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Usefulness of Single Photon Emission Computed Tomography/Computed Tomography Fusion-Hybrid Imaging to Evaluate Coronary Artery Disorders in Patients with a History of Kawasaki Disease

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Background: The coronary arterial lesions of Kawasaki disease are mainly dilative lesions, aneurysms, and stenotic lesions formed before, after, and between aneurysms; these lesions develop in multiple branches resulting in complex coronary hemodynamics. Diagnosis of myocardial ischemia and infarction and evaluation of the culprit coronary arteries and regions is critical to evaluating the treatment and prognosis of patients. This study used hybrid imaging, in which multidetector computed tomographic (CT) images for coronary CT angiography (CCTA) and stress myocardial perfusion single-photon emission CT (SPECT) images were fused. We investigated the diagnosis of blood vessels and regions responsible for myocardial ischemia and infarction in patients with complex coronary arterial lesions; in addition, we evaluated myocardial lesions that developed directly under giant coronary artery aneurysms.

Methods: The subjects were 17 patients with Kawasaki disease with multiple coronary arterial lesions (median age, 18.0 years; 16 male). Both CCTA using 64-row CT and adenosine-loading myocardial SPECT were performed. Three branches, the right coronary artery (RCA), left anterior descending branch (LAD), and left circumflex branch, were evaluated with the conventional side-by-side interpretation, in which the images were lined up for diagnosis, and hybrid imaging, in which the CCTA and SPECT images were fused with computer processing. In addition, the myocardial lesions directly under giant coronary artery aneurysms were investigated with fusion imaging.

Results: Images sufficient for evaluation were acquired in all 17 patients. In the RCA, coronary arterial lesions were detected with CCTA in 16 patients. The evaluations were consistent between the side-by-side and fusion interpretation in 14 patients, and the blood vessel responsible for the myocardial ischemic region was identified in 2 patients. In the left circumflex branch, coronary arterial lesions were confirmed with 3-dimensional CT in 5 patients, and the the culprit coronary arteries for myocardial ischemia/infarction were confirmed with the fusion interpretation but not with the side-by-side interpretation. In the LAD, coronary arterial lesions were present in all patients, and the diagnosis was made with the fusion interpretation in 10 patients. In the LAD, small-range infarct lesions were detected directly under the giant coronary artery aneurysm in 8 patients, but were not confirmed with the side-by-side interpretation.

Conclusion: Fusion imaging was capable of accurately evaluating myocardial ischemia/infarction as cardiovascular sequelae of Kawasaki disease and confirming the culprit coronary arteries. In addition, analysis of fusion images confirmed that small-range infarct lesions were concomitantly present directly under giant coronary artery aneurysms in the anterior descending coronary artery.

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Key words: Kawasaki disease, single-photon emission computed tomography/computed tomography fusion-hybrid imaging, coronary arterial lesions, myocardial ischemia

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Introduction

Kawasaki disease is an acute systemic vasculitis which develops mostly in infants; the number of infants receiving new diagnoses each year is more than 10,000 and has recently been increasing in Japan. The most problematic sequelae of Kawasaki disease are coronary arterial lesions (CALs), including coronary artery aneurysms. These lesions occur in approximately 3.0% of cases, despite recent advances in acute-phase treatment[1]. Acute-phase CALs start as dilative lesions and form aneurysms. Vascular remodeling constantly occurs in the dilated coronary artery, recessing the coronary artery aneurysm in more than half of cases; however, progression to stenotic lesions is not uncommon. When the size of an acute-phase coronary artery aneurysm exceeds 4 mm, the vascular intima grows[2]. As a result, stenotic lesions developed in aneurysms of 6 to 8 mm 5, 10, and 15 years after the onset of Kawasaki disease in 6%, 28%, and 52% of cases, respectively, and in aneurysms larger than 8 mm in 44%, 62%, and 74% of cases, respectively. Moreover, coronary artery aneurysms are formed on the bilateral sides of the artery in many cases, and lesions are often mixed, ranging from dilative to stenotic lesions. These lesions lead to complex coronary hemodynamics.

