achieving BP control. Blood pressure was controlled not to exceed the normal systolic BP—the 5th percentile of normal—when there was a risk of progressive CAA expansion.¹² Although the urine volume decreased with decreased BP, it was managed by temporary haemodialysis.

Antithrombotic therapy is also essential for patients with super GCCAs (Supplementary material online, Table S2).^{1,13} Cardiac CT in our case showed a highly dilated RCA and LAD with severely diminished peripheral coronary blood flow. Thrombus formation was

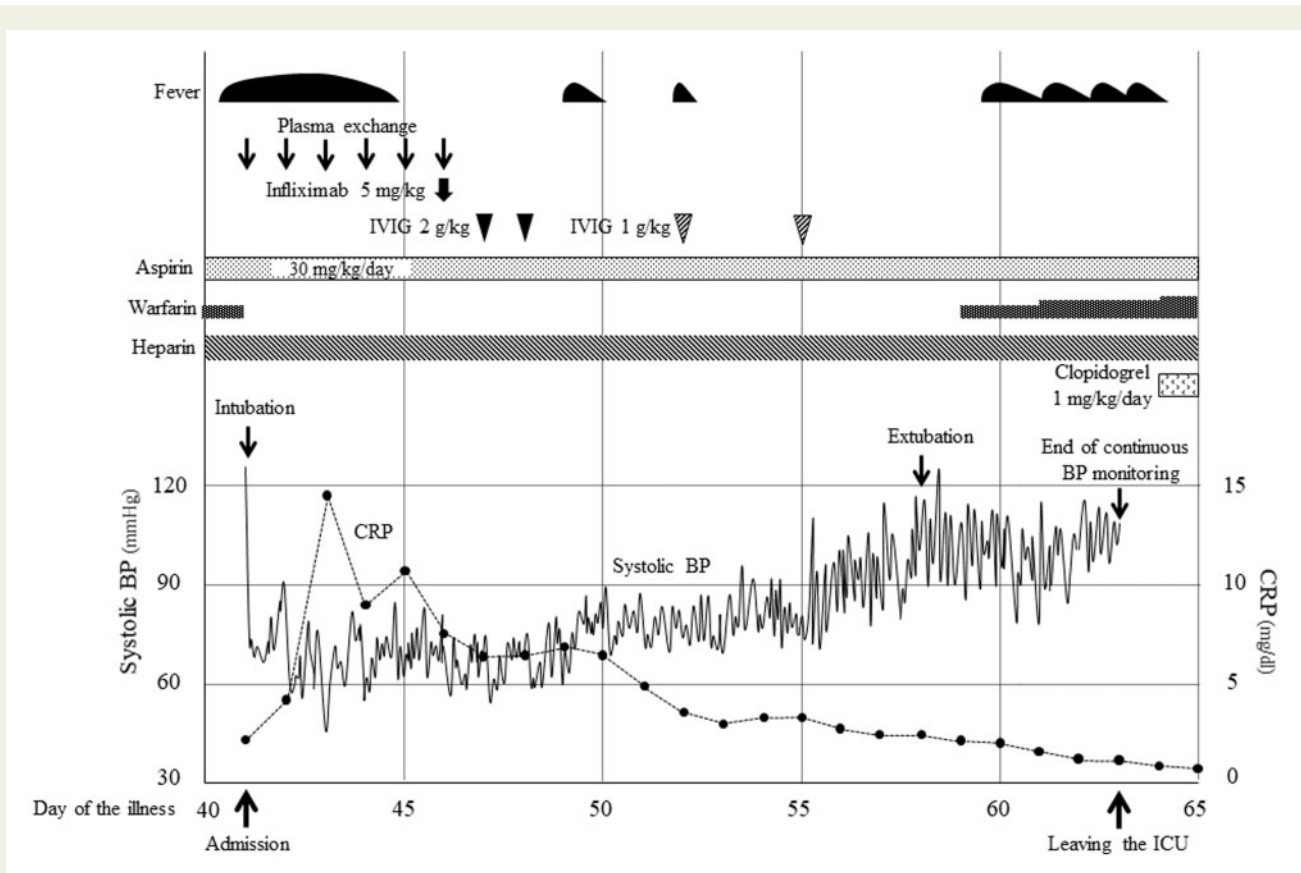


Figure 2 Clinical course. BP, blood pressure; CRP, C-reactive protein; ICU, intensive care unit; IVIG, intravenous immunoglobulin.

