Rupture of a coronary artery aneurysm in Kawasaki disease: A rare case and review of the literature for the past 15 years

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We describe the rare case of a 3-month-old boy who had a ruptured coronary artery aneurysm (CAA) in the right coronary artery (RCA) combined with multiple CAAs in the left circumflex and left anterior descending coronary arteries. We also present a statistical analysis of all the ruptured CAAs previously reported and review the literature of the past 15 years, focusing on the location, etiology, diagnosis, management, and prognosis of giant CAAs.

CLINICAL SUMMARY

A 3-month-old Japanese boy was admitted to a neighborhood hospital with reported fever 2 days in duration and neck pain. He was treated for Kawasaki disease with intravenous immunoglobulin (IVIG; 2 g/kg) on days 5 and 8 of

illness and with prednisolone sodium metazoate (INN prednisolone; 2 mg/kg/d). He was transferred to our hospital for further management. At admission, the patient's abnormal laboratory findings included a white blood cell count of 15,600 cells/mm³, a neutrophil percentage of 71%, a platelet count of 27,000 cells/mm³, an aspartate aminotransferase level of 161 IU/mL, a sodium level of 136 mmol/L, a C-reactive protein level of 11.1 mg/dL, and hypoalbuminemia. Despite the treatment, the RCA aneurysm enlarged progressively, reaching 14.2 mm in maximal diameter by hospital day 23 of the illness, as shown by echocardiography (Figure 1). At 2:00 AM on hospital day 24, the patient suddenly lost consciousness, bradycardia developed, and the radial arterial pulse was not palpable. Despite immediate cardiopulmonary resuscitation, the heart was not beating and did not begin to beat even with open heart massage. After median sternotomy and pericardiotomy, the RCA aneurysm rupture was confirmed. We attempted to suture the ruptured coronary arterial wall, but it was too fragile to suture. The heart did not regain spontaneous contractions, even with extracorporeal membrane oxygenation support for 5 days, and the patient died. Pathologic studies revealed thickened aneurysmal wall with the presence of the inflammatory.

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FIGURE 1. Preoperative echocardiographic images. Images to right demonstrate markedly enlarged vessels (arrows) and pericardial effusion (PE). RCA, Right coronary artery; LV, left ventricle; LA, left atrium; LCA, left circumflex coronary artery; Ao, aorta; Φ, diameter.

TABLE 1. Summary of medical course of the ruptured coronary artery aneurysm

Study	Study design	Age	Sex	Fever onset to presentation (d)	Fever onset to treatment (d)	IVIG (mg/kg)	Steroid	Fever onset to rupture (d)	Surgical procedure	Outcome
Rowley, 1997, US	Case report (autopsy)	10 y	Boy	—	—	2000 for 1 d	—	13	None	Died
	Case report (autopsy)	22 mo	Girl	—	—	None	—	Unknown	None	Died
Koutlas, 1997, US	Case report	3 y	Boy	—	14	2000 for 1 d	—	16	CABG, then PCPS, then transplant (POD 4)	Survived
Suzuki, 1999, Japan	Case report (autopsy)	4 y	Girl	4	6	400 for 5 d	+	22	None	Died
Maresi, 2001, Italy	Case report (autopsy)	2 mo	Boy	—	—	—	—	7	None	Died
Vanlieferinghen, 2002, France	Case report (autopsy)	6 mo	Girl	7	—	—	—	14	None	Died
Donna, 2003, US	Case report (autopsy)	11 mo	Boy	4	—	—	—	16	None	Died
Mok, 2003, China	Case report	5 y	Boy	—	9	400 for 3 d	—	29	Pericardial window at bedside, then emergency CABG with SVG	Survived
Wilson, 2004, New Zealand	Case series (autopsy)	2 mo	Girl	2	3	+ (no details)	—	3	None	Died
Imai, 2006, Japan	Case series (autopsy)	5 y	Boy	2	3	+ (no details)	—	13	None	Died
Miyamoto, 2013, Japan	Case series (autopsy)	3 mo	Boy	2	4	2000 for 2 d	+	24	Pericardial window, repair of ruptured CAA with direct closure.	Died

None of the reports listed cyclosporine use. *IVIG*, Intravenous immunoglobulin; *CABG*, coronary artery bypass grafting; *PCPS*, percutaneous cardiopulmonary support; *POD*, postoperative day; *SVG*, saphenous vein graft; *CAA*, coronary artery aneurysm.

DISCUSSION

Rupture of a coronary aneurysm can occur within the first few months after Kawasaki disease, but it is an exceedingly rare occurrence. As of our last search date (September, 1 2013), a total of 9 other studies incorporating 10 patients have described variations in the ruptured CAA since in 1997 (Tables 1 and 2). Among these, the aneurysms became apparent within 1 to 2 weeks after the onset of fever, rather than the usual course of 2 to 3 weeks. Leukocytosis was found to be typical during the acute stage of Kawasaki disease, with a predominance of immature and mature granulocytes. Approximately 50% of patients had reported white blood cell counts exceeding 10,000 cells/mm³. Acute-phase reactants, such as C-reactive protein, were rapidly elevated within 2 weeks in 3 cases. On the basis of histologic investigation of 37 autopsy cases, Amano and colleagues¹ classified arterial lesions into the following 6 types according to the morphogenesis of arteritis: (1) endothelial degeneration and increased vascular permeability, (2) edema and degeneration of media, (3) necrotizing panarteritis, (4) granulation formation, (5) scar formation, and (6) aneurysm formation. In our case of a ruptured CAA, the wall of the aneurysm showed various changes according to the duration of the disease. Efficacy of IVIG and steroid (prednisolone at 2 mg/kg/d) therapy has been reported in the treatment of severe Kawasaki

