Original Article

Hyperintense posterior cerebral artery sign in patients with reversible cerebral vasoconstriction syndrome

Masaaki Imai, Masami Shimoda, Shinri Oda, Kaori Hoshikawa, Takahiro Osada, Rie Aoki, Azusa Sunaga

Department of Neurosurgery, Tokai University Hachioji Hospital, Ishikawa Machi, Hachioji, Tokyo, Japan.

E-mail: Masaaki Imai - imai101@is.icc.u-tokai.ac.jp; *Masami Shimoda - mashimoda-nsu@umin.ac.jp; Shinri Oda - shinri_yat1116@yahoo.co.jp; Kaori Hoshikawa - gaosuz@infoseek.jp; Takahiro Osada - t-osada@is.icc.u-tokai.ac.jp; Rie Aoki - s9021@nms.ac.jp; Azusa Sunaga - a.sunaga@tokai.ac.jp

*Corresponding author:
Masami Shimoda,
Department of Neurosurgery,
Tokai University Hachioji
Hospital, Ishikawa Machi,
Hachioji, Tokyo, Japan.

mashimoda-nsu@umin.ac.jp

ABSTRACT

Background: This study investigated hyperintense vessel signs (HVS) on fluid-attenuated inversion recovery imaging in the P1–2 portions of posterior cerebral arteries (PCAs) as a "hyperintense PCA sign" and HVS of cortical arteries. We retrospectively examined whether these signs would be useful in diagnosing reversible cerebral vasoconstriction syndrome (RCVS) in the acute phase.

Methods: Eighty patients with RCVS who underwent initial magnetic resonance imaging (MRI) within 7 days of onset were included in this study. HVS and related clinical factors were examined.

Results: On initial MRI of RCVS patients, hyperintense PCA sign and HVS of cortical arteries were seen in 21 cases (26%) and 38 cases (48%), respectively. In patients showing hyperintense PCA sign, vasoconstriction of the A2–3 portion was a significant clinical factor. Conversely, vasoconstriction of the M1 and P1 portions and the presence of white matter hyperintensity on initial and chronic-stage MRI were significantly associated with the presence of HVS in cortical arteries.

Conclusion: Because rich collateral flow exists around PCAs, the frequency of hyperintense PCA sign is not high. However, hyperintense PCA sign findings in patients with suspected RCVS offer credible evidence of extreme flow decreases due to vasoconstriction in peripheral PCAs and other arteries associated with the collateral circulation of PCAs. Conversely, HVS in cortical arteries tend to reflect slow antegrade circulation due to vasoconstriction of peripheral vessel and major trunks. Both signs appear useful for auxiliary diagnosis of acute-phase RCVS.

Keywords: Fluid-attenuated inversion recovery, Hyperintense vessel sign, Posterior cerebral artery, Reversible cerebral vasoconstriction syndrome

INTRODUCTION

"Hyperintense vessel signs" (HVS) or "intra-arterial high signals" are seen when occlusion of a blood vessel is depicted as high signals on fluid-attenuated inversion recovery (FLAIR) imaging.[12] In this sign, the delayed/stagnant part of blood flow due to retrograde collateral circulation to the distal artery branch of the occluded part is depicted as a relative hyperintensity structure.[16] HVS often reflect the condition of the middle cerebral artery (MCA) in the Sylvian fissure, particularly the insular-opercular segment. In FLAIR imaging of some patients with reversible cerebral vasoconstriction syndrome (RCVS), we recently identified HVS in peduncular and/or ambient segments (P1–2 segments) of posterior cerebral arteries (PCAs). We referred

to such HVS on FLAIR in the peduncular and/or ambient segments (P1–2 segments) of a PCA as "hyperintense PCA signs" (HPS).