Morphologic evaluation with coronary arteriography (CAG) is essential to evaluate CAL, but a disadvantage is its high invasiveness. For diagnosing CAL in adults, coronary computed tomographic angiography (CCTA) has high diagnostic accuracy: a sensitivity of 99%, a specificity of 64%, and a negative predictive value of 64%[3]. The usefulness of CCTA for diagnosing CAL in children has also been reported[4] However, in patients with tachycardia or severe vascular calcification, accurate images are difficult to obtain and evaluating stenotic lesions has a reduced positive predictive value[5]. On the other hand, the modality most frequently used for the evaluation of myocardial ischemia is the imaging of stress myocardial perfusion with single-photon emission computed tomography (SPECT). In adults, the sensitivity and specificity of detecting coronary artery stenosis of ≥50% were reported to be 86% and 74%, respectively[6], whereas the incidence of cardiac accidents was reported to be ≤1% when the stress myocardial blood flow image was normal on the prognosis judgment[7]. Adenosine-stress myocardial SPECT is safe for children[8]. However, the main concern about SPECT is the difficulty of confirming culprit coronary arteries for myocardial ischemia. The blood-supplied regions of the myocardium are determined with a 17-segment model established by the American Heart Association, but large individual variations are present in the regions perfused by the coronary arteries[9]. When the hemodynamics are complex because of multivessel disease, myocardial ischemia is difficult to confirm with SPECT imaging[5].

Cardiac SPECT/CT hybrid imaging compensates for these disadvantages and is considered a method for accurately diagnosing ischemic regions and culprit coronary arteries; its usefulness for adults is widely documented[10]. We hypothesized that evaluation with fusion imaging is also beneficial for the CALs of Kawasaki disease showing complex coronary hemodynamics, and we evaluated these lesions with fusion imaging to confirm usefulness. In Kawasaki disease, a giant coronary artery aneurysm might damage blood vessels branching from the aneurysm region and form an infarct lesion directly under the aneurysm, but there has been no reliable evidence of this. Additionally, we speculate that the presence of infarction under an aneurysm can also be demonstrated with fusion imaging.

Materials and Methods

Subjects

The subjects were 17 patients with Kawasaki disease who were being followed up at the outpatient clinic of our hospital and were examined with SPECT/CT fusion-hybrid imaging. Evaluations made by the side-by-side interpretation and fusion imaging of SPECT and CCTA were retrospectively compared.

The examinations were performed after the test contents were sufficiently explained to the patients and their families and consent was obtained.

Methods

CCTA examinations

Images were acquired with a 64-row CT scanner (LightSpeed; GE Medical System, Milwaukee, WI, USA). One hour before CCTA, a β-blocker (atenolol) was administration to all patients; the dose was 50 mg for patients 15 years or older and 25 mg for patients younger than 15 years. No other drug was administered.

Images were acquired as previously reported[11]. Briefly, before the helical scan, preliminary acquisition was performed to decide the initiation and completion positions of acquisition and the acquisition gate. The minimum gantry rotation time was 0.35 seconds, tube voltage was 120 kV, and tube current ranged from 280 to 750 mA; electrocardiographic (ECG) modulation was used.

The contrast medium iopamidal (Iopamiron 370, Bayer AG, Leverkusen, Germany) was administered at a dose of 0.8 mL/kg. The intravenous infusion rate of contrast medium was body weight (kg)×0.08 mL/second with a saline boost of 20 mL.

The region of interest was set to the ascending aorta. An ECG gated helical scan was performed. The tracheal bifurcation over the diaphragm was scanned during a single breath hold by the patient lasting 5 to 7 seconds. To select the optimum cardiac cycle, retrospective ECG gating was performed, and images from early systole to late diastole were retrospectively reconstructed. All images acquired at 0.625-mm thickness were reconstructed.

Stress myocardial perfusion SPECT imaging

A 1-day ECG-gated rest/adenosine stress method (myocardial perfusion imaging protocol) was applied to all patients.

Technitium-99m-tetrofosmin (296 MBq) was intravenously injected while that patient was at rest, and 740 MBq was intravenously injected at 3 minutes after a continuous intravenous injection of adenosine was started. Adenosine was administered at a dosage of 120 μg/kg/minute for 6 minutes.