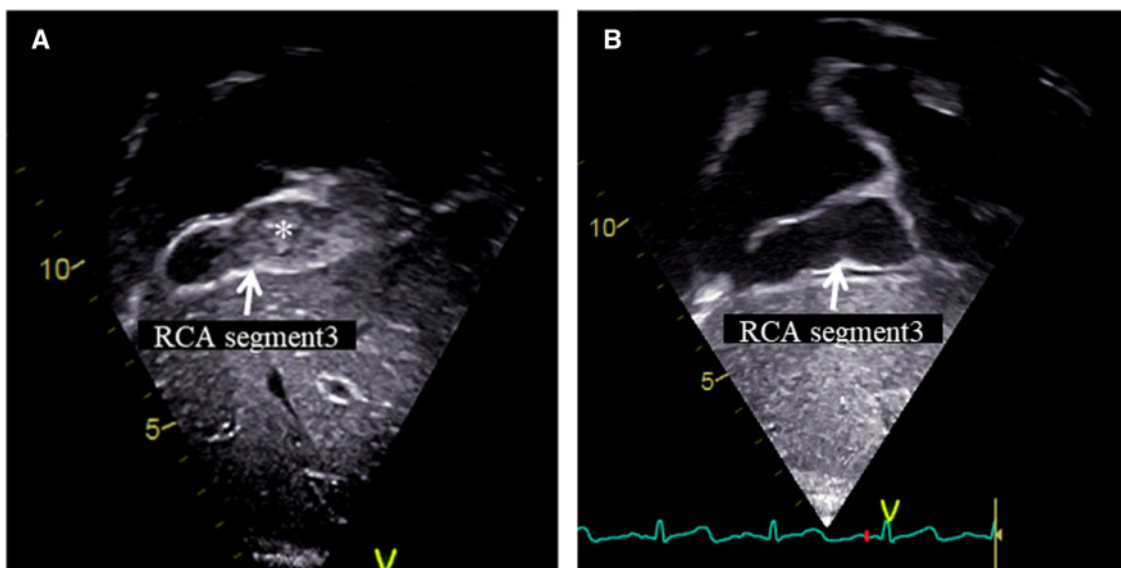


Figure 3 (A) On the 67th day of the illness, subcostal view echocardiography shows a thrombus (*) in the giant coronary artery aneurysm of the right coronary artery segment 3. (B) Echocardiography at discharge shows the disappearance of the thrombus in the giant coronary artery aneurysm of the right coronary artery segment 3. RCA, right coronary artery.

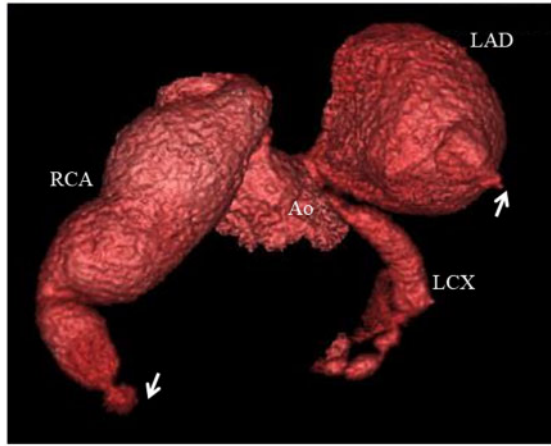
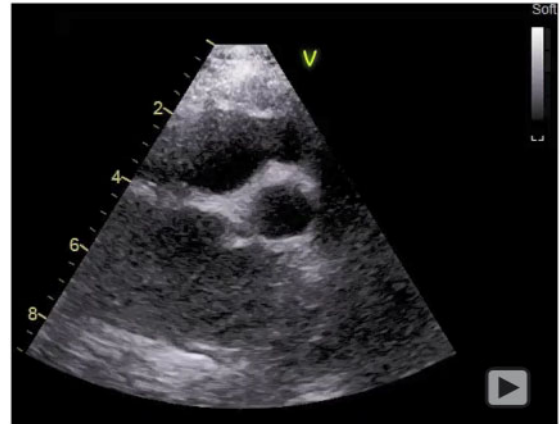


Figure 4 Three-dimensional cardiac computed tomography image 4 months after onset. Image showing marked enlargement of the right coronary artery and left anterior descending branch and no visualization of the segment 3 and segment 7 by contrast media (arrows). Ao, aorta; LAD, left anterior descending branch; LCX, left circumflex; RCA, right coronary artery.