In the past, HVS on FLAIR images have been reported as a neuroradiological finding in the acute phase of RCVS.[1,7,17] Although Chen *et al.* reported the presence of HVS on FLAIR images in 22% of RCVS patients, that study evaluated the sign of cortical arteries in the MCA and PCA regions.[1] However, we could not find any mention of HPS in patients with RCVS. In addition, in the literature on other areas of stroke, Krings *et al.* reported a hyperdense PCA sign on computed tomography,[9] but few reports have mentioned HPS on FLAIR. The reason for the few references to HPS seems to be that HPS are clinically rare. Because rich collateral flows exist around PCAs,[4] the flows in proximal PCAs (P1–2) would be expected to be maintained through rich collaterals even when peripheral PCA flow decreases. However, once HPS are obtained in patients with suspected RCVS, we can obtain reliable findings of extreme flow decrease due to vasoconstriction in peripheral PCAs and other arteries associated with the collateral circulation of PCAs.

At present, as vasoconstriction vessels are located peripherally during the acute phase,[17,18] the diagnosis of RCVS is reportedly missed in one-third of patients who undergo initial magnetic resonance angiography (MRA) within 10 days of headache onset.[3,5] In such patients with RCVS who are difficult to diagnose during the acute phase, we retrospectively examined whether HPS and HVS of cortical arteries would prove useful for the neuroradiological diagnosis of RCVS in the acute phase.

MATERIALS AND METHODS

Normal control group

The normal control group comprised 166 patients who visited our hospital with neurological conditions other than cerebrovascular disorders, brain tumor, demyelinating diseases, dementia, or metabolic diseases, and who underwent MRI of the head that showed no abnormalities (50 men, 116 women; mean age, 54 ± 16 years). Normal MRI findings were defined as a lack of arteriosclerotic stenosis of major intracranial arteries (including PCAs), asymptomatic or symptomatic cerebral infarction, cerebral hemorrhage including microbleeds, or hydrocephalus. Regarding periventricular and deep and subcortical white matter hyperintensity (DSWMH), grades 0–1 of the Fazekas scale[6] were regarded as normal.

Patient population

Patients diagnosed with RCVS in our institution according to our previously reported criteria for RCVS[17,18] were included in our database. That is, patients diagnosed with RCVS in our institution according to the following five criteria for RCVS were included in our database: (i) acute and severe headache (often thunderclap headache [TCH]) with or without focal deficits or seizures; (ii) a uniphasic course without any new symptoms more than 1 month after clinical onset; (iii) segmental, multifocal vasoconstriction of cerebral arteries as shown by digital subtraction angiography (DSA) or indirect angiography (e.g., MRA or three-dimensional computed tomography [CT] angiography); (iv) no evidence of aneurysmal subarachnoid hemorrhage (SAH); and (v) complete or substantial normalization of arteries on follow-up DSA or indirect angiography obtained within 12 weeks after clinical onset.[5] Cerebrospinal fluid analysis was not routinely performed for patients in this study.

Our database included 102 RCVS patients between October 2010 and November 2020. We excluded 22 RCVS patients who visited our hospital in the subacute or chronic phase and who were therefore not examined by initial MRA or MRI within 7 days of RCVS onset. The remaining 80 RCVS patients who underwent initial MRI within 7 days of RCVS onset were included in this retrospective study. As much as possible, we performed sequential MRA during the period from onset to remission of TCH and within 14 days after TCH remission. No significant differences in demographic variables were present between enrolled and excluded patients.

Imaging protocol

The distinction between RCVS and primary angiitis of the central nervous system was diagnosed with reference to the RCVS2 score.[15] At all-time points, serial MRI included axial conventional T1-weighted imaging (T1WI), FLAIR imaging, diffusion-weighted imaging, and MRA, all performed using a 1.5-T superconducting magnet (Signa EXCITE or HDX; GE Medical Systems, Milwaukee, WI) with a quadrature head coil. Pulse sequences were as follows: FLAIR (repetition time (TR)/echo time (TE), 8000/120 ms; inversion time (TI), 2000 ms; section thickness/section gap, 7.0/1.0 mm; field of view (FOV), 24 × 24 cm; number of excitations (NEX), 1; matrix, 256 × 224), T1WI (TR/TE, 2000/24 ms; TI, 750 ms; section thickness/section gap, 7.0/1.0 mm; FOV, 24 × 24 cm; NEX, 2; matrix, 256 × 192), and three-dimensional time-of-flight MRA (TR/TE, 27/6.8 ms; flip angle, 16°; bandwidth, 14.7 Hz; FOV, 18 × 18 cm; slab thickness, 70 mm; slice thickness, 1.2 mm; matrix 256 × 192, and NEX, 1). MRI scanning was completed within 13–15 min.