The SPECT data were collected with a dual-head detector camera (Infinia; GE Medical System) with the following settings: low-energy general-purpose collimator and 20% symmetric window 140 keV; 64×64 matrix circular orbit with step-and-shoot acquisition at 5° intervals over 180° ; and 30 seconds/projection for stress imaging and 50 seconds/projection for rest imaging. After gating with the detection of ECG R waves, 16 frames were acquired per single cardiac cycle. In each patient, all collected non-ECG-gated data were reconstructed with workstation software. Polar maps of perfusion, wall movement, and wall thickness were prepared, and the left ventricular end-diastolic volume and left ventricular ejection fraction were also calculated from the gated SPECT data with a commercial software program (Cedars QGS/QPS; Cedars-Sinai Medical Center, Los Angeles, CA, USA).

Fusion image preparation

The CCTA and SPECT images were fused by means of a software system/program (CardIQ, GE Healthcare). The fusion method has previously been described in detail[12]. Briefly, this software system/program provides tools to optimally align the axial source SPECT and CT images through the use of the heart muscle contour on SPECT and CT to project the SPECT image on the surface of the left ventricular epicardium to provide fused images. The preset for the projection color scale on the left ventricular epicardium was adopted from the corresponding individual SPECT images and was not changed during the fusion process.

Image analysis

Two radiologists interpreted the CTA images, and another 2 radiologists interpreted the SPECT images obtained during rest and stress tests. They individually prepared diagnostic reports, and consistency was verified. Finally, diagnoses were made with the SPECT/CT side-by-side interpretation. Cases with consistent and inconsistent SPECT/CT findings were re-evaluated with the fusion interpretation and reviewed. The final reports were discussed by pediatric cardiologists and radiologists, and the final diagnosis was made after a consensus was reached.

Results

Subjects

The subjects were 17 patients (16 male and 1 female) who ranged in age from 10 to 34 years (median age, 18.0 years). The onset time of Kawasaki disease ranged from 4 months to 6 years and 11 months old (median age, 2 years), and the time to examination after onset ranged from 4 to 33 years (mediantime, 14 years). Sixteen patients, excluding 1, had a past medical history of giant coronary artery aneurysm after the acute phase (**Table 1 A**). Eight patients had received a coronary artery bypass graft (CABG), and 2 patients had received treatment with (percutaneous coronary intervention) (**Table 1B**). Including referred patients, the age of patients at the time of first CAG at our hospital ranged from 0.1 to 33.0 years (median, 6.2 years) after onset. The SPECT/CT was performed 4.0 to 33.0 years (median: 14.0 years) after the onset of Kawasaki disease. The acquired SPECT/CT images were sufficient for locating CALs and judging ischemia and infarction in all patients. The absence of occlusion of the anastomosed region was confirmed on fusion imaging in all patients who underwent coronary artery bypass grafting (CABG). No ischemia was observed in the regions perfused with the bypass grafts in any patients undergoing CABG.

Right Coronary Artery

Right CALs were detected with CCTA in 16 of the 17 patients. Ischemia and infarction were detected in the region perfused by the right coronary artery (RCA) on SPECT in 2 and 8 patients, respectively (**Table 2**). The imaging diagnosis made with the side-by-side interpretation was corrected with the fusion interpretation in 2 pa-

Table 1A Patients profile: the first coronary arteriography

Case	Sex	Age (years)	Age of onset (months)	Presence of GAN at acute phase	Years from KD onset to 1st CAG at our hospital	RCA finding of 1st CAG	LCA finding of 1st CAG
1	M	19	7	RCA	12.9	#1 GAN 16×24 mm	#5–6 mAN
2	M	18	24	LCA	14.0	#1–2 LS 90%–95%	#5 sAN #6 mAN, LS50% at distal site
3	M	26	7	-	5.8	#2 mAN, LS 99% at distal site #4 Occ #4AV collateral to #15	
4	M	25	4	LCA	9.0	#2 LS 50%	#6 GAN, LS 50%–75% at proximal site #7 GAN, LS 50% at proximal site
5	M	10	70	RCA and LCA	0.3	#1–2–3 GAN #3–4 mAN	#5–7–11–12 GAN
6	M	23	11	RCA	19.2	#2 GAN #4 to Cx collateral	#6 SS
7	M	13	12	RCA and LCA	5.3	#1 Occ	#6 GAN, LS 90% at distal site
8	M	29	52	RCA and LCA	22.7	#1 Occ	#6 Occ
9	F	33	13	RCA and LCA	0.4	#1–2 GAN	#5–6 GAN
10	M	12	21	RCA	0.1	#1–3 GAN	#5–6–11 mAN
11	M	34	33	LCA	33.3	#1 to #7 collateral #2 Occ #4PD, AV to #15 collateral	#5 sAN #6 GAN, Occ at distal site #7 to #1 collateral
12	M	15	83	LCA	0.2	#1 Occ #4 PD to #13 collateral	#6–8 GAN
13	M	19	73	RCA and LCA	2.2	#1–2 GAN	#6–7 GAN
14	M	16	46	LCA	6.8	#1 mAN #2 mAN	#5–6–11 GAN
15	M	17	48	LCA	6.2	#2 mAN	# 6–7 mAN
16	M	11	13	LCA	0.5	#1 regression	#6–7 mAN
17	M	13	29	RCA and LCA	8.2	#1 GAN #2 GAN	#5–6–11 mAN #6–7 GAN

