

# Cerebral Hypoperfusion During Acute Kawasaki Disease

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**Background and Purpose**—Kawasaki disease is a febrile disease of children notable for systemic vasculitis. There have been many previous reports of various complications, including disorders of the central nervous system. We evaluated cerebral perfusion during the acute stage in patients with Kawasaki disease.

**Methods**—Single-photon emission-computed tomography (SPECT) with  $^{99m}\text{Tc}$ -hexamethylpropyleneamine oxime was performed in 21 children with acute stage Kawasaki disease. Follow-up SPECT and MRI were performed about 1 month after the first SPECT in patients who exhibited abnormal SPECT findings during the acute stage.

**Results**—In 6 of 21 children SPECT imaging demonstrated localized cerebral hypoperfusion without abnormal neurological findings or clinical symptoms, and the follow-up SPECT and MRI approximately 1 month after the first SPECT revealed no abnormalities.

**Conclusions**—Some patients with Kawasaki disease have transient localized cerebral hypoperfusion at the acute stage. (*Stroke*. 1998;29:1320-1321.)

**Key Words:** cerebral circulation ■ hypoperfusion ■ Kawasaki disease ■ tomography, emission computed

Kawasaki disease (KD) is an acute illness of early childhood characterized by prolonged fever, diffuse mucosal inflammation, indurative edema of the hands and feet, a polymorphous skin rash, and nonsuppurative lymphadenopathy.<sup>1</sup> KD is also called mucocutaneous lymph node syndrome in the early literature.<sup>2</sup> The histopathologic findings in KD comprise pan-vasculitis with endothelial necrosis and the infiltration of mononuclear cells into small- and medium-sized blood vessels.<sup>3,4</sup> KD has many complications, including involvement of the nervous system, with the most important being cardiac involvement. Neurological complications, including cerebral infarction, aseptic meningitis, facial palsy, sensorineural hearing loss, hemiparesis, ataxia, and encephalopathy, have been previously reported.<sup>5-11</sup> We performed single-photon emission computed tomography (SPECT) in children with KD to investigate brain perfusion in the acute stage.

## Subjects and Methods

Twenty-one children (10 girls and 11 boys; aged 3 months to 4 years; mean age, 1.7 years) with acute KD on admission to our hospital between February 1996 and December 1997 were included in this study (see the Table). Their parents gave informed consent for their participation in the study. The patients met the specific diagnostic criteria for KD.<sup>1</sup> The day of onset of fever was considered the first day of illness. All patients were treated with high-dose intravenous immunoglobulin ( $400 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$  for 5 days) and oral aspirin administration.

[ $^{99m}\text{Tc}$ ]hexamethylpropyleneamine oxime ( $^{99m}\text{Tc}$ -HMPAO) SPECT scanning was performed from 10 to 15 minutes after an intravenous injection of 110 to 300 MBq of  $^{99m}\text{Tc}$ -HMPAO in children with KD on days 4 to 16 (mean  $\pm$  SD,  $8.1 \pm 3.7$  days) of

illness. The  $^{99m}\text{Tc}$ -HMPAO was prepared from a freeze-dried kit (Ceretek; Amersham International) by adding 1110 MBq of freshly eluted  $^{99m}\text{Tc}$  perchlorate to 5 mL of a saline solution. The injection was performed within 30 minutes after preparation. The scanning equipment consisted of a rotating, large field-of-view gamma camera fitted with a low-energy and high-resolution collimator. Follow-up SPECT and MRI were performed approximately 1 month after the first SPECT in patients who exhibited abnormal SPECT findings during the acute stage. MRI was performed using a 1.5-T scanner with a spin-echo T1-weighted sequence of 560/14/2 ms (repetition time/echo time/excitations) and a T2-weighted sequence of 3000/90/1 ms.

## Results

Six (29%) of the 21 patients exhibited localized cerebral hypoperfusion on SPECT during the acute stage (see the Figure). The SPECT abnormalities were not related to the maximum serum C-reactive protein level or the duration of the fever (Table). All 6 patients with abnormal first SPECT findings exhibited normal follow-up SPECT and MRI findings at about 1 month after the first SPECT, and no definite abnormal neurological findings or clinical symptoms were seen in the acute and convalescent stages. Patient 11, who had no abnormalities on SPECT in the present study, exhibited transient dilatation of the coronary arteries, and patient 21 had transient mitral regurgitation on 2-dimensional echocardiography.

## Discussion

We suggest that the transient localized cerebral hypoperfusion observed on SPECT in the present 5 patients might have been caused by cerebral vasculitis. KD is characterized by

Received March 9, 1998; final revision received April 13, 1998; accepted April 13, 1998.