Definitions of variables

TCH was defined as a severe pain peaking within seconds. The presence of TCH was diagnosed by a thorough interview of the patient. TCH remission was defined as "the time at which the last TCH improved." Hypertensive emergency

was defined as systolic blood pressure over 180 mmHg or diastolic blood pressure over 120 mmHg.

White matter hyperintensity (WMH) was defined as hyperintensity on FLAIR imaging without hypointensity on T1WI. Progression of WMH after RCVS was assessed by comparison of MRI at onset and 3 months after onset. We assessed progression of periventricular WMH using the Fazekas scale,[6] and WMH progression was considered present if the visual rating increased by at least one grade. Progression of DSWMH after RCVS was defined as the occurrence of new WMH in at least one of four regions of subcortical white matter (frontal, parietal, occipital, or temporal), the basal ganglia, and the infratentorial region. Localization of vasoconstriction of the cerebral arteries was evaluated on MRA. Centripetal propagation of vasoconstriction (CPV) was defined as vasoconstriction that progressed from distal arteries at the time of TCH (i.e., on MRA obtained within 72 h of RCVS onset) to the major cerebral arteries of the circle of Willis defined as the internal cerebral artery, A1 portion of the anterior cerebral artery (ACA), and/or P1 portion of a PCA, and M1 portion of the MCA, basilar artery, and vertebral artery on MRA obtained within 48 h of TCH remission.

We divided RCVS patients into two groups depending on the presence or absence of HPS. Furthermore, we divided RCVS patients into two groups depending on the presence or absence of HVS in a cortical artery, and we investigated differences in clinical features. HVS was defined as focal, tubular, or serpentine hyperintensities in the subarachnoid space, relative to those in the cerebrospinal fluid and corresponding with the typical arterial course.[11] Furthermore, we defined HPS as hyperintensities of a PCA within the ambient cistern, medial to the tentorium cerebelli that typically visualized in 1 or 2 adjacent slices and that can extend into the quadrigeminal cistern on FLAIR imaging [Figures 1 and 2]. In other words, we defined HPS as HVS of the P1 and/or P2 portion (P1–2) of a PCA. We defined "HVS in a cortical artery" as HVS in the ACA, MCA, or a PCA at the level of a cortical artery [Figure 3].

MRI findings were interpreted by at least two senior stroke neurosurgeons (M.S. and S.O., with 38 and 33 years of experience, respectively). When neurosurgeons disagreed about findings, they consulted with each other to reach a consensus decision. Outcomes were assessed at 3–6 months after onset using modified Rankin scale scores.

Treatment protocol

Vasoactive medications such as triptans were stopped, and symptomatic analgesic treatment was used in all patients without a standard protocol. Oral administration of cilostazol or lomerizine hydrochloride was recommended
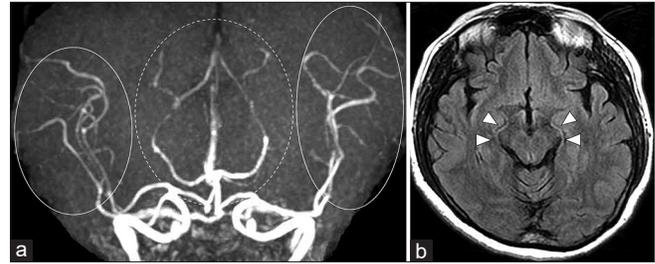
Figure 1: Images from a 55-year-old woman with reversible cerebral vasoconstriction syndrome. (a) The initial magnetic resonance angiography obtained 8 h after onset of thunderclap headache shows vasoconstrictions in bilateral P2–3 portions of the posterior cerebral arteries (dotted circle), and bilateral M2–3 portions of the middle cerebral artery (circle). (b) Fluid-attenuated inversion recovery obtained at the same time as magnetic resonance angiography shows bilateral hyperintense posterior cerebral arteries signs in the crural and ambient cisterns (white arrowheads).
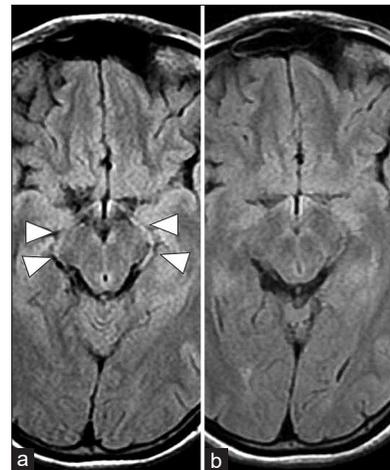
Figure 2: Images from a 17-year-old woman with reversible cerebral vasoconstriction syndrome. (a) Fluid-attenuated inversion recovery obtained 4 days after onset of Thunderclap headache shows bilateral hyperintense posterior cerebral arteries signs (HPSs) in the crural and ambient cisterns (white arrowheads). (b) In the chronic phase of fluid-attenuated inversion recovery, findings of HPS have disappeared.