sAN: small aneurysm (≤4 mm)
mAN: medium size aneurysm (>4 and <8 mm)
GAN: giant aneurysm (≥8 mm)
Occ: occulusion
SS: segmental stenosis
LS: legional stenosis

tients (cases 10 and 11), and the ischemic and infarct regions and culprit coronary arteries were additionally confirmed with the fusion interpretation.

Left Anterior Descending Coronary Artery

The CALs of the left anterior descending (LAD) coronary artery were confirmed with CCTA in all 17 patients. Ischemia and infarction were detected on SPECT in 7 and 12 patients, respectively (**Table 3**). The locations of ischemia and infarction were not consistent between SPECT and CCTA in 13 patients on the side-by-side interpretation. The diagnosis was corrected with the fusion interpretation in 13 patients, and penetrating and small branches not identifiable with the side-by-side interpretation, such as first diagonal branch (D1), were confirmed as culprit coronary arteries for ischemia or infarction with the fusion interpretation in 6 patients. A finding considered as ischemia with the side-by-side interpretation was corrected with the fusion interpretation in 1 patient, and infarction was additionally confirmed with the fusion interpretation in another patient. The diagnosis was corrected in 13 patients, and the most frequent correction was the presence of infarction directly under the aneurysm newly identified with the fusion interpretation in 11 patients (**Fig. 1**). Ten patients had a giant aneurysm in the LAD.

Circumflex Branch of the Left Coronary Artery

The CALs were detected with CCTA in the circumflex branch (CX) in 5 of the 17 patients. Ischemia and infarction were detected on SPECT in 2 (cases 2 and 4) and 3 (cases 11, 13, and 14) patients, respectively (**Table 4**). No

Table 1B Patients profile: coronary computed tomographic angiography, intervention

Case	Duration from KD onset to CT exam (years)	CT finding of RCA	CT finding of LCA	Number of branches of CAL	PCI	CABG	Number of grafts	Patency	Graft type
1	18	#1 GAN	#6 sAN	2	-	-			
2	17	#2 SS	#6 sAN, Calc, LS 50% at distal site #11 Regression	3	-	-			
3	25	#2 SS #4AV to #15 collateral	#6 LS 50%	2	-	-			
4	24	#1 LS 50% #2 LS 90%, Calc #4 sAN (Bifurcation site of AV and PD)	#6 GAN, LS 90% at distal site #7 sAN, Calc, LS 50% at distal site	2	+	-			
5	4	#1–#2 GAN	#5–#7–#11 GAN	3	-	-			
6	23	#1 Occ #3 bypass anastomosis	#6 SS #7 bypass anastomosis	2	-	+	2	yes	LITA-LAD RITA-RCA
7	12	#1–#2 SS	#6 Occ #7 bypass anastomosis	2	-	+	1	yes	LITA-LAD
8	25	#1–#2 SS #3 bypass anastomosis	#5–6–11 GAN #6 Occ #8 and D1 bypass anastomosis	3	-	+	2	yes	LITA-D1-LAD RITA-RCA
9	32	#1–#2 SS	#6 sAN #8 bypass anastomosis #9 bypass anastomosis (occluded)	2	-	+	2	yes (once occluded)	LITA-LAD RITA-D1
10	11	#1–#2 SS #4AV, PD to #15 collateral	#5–#6 Regression, Calc #7 sAN	2	-	-			
11	33	#2 Occlusion #15→#4PD, AV collateral	#5 sAN #6 Occ #11sAN, 75% stenosis #1→#7 collateral	3	-	-			
12	9	#1–#2 SS #15→#4PD, AV collateral	#6 GAN, LS 75% at distal site	2	-	-			
13	13	#1 SS #2 Occ #3 bypass anastomosis	#6 Occ #7 bypass anastomosis #9 bypass anastomosis	2	-	+	2	yes	LITA-D1-LAD GEA-RCA
14	12	#1–#2 sAN	#5–#6–#11 GAN	3	-	-			
15	14	#2–#3 sAN	#6–#7 sAN #7 bypass anastomosis	2	-	+	1	yes	LITA-LAD#7
16	10	-	#6–7 sAN #7 bypass anastomosis	1	-	+	1	yes	LITA-LAD
17	11	#1–#2 GAN #4PD sAN	#5–6–11 GAN #7 and D1 bypass anastomosis	3	+	+	1	yes	LITA-D1-LAD