disease. Patients should be treated with 2-g/kg IVIG in a single infusion accompanied by aspirin.² This therapy should be started within the first 10 days of illness, as manifested by elevated C-reactive protein. About 20% of patients with Kawasaki disease do not have relief from fever with the initial IVIG plus aspirin therapy³; however, the effects of steroids on coronary artery abnormalities are still unknown. An immunologic study has shown that hypercytokinemia is observed in patients with Kawasaki disease and that cytokines are elevated in the acute phase of Kawasaki disease. It has been reported that inflammatory cytokines are elevated in the acute phase of Kawasaki disease, and IVIG and prednisolone rapidly ameliorate symptoms by reducing cytokine levels. Inflammatory cytokines may mediate endothelial damage and lead to coronary artery abnormalities.^{4,5} According to a previous study, however, some patients who died of ruptured CAA were treated with IVIG and steroids, and most patient had progressive enlarging coronary aneurysms larger than 10 mm in diameter.⁵ We think that patients with enlarged coronary aneurysms should be monitored closely, and optimal surgical timing is within 1 month after the onset of the fever. Especially in cases with giant aneurysm larger than 10 mm in diameter with rapid progressive enlargement, despite intensive care, control of blood pressure, and heart rate with β -blockers or calcium-channel antagonists under general anesthesia, we should

TABLE 2. Summary of laboratory and cardiac findings of the ruptured coronary artery aneurysm

Study	Hb (g/dL)	WBCs ($\times 10^3/\text{mm}^3$)	Platelets ($\times 10^3/\text{mm}^3$)	AST (IU/L)	ALT (IU/L)	CRP (mg/dL)	Echocardiogram	Ruptured position	Pathology
Rowley, 1997, US	—	—	—	—	—	—	—	—	Inflammatory cells present in intima, media, and adventitia of vessels; IgA-producing cells present in all 3 layers
	—	—	—	—	—	—	—	—	Inflammatory cells present in intima, media, and adventitia of vessels; IgA-producing cells present in all 3 layers
Koutlas, 1997, US	9.0	20	835	—	—	—	Day 15, LMCA 15 mm, RCA 5 mm	LMCA	—
Suzuki, 1999, Japan	10.0	11.3	22	184	181	21.0	Day 6, LMCA 4 mm, RCA 3.3 mm; day 15, LMCA 5 mm, RCA, 4 mm; day 22, giant aneurysm, LMCA 15 mm, RCA 10 mm	LMCA (0.7-3 cm from ostium)	Proliferation of fibroblasts and myofibroblasts; inflammatory infiltrates of lymphocytes and plasma cells
Maresi, 2001, Italy	—	27.59	895	—	—	—	—	LMCA (1 cm from ostium)	At site of rupture, inflamed wall epicardium; similar inflammation in adventitia of remaining coronary vessels
Vanlieferinghen, 2002, France	—	11.7	—	—	—	—	—	LMCA	Autopsy showed cardiac tamponade caused by important ruptured aneurysm of LCA
Donna, 2003, US	—	—	—	—	—	—	—	Proximal LAD	Massive vessel wall destruction characterized by loss of elastic and muscular layers due to dense lymphoplasmacytic infiltrate
Mok, 2003, China	—	—	111	—	—	—	Day 6, LMCA 4.7 mm, RCA 18.6 mm; day 28, RCA 30 mm	Proximal RCA	Not listed
Wilson, 2004, New Zealand	—	—	—	—	—	—	—	Proximal LAD	Severe segmental necrotizing arteritis of all coronary arteries; mild to moderate fibrous intimal proliferation associated focally with organizing thrombus; focal fibrinoid necrosis
Imai, 2006, Japan	—	29.4	—	—	—	16.6	Day 7, LAD 8.1 mm; day 12, LAD 18 mm	Proximal LAD	Inflammatory cell infiltration in proximal or distal portion of aneurysm in both right and left coronary arteries, more prominent in intima and adventitia than media; fibrocellular intimal thickening, rich in cells including smooth muscle cells, covering media
Miyamoto, 2013, Japan	7.2	15.6	27	161	120	11.1	Day 13, RCA 5.0 mm, LCA 3.1 mm; day 23, RCA 14.2 mm	Proximal RCA	Internal elastic membrane of coronary artery wall disappeared, leading to rupture and extending artery wall under influence of blood pressure

Hb, Hemoglobin; WBCs, white blood cells; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; LMCA, left main coronary artery; RCA, right coronary artery; LAD, left anterior descending coronary artery; LCA, left circumflex coronary artery; —, not listed in thesis.

suspect the possibility of the rupture. The patient should undergo coronary artery bypass grafting as soon as possible. Early intervention may offer the only chance for survival.

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