for the prevention of cerebral vasoconstriction. Administration of steroids was avoided. For patients with severe TCH, low-dose propofol (30–50 mg/h) was infused intravenously. For five of the ten patients who experienced a hypertensive emergency, nicardipine was used with intravenous infusion of the dose adapted to normalize blood pressure levels.

Institutional review board approval

Study approval was obtained from the Institutional Review Board for Clinical Research (approval no. 21R-037) and Conflict of Interest Management Committee (approval
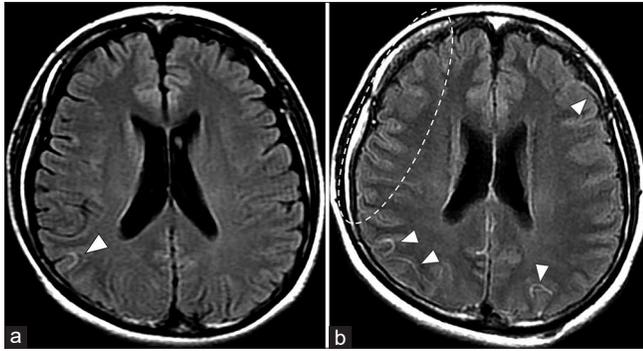
Figure 3: Images from a 31-year-old woman with reversible cerebral vasoconstriction syndrome. (a) Initial fluid-attenuated inversion recovery obtained 2 days after onset shows Hyperintense vessel signs in the right cortical artery (white arrowheads). (b) At 11 days after onset, centripetal propagation of vasoconstriction in bilateral P1–2 portions of the posterior cerebral arteries, left M1 portions, basilar artery, and right vertebral artery are apparent on follow-up magnetic resonance angiography. Fluid-attenuated inversion recovery obtained at the same time as magnetic resonance angiography shows multiple hyperintense vessel signs of the cortical artery (white arrowheads and dotted circle).

no. 21-037) at our university. We performed MRI after obtaining oral informed consent from each patient.

Statistical analysis

In patients with RCVS, the significance of clinical factors potentially associated with HPS and HVS in a cortical artery was determined by the two-tailed Fisher's exact test. Continuous variables (age and timing of initial MRI after onset) were tested using an independent sample two-tailed Student's *t*-test. Clinical factors showing a significance level of $P < 0.10$ were entered into multivariate logistic regression analysis with the presence of HPS and HVS in a cortical artery as the dependent variable. All statistical analyses were performed using commercially available software (Statistical Package for the Social Sciences [SPSS] for Windows version 22.0; Mehta and Patel/SPSS, Chicago, IL).

RESULTS

Incidence of HPS in the normal control group

Among the 166 patients in the normal control group (without asymptomatic arteriosclerotic stenosis of the PCA), the prevalence of HPS was 2% (3/166).

Pre-onset clinical features and HVS

[Table 1] summarizes HVS in various cerebral arteries on FLAIR imaging in RCVS patients. Of the major trunks of the cerebral artery, even if vasoconstriction of M1 and A1 was present, HVS of the M1 and M2 portions of the MCA and

Table 1: Hyperintense vessel sign on MRI in patients with reversible cerebral vasoconstriction syndrome.