sAN: small aneurysm (=<4 mm)
mAN: medium size anrurysm (4< <8 mm)
GAN: giant aneurysm (=>8 mm)
Occ: occulusion
SS: segmental stenosis
LS: legional Stenosis
LITA: left internal thoracic artery
RITA: right internal thoracic artery
GEA: gastroepiploic artery
D1: first diagonal branch
AV: atrio-ventricular branch
PD: posterior descending artery
CABG: coronary artery bypass grafting

Table 2 Right coronary artery: findings of side-by-side interpretation and fusion interpretation

Case	Presence or absence of ischemia SPECT	Presence or absence of infarction SPECT	Consistence of ischemic/infarct regions between CT and SPECT on the side-by-side evaluation	Presence or absence of ischemia fusion	Presence or absence of infarction fusion	Comparison between side-by-side and fusion	Comment
13	+	+	Consistent	+	+	Equivalent	
2	+	-	Consistent	+	-	Equivalent	
10	-	+	Consistent	+	+	Diagnosis was corrected by fusion	Correction of blood vessels responsible for ischemic/infarct regions by fusion
11	-	+	Consistent	+	+	Diagnosis was corrected by fusion	Correction of blood vessels responsible for ischemic/infarct regions by fusion
3	-	+	Consistent	-	+	Equivalent	
4	-	+	Consistent	-	+	Equivalent	
6	-	+	Consistent	-	+	Equivalent	
8	-	+	Consistent	-	+	Equivalent	
9	-	+	Consistent	-	+	Equivalent	
5	-	-	Consistent	-	-	Equivalent	
7	-	-	Consistent	-	-	Equivalent	
12	-	-	Consistent	-	-	Equivalent	
1	-	-	Consistent	-	-	Equivalent	
14	-	-	Consistent	-	-	Equivalent	
15	-	-	Consistent	-	-	Equivalent	
17	-	-	Consistent	-	-	Equivalent	
16	-	-	Consistent	-	-	Equivalent	

significant CALs were confirmed in the CX with CCTA in 3 patients (cases 2, 4, and 13); however, ischemia was confirmed in the CX-perfused region with the fusion interpretation in 2 patients (cases 2 and 4), and infarction was confirmed in 1 (case 13). A CAL accompanied by marked stenosis or occlusion was present in both the RCA and LAD in all these cases. Ischemia was present in the LAD-perforating branch and RCA-perfused regions in case 2. Ischemia in the LAD-perfused region and infarction in the RCA-perfused region were noted in case 4. Furthermore, ischemia in the LAD D1-perfused region and ischemia and infarction in the RCA-perfused region were noted in case 13. The diagnosis of the CX was corrected with the fusion interpretation in 5 patients, and subdivided blood vessels were confirmed as those responsible for ischemia and infarction. No giant aneurysms of the CX or underlying myocardial infarct lesions were present in the patients.