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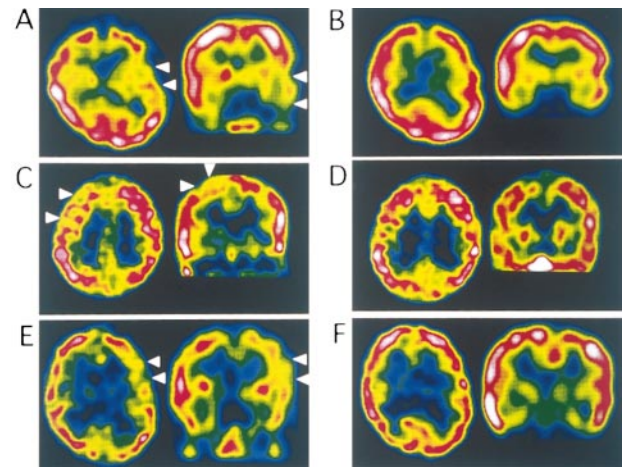
Data for 21 Children With Kawasaki Disease

Patient No./Age/Sex	Duration of Fever, days	Maximum Serum CRP, mg/dL	Days of SPECT	SPECT Findings
1/5 mo/M	8	6.82	8	Hypoperfusion in the left temporal region
2/3 y/M	9	22.2	9	Hypoperfusion in the right frontal region
3/18 mo/F	5	3.56	5	Hypoperfusion in the left frontotemporal region
4/4 y/F	9	12.5	15	Hypoperfusion in the left occipital region
5/7 mo/F	7	10.7	7	Hypoperfusion in the left temporal region
6/3 mo/F	7	16.5	5	Hypoperfusion in the left parietal region
7/10 mo/F	10	18.0	11	Normal
8/14 mo/M	6	4.75	5	Normal
9/5 mo/M	5	6.02	4	Normal
10/18 mo/M	8	13.3	8	Normal
11/3 y/M	21	23.9	16	Normal
12/15 mo/F	9	23.1	4	Normal
13/6 mo/F	10	13.5	10	Normal
14/2 y/F	9	11.4	12	Normal
15/2 y/M	7	15.0	12	Normal
16/13 mo/F	5	13.9	5	Normal
17/2 y/M	8	9.80	9	Normal
18/18 mo/M	6	19.3	4	Normal
19/11 mo/M	6	13.0	4	Normal
20/2 y/M	6	2.98	9	Normal
21/21 mo/F	7	11.0	5	Normal

SPECT indicates single photon emission computed tomography; CRP, C-reactive protein.

systemic vasculitis, so there may be cerebral vasculitis in KD. Cerebral infarction, 1 of the neurological complications of KD, may be caused by cerebral arteritis. It has been reported that SPECT reveals hypoperfusion areas in cerebral vasculitis, including, for example, systemic lupus erythematosus, microscopic polyangiitis, and Sneddon's syndrome (livedo racemosa and cerebral infarction).<sup>12-14</sup> The case of a boy with KD who developed asymptomatic cerebral infarction has been reported,<sup>10</sup> and it has also been reported that patients with asymptomatic cerebral vasculitis with systemic lupus erythematosus, microscopic polyangiitis, and Sneddon's syndrome showed cerebral hypoperfusion on SPECT.<sup>12-14</sup>

This is the first report of localized cerebral hypoperfusion observed on SPECT in the acute stage of KD. Our study emphasizes that patients with KD may have localized cerebral hypoperfusion during the acute stage. The abnormalities observed on SPECT in all 5 patients were transient, and neurological examination revealed no abnormalities in the acute and convalescent stages. However, long-term follow-up evaluation and the study of many patients with appropriate case controls are necessary to conclude whether patients with transient cerebral hypoperfusion have sequelae, including cognitive or behavioral problems.



[<sup>99m</sup>Tc]hexamethylpropyleneamine oxime single-photon emission-computed tomography (SPECT) in the acute and convalescent stages. A, In patient 1, a 5-month-old boy, the first SPECT revealed decreased regional cerebral blood flow in the left temporal area (arrowheads) on day 8 of illness. The second SPECT (B) revealed no abnormalities on day 50 of illness. C, In patient 2, a 3-year-old boy, the first SPECT revealed decreased regional cerebral blood flow in the right frontal area (arrowheads) on day 9 of illness. The second SPECT (D) revealed no abnormalities on day 37 of illness. E, In patient 3, an 18-month-old girl, the first SPECT revealed decreased regional cerebral blood flow in the left frontotemporal area (arrowheads) on day 5 of illness. The second SPECT (F) revealed no abnormalities on day 47 of illness.

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