	Number of cases	
	Initial MRI	Follow-up MRI at time of TCH remission
A1 and/or A2 portion of the ACA	0	0
M1 and/or M2 portion of the MCA	0	0
P1 portion of a PCA	2	2
P2 portion of a PCA	20	17
P1 and/or P2 portion of a PCA	21	17
Basilar artery	3	2
Vertebral artery	1	0
PICA	1	1
Cortical artery of the ACA	2	2
Cortical artery of the MCA	34	21
Cortical artery of a PCA	19	18

ACA: Anterior cerebral artery, MCA: Middle cerebral artery, PCA: Posterior cerebral artery, MRI: Magnetic resonance imaging

A1 and A2 portions of the ACA were not observed on initial or follow-up MRI. Among the major trunks of the cerebral artery, HPS was the most common, appearing in 21 of 80 cases, 26%. Most HPS were in the P2 portion of a PCA (20 of 21 cases) and HPS in the P1 portion were seen in only two cases. RCVS in patients with HVS in a cortical artery (ACA, MCA, and PCA) was seen in 38 patients (48%).

The sensitivity and specificity of HPS on initial MRI as a diagnostic method (or "marker?") for RCVS were 26% (21/80) and 98% (163/166), respectively, with reference to the normal control group. In RCVS patients with findings of HPS and HVS for a cortical artery, no relevant pre-onset clinical factors were found [Table 2].

Findings of MRI and post-onset clinical factors

Among all patients, 73% (58 of 80 cases) underwent MRI during the acute phase within 72 h of onset. Among the localizations of vasoconstriction, vasoconstriction of A2–3 was significantly associated with the presence of HPS [Table 3]. In RCVS patients with findings of HPS, none of vasoconstriction other than A2–3, timing of initial MRI after onset, associated lesions on MRI, or CPV showed significant associations [Table 3]. However, no significant differences were evident, 12 of the 21 cases (57%) in which HPS findings were found on initial MRI showed a high rate of CPV findings on subsequent MRI.

In RCVS patients with findings of HVS in a cortical artery, timing of initial MRI after onset and CPV showed no significant association [Table 3]. On the other hand, vasoconstriction of the M1 portion of the MCA and P1 portion of a PCA was significantly associated in RCVS patients with findings of HVS in

Table 2: Comparison of clinical features of hyperintense vessel sign of P1–2 and findings of hyperintense vessel sign in a cortical artery in patients with RCVS.

	Hyperintense PCA sign on initial MRI			Hyperintense vessel sign in a cortical artery (ACA, MCA, PCA) on initial MRI			All patients
	Present	Absent	*P*-value	Present	Absent	*P*-value	
Number of patients (%)	21 (26)	59 (74)		38 (48)	42 (52)		80
Age (years)							
Mean±SD	45±16	38±13	0.075	40±14	40±14	0.780	40±14
Range	15-70	13-61		13-70	15-67		13-70
Sex (male/female)	3:18	12:47	0.748	5:33	10:32	0.262	15:65
History of RCVS (%)	5 (24)	15 (25)	1.000	10 (26)	10 (24)	0.803	20 (25)
History of migraine	15 (71)	39 (66)	0.789	27 (71)	27 (64)	0.634	54 (68)
(With aura) (%)	5 (24)	10 (17)	0.523	7 (18)	8 (19)	1.000	15 (19)
Trigger (%)							
Pregnant or postpartum	3 (14)	10 (17)	1.000	5 (13	8 (19)	0.554	13 (16)
Emotional situations	13 (62)	22 (37)	0.073	19 (50)	16 (38)	0.368	35 (44)
Bathing-related	3 (14)	6 (10)	0.691	3 (8)	6 (14)	0.487	9 (11)
SSRI use	6 (29)	10 (17)	0.341	7 (18)	9 (21)	0.786	16 (20)
Hypertensive emergency	4 (19)	5 (8)	0.232	6 (16)	3 (7)	0.296	9 (11)