Discussion

The CALs of Kawasaki disease start with dilative lesions in the acute phase and develop into diverse lesions, such as coronary artery occlusion, by thrombus formation in aneurysms and progression of stenotic lesions due to vascular remodeling. Small aneurysms are likely to spontaneously regress, and about half of these aneurysms regress to a normal appearance on catheter contrast angiography within 1 to 2 years[13]. However, giant aneurysms with an inner diameter exceeding 8 mm do not completely regress and cause thrombotic occlusion and stenotic lesions at a high frequency. Although the long-term survival rate is favorable when management and treatment are appropriate, CABG, percutaneous coronary intervention, and cardiac events, such as myocardial infarction, occur in more than 70% of cases[14]. Histological examination has observed long-term expression of active growth factors in coronary artery aneurysms, demonstrating long-term active vascular remodeling[15]. Therefore, long-term observation is necessary for patients with Kawasaki disease complicated by CALs, as well as repeated evaluation of the coronary artery morphology and active evaluation of myocardial ischemia in patients with a morphological risk. The prognosis is also poor in patients with impaired cardiac function[16]. The biggest causes of aggravation of cardiac function are myocardial infarction and ischemia, and early discovery and treatment of these cardiac events are necessary. An excellent modality for evaluating coronary artery morphology is

Table 3 Left anterior descending: findings of side-by-side interpretation and fusion interpretation

Case No	Presence or absence of ischemia SPECT	Presence or absence of infarction SPECT	Consistence of ischemic/infarct regions between CT and SPECT on the side-by-side evaluation	Presence or absence of ischemia fusion	Presence or absence of infarction fusion	Comparison between side-by-side and fusion	Comment
2	+	+	Inconsistent	+	+	Diagnosis was corrected by fusion	Identification of infarction directly below the aneurysm with fusion Correction of blood vessels responsible for ischemic/infarct regions with fusion
10	+	+	Inconsistent	+	+	Diagnosis was corrected with fusion	Identification of infarction directly below the aneurysm with fusion Correction of blood vessels responsible for ischemic/infarct regions by fusion
11	+	+	Inconsistent	+	+	Diagnosis was corrected with fusion	Identification of infarction directly below the aneurysm with fusion Correction of blood vessels responsible for ischemic/infarct regions by fusion
13	+	+	Inconsistent	+	+	Diagnosis was corrected with fusion	Identification of infarction directly below the aneurysm with fusion Correction of blood vessels responsible for ischemic/infarct regions by fusion
17	+	+	Inconsistent	+	+	Diagnosis was corrected with fusion	Identification of infarction directly below the aneurysm with fusion
16	+	+	Inconsistent	-	+	Diagnosis was corrected with fusion	Identification of infarction directly below the aneurysm by Fusion No ischemic finding was noted on the fusion method
4	+	-	Inconsistent	+	+	Diagnosis was corrected by fusion	Identification of infarction directly below the aneurysm by fusion Correction of blood vessels responsible for ischemic/infarct regions with fusion
5	-	+	Inconsistent	-	+	Diagnosis was corrected with fusion	Identification of infarction directly under the aneurysm
7	-	+	Inconsistent	-	+	Diagnosis was corrected with fusion	Identification of infarction directly under the aneurysm
8	-	+	Inconsistent	-	+	Diagnosis was corrected with fusion	Identification of infarction directly under the aneurysm
12	-	+	Inconsistent	-	+	Diagnosis was corrected by fusion	Identification of infarction directly under the aneurysm
14	-	+	Inconsistent	-	+	Diagnosis was corrected with fusion	Correction of blood vessels responsible for ischemic/infarct regions with fusion
6	-	+	Consistent	-	+	Equivalent	
9	-	-	Inconsistent	-	+	Diagnosis was corrected with fusion	An infarct region was newly identified with fusion
1	-	-	Consistent	-	-	Equivalent	
3	-	-	Consistent	-	-	Equivalent	
15	-	-	Consistent	-	-	Equivalent	

CAG. However, patients with Kawasaki disease complicated by CALs require repeated evaluations for a long time, and invasiveness on CAG is a large burden.