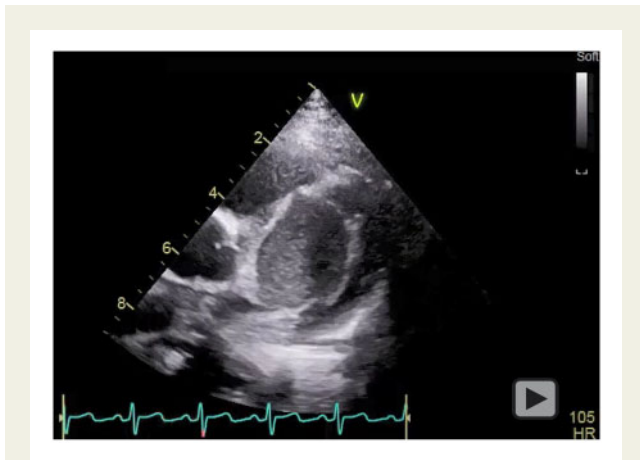
observed again in the peripheral RCA, necessitating further warfarin dose adjustment. In addition, the CMR findings suggested ischaemia and fibrosis in the RCA perfusion region of the LV. Although LGE is



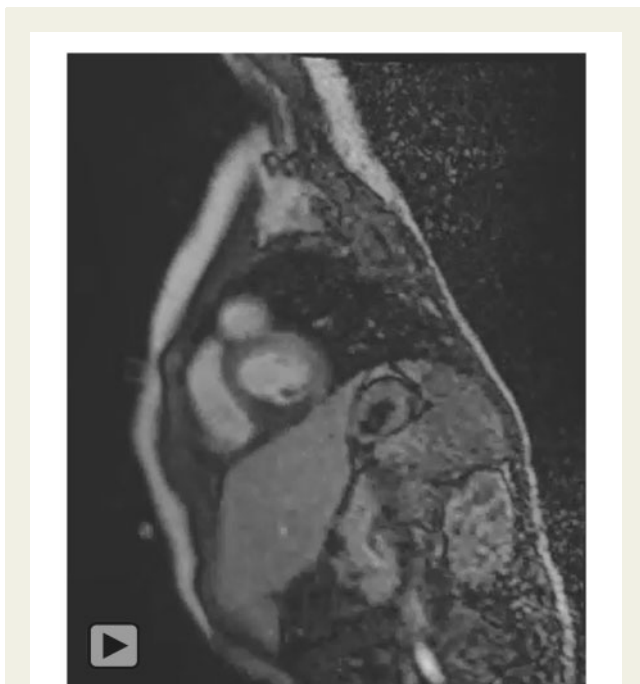
Video 1 Right coronary artery segments 1.



Figure 5 (A) Myocardial perfusion imaging by first-pass contrast-enhanced cardiac magnetic resonance imaging at 4 months after onset. It shows subendocardial hypoperfusion from the ventricular septum to the inferior wall region of the left ventricle when a coronary artery vasodilator, adenosine, was loaded. (B) Late gadolinium enhancement cardiac magnetic resonance imaging at 4 months after onset is observed from the ventricular septum to the inferior wall region of the left ventricle (*) at rest.



Video 2 Left anterior descending branch segment 6.



Video 3 Cine steady-state free precession cardiac magnetic resonance imaging.

rare in patients with KD, it is reportedly associated with long-term LV dysfunction.¹⁴ Fortunately, in our case, the acute phase of KD was concluded without neurological sequelae. Nevertheless, since the risk level is classified as 5.1 in the American Heart Association 2017 statement, a high risk of cardiovascular events exists and careful follow-up, with focus on oral medications and exercise restriction is required.¹

Conclusion

Strict BP control with continuous arterial pressure monitoring under general anaesthesia could be useful in patients with KD and GCAA at a high risk of CAA rupture.

Lead author biography



Dr Yuji Moritoh is a deputy manager at the Department of Paediatric Cardiology, Hiroshima Citizens Hospital. In 2018, he was a winner of the Excellent Paper Award of Japan Foundation for Pediatric Research.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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