As the modalities for evaluating coronary artery morphology have recently diversified, CCTA has become an accepted substitute for CAG in the observation of Kawasaki disease associated coronary artery aneurysms owing to its high spatial resolution[17]. However, angiography alone overestimates the ischemic region in patients showing complex hemodynamics, such as those with multivessel disease[18]; thus, evaluation with contrast imaging alone is not sufficient in patients with Kawasaki disease who have lesions in multiple vasculature. On the other hand, adenosine stress myocardial ^{99m}Tc SPECT is

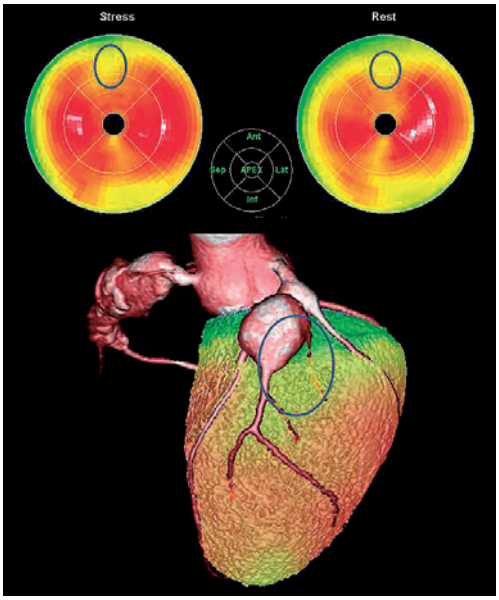

Fig. 1 Upper, SPECT Bull's eye; lower, hybrid image. In the upper SPECT images, Tc uptake decreased during both rest and stress in the region enclosed in the blue circle, suggesting infarction. However, a perfusion defect was noted only in the proximal region, as the distal region could not be evaluated on the basis of the general perfusion defect patterns; thus, the diagnosis could not be made with the side-by-side interpretation. In this hybrid image, a region with reduced perfusion was noted directly under the giant aneurysm (**blue circle**).

less invasive, and myocardial ischemia can be evaluated even in children in whom exercise tests are difficult to perform. In cardiac SPECT/CT hybrid imaging, both the specificity (from 63% to 95%) and positive predictive value (from 31% to 77%) of CAL evaluation increased compared with those of CCTA alone[19] which has evidence of its utility in adults. Particularly more accurate diagnosis was achieved in multivessel disease, moderate or severe stenosis, and lesions accompanied by collateral circulation, which cannot be clearly evaluated with the side-by-side method[20]. Regarding prognosis, the incidence of cardiac events (death or myocardial infarction) was significantly higher in patients in whom the findings of SPECT and CCTA were consistent on SPECT/CT analysis[21].

We investigated the usefulness of the SPECT/CT fusion method for patients with Kawasaki disease-associated coronary artery disorder. This method is useful for multivessel disease, such as Kawasaki disease, and the blood vessels responsible for myocardial ischemic lesions were accurately identified. The diagnoses made with the side-by-side method were corrected in 2 of 16 patients with RCA lesions and 10 of 17 patients with LAD lesions. In all these cases, the ischemic region and culprit coronary arteries were confirmed with the fusion interpretation. In particular, fusion imaging initially clarified the occurrence of infarction directly under giant aneurysms in the LAD. This pattern indicates a perfusion defect only in the proximal region without confirming a defect in the distal region; the culprit coronary arteries could not be confirmed with the side-by-side interpretation, because they cannot be confirmed with the general ischemia and infarction-induced perfusion defect patterns. The aneurysm was giant in most cases in which myocardial infarction occurred directly under the aneurysm. Two mechanisms are considered for the occurrence of infarction directly under the giant coronary artery aneurysm. In one mechanism, the microvasculature branching from the giant aneurysm region is exposed to and occluded during giant aneurysm formation by severe inflammation, which causes infarction. In the other mechanism, thrombus formation occurs in the aneurysm after giant aneurysm formation, and small branches from the aneurysm are occluded and become infarcted directly under the aneurysm. Infarction directly under giant aneurysms could not be judged with the side-by-side interpretation and was initially evaluated with the fusion interpretation. The diagnosis of the LAD was corrected with the fusion interpretation in 13 cases. The most frequent correction was due to confirmation of infarction directly under aneurysms (11 patients), while other corrections were confirmation of thin branches, such as the penetrating branch and D1, as the culprit coronary arteries for ischemia and infarction; this confirms the high precision of the fusion interpretation. In the CX, although CAL was not demonstrated with CCTA, ischemia or infarction was noted in the CX-perfused region in 3 patients. All cases were accompanied by severe stenosis or occlusion of the RCA and LAD; the perfusion defect region was small and located in the boundary between the RCA and LAD, where multivessel disease was difficult to diagnose. In the RCA, the diagnosis was corrected with the fusion interpretation only in 2 of 14 patients, and the RCA branch was ultimately identified as being responsible for ischemia or infarction. The most frequent finding accompanying a giant RCA aneurysm is lotus-like neovascularization through the vasa vasorum of the aneurysm after its occlusion; this finding is followed by recanalization, termed segmental stenosis, which is a characteristic finding of Kawasaki disease CAL. As the myocar-

Table 4 Left circumflex: findings of side-by-side interpretation and fusion interpretation

Case	Presence or absence of ischemia SPECT	Presence or absence of infarction SPECT	Consistence of ischemic/infarct regions between CT and SPECT on the side-by-side evaluation	Presence or absence of ischemia fusion	Presence or absence of infarction fusion	Comparison between side-by-side and fusion	Comment
2	+	-	Inconsistent	+	-	Fusion is superior	Correction of blood vessels responsible for ischemic/infarct regions with fusion
4	+	-	Inconsistent	+	-	Fusion is superior	Correction of blood vessels responsible for ischemic/infarct regions with fusion
11	-	+	Inconsistent	-	+	Fusion is superior	Correction of blood vessels responsible for ischemic/infarct regions with fusion
13	-	+	Inconsistent	-	+	Fusion is superior	Correction of blood vessels responsible for ischemic/infarct regions with fusion
14	-	+	Inconsistent	-	+	Fusion is superior	Correction of blood vessels responsible for ischemic/infarct regions with fusion
5	-	-	Consistent	-	-	Equivalent	
8	-	-	Consistent	-	-	Equivalent	
17	-	-	Consistent	-	-	Equivalent	
1	-	-	Consistent	-	-	Equivalent	
3	-	-	Consistent	-	-	Equivalent	
6	-	-	Consistent	-	-	Equivalent	
7	-	-	Consistent	-	-	Equivalent	
9	-	-	Consistent	-	-	Equivalent	
10	-	-	Consistent	-	-	Equivalent	
12	-	-	Consistent	-	-	Equivalent	
15	-	-	Consistent	-	-	Equivalent	
16	-	-	Consistent	-	-	Equivalent	

dial blood flow demand of the right ventricle is lower than that of the left ventricle, blood flow through segmental stenosismay still be able to supply the myocardial blood flow of the right ventricle. Thus, collateral circulation, which is formed in the LAD with severe stenosis and occlusion, is observed less often in the RCA. In addition, the hemodynamics of the RCA are not as complex as those of the LAD with stenosis or occlusion. This lower complexity may have been the reason for fewer corrections of the diagnosis with the fusion interpretation in the RCA than in the LAD.

Study Limitations

The previous side-by-side evaluations of SPECT, CCTA, and a new method, SPECT/CT fusion-hybrid imaging, were retrospectively evaluated in patients with Kawasaki disease who had multivessel disease exhibiting complex hemodynamics. We did not performed CAG for morphological diagnosis or evaluate fractional flow reserve or coronary flow reserve for myocardial ischemia[22]. For coronary morphological diagnosis, CAG has been considered a gold standard. However, according to the Japanese circulation guideline[17], CCTA is also recommended for morphological evaluation, especially during follow up. The guideline[17] and the other report[22] also recommend stress perfusion image scintigraphy for evaluating myocardial ischemia, as well as for evaluating fractional flow reserve and coronary flow reserve. We suspect that our new finding, "myocardial infarction directly under giant aneurysm in the LAD," is be caused by occlusion of microvasculature branching from the giant aneurysm. Evaluating fractional flow reserve or coronary flow reserve for such microvasculature is quite difficult.

Conclusion

We have shown that SPECT/CT fusion-hybrid imaging is useful for evaluating Kawasaki disease CALs in patients with multivessel disease, particularly in the LAD-perfused region. Patients with Kawasaki disease who have CAL require lifelong observation, and for these patients SPECT/CT is a less-invasive and useful examination.

Conflict of Interest: The authors declare no conflict of interest.

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