PCA: Posterior cerebral artery, hyperintense PCA sign, hyperintense vessel sign in P1 and/or P2 of a posterior cerebral artery; ACA: Anterior cerebral artery, SD: Standard deviation; RCVS: Reversible cerebral vasoconstriction syndrome, SSRI: Selective serotonin reuptake inhibitor, TCH: Thunderclap headache. Values represent n (%) unless otherwise stated. Percentages in the "Number of patients" row show percentages of the total number of patients, whereas percentages in the "Present" and "Absent" columns indicate percentages of patients with presence or absence of hyperintense vessel sign in P1 and/or P2 (or hyperintense vessel sign in a cortical artery), respectively

a cortical artery on initial MRI [Table 3]. Among the associated lesions, the only significant association with the presence of HVS in a cortical artery was the presence of DSWMH on initial MRI (*P* = 0.036) and progression of DSWMH on MRI in the chronic phase (*P* = 0.042). Of the 28 patients who displayed DSWMH on initial MRI, 20 showed progress of DSWMH in the chronic phase. Conversely, of the 29 patients with progression of DSWMH in the chronic phase, 20 had DSWMH on initial MRI, representing a significant difference (*P* < 0.001).

After 3–6 months, modified Rankin scale score was 0 in all 80 of these RCVS patients, and all were able to resume prior daily activities.

Changes to findings of HPS and HVS in a cortical artery on follow-up MRI

On follow-up MRI at the time of TCH remission, the frequency of clarification of findings and new findings of HPS and HVS in a cortical artery was low, at about 10% [Table 3]. Conversely, the frequency of disappearance of findings of HPS and HVS in a cortical artery tended to be as high as about 40% [Table 3].

Clinical factors related to HPS and HVS in a cortical artery on multivariate analysis

Multivariate step-wise logistic regression analysis revealed that the presence of vasoconstriction in the A2–3 portion

was significantly associated with the presence of HPS (*P* = 0.011) [Table 4]. Multivariate logistic regression analysis identified the presence of vasoconstriction in the M1 portion (*P* = 0.042) and ("or?") P1 portion (*P* = 0.025) on initial MRA, DSWMH on initial MRI (*P* = 0.030), and progression of DSWMH at the time of chronic stage (*P* = 0.030) were all significantly associated with the presence of HVS in a cortical artery [Table 4].

Inter-reader reproducibility

Inter-reader agreement was excellent for both HPS (97.5% agreement, κ = 0.935 (95% confidence interval [CI] 0.780–0.982) and HVS of cortical arteries (93.8% agreement, κ = 0.875 (95%CI 0.724–0.942)) on initial MRI in RCVS patients.

DISCUSSION

Mechanism and clinical significance of HPS findings in RCVS

While the mechanisms underlying HVS remain to be established, stationary blood and slow antegrade or retrograde collateral circulation at a site peripheral to arterial occlusion or severe stenosis have been suggested as possible explanations for HVS.[10,12] Therefore, for example, for HVS of M1 or A1 to occur, an occlusion or severe stenosis must be present in the ICA, as the artery proximal to the M1 or A1.

Table 3: Findings of MRI and post-onset factors in RCVS patients with hyperintense vessel sign of P1–2 and hyperintense vessel sign in a cortical artery.

	Hyperintense PCA sign			Hyperintense vessel sign of cortical arteries (ACA, MCA, PCA)			All patients
	Present	Absent	*P*-value	Present	Absent	*P*-value	
Number of patients (%)	21 (26)	59 (74)		38 (48)	42 (52)		80
Timing of initial MRI after onset (days)							
Mean±SD (days)	3±2	3±2	0.517	3±2	3±2	0.939	3±2
Range (days)	1–7	1–7		1–7	1–7		1–7
Initial MRI obtained within 72 h after onset (%)	14 (67)	44 (75)	0.406	26 (68)	32 (76)	0.446	58 (73)
Localization of vasoconstriction vessel on initial MRA (%)							
A1 portion	0	3 (5)	0.563	2 (5)	1 (2)	0.601	3 (4)
A2–3 portion	8 (38)	8 (14)	0.025	7 (18)	9 (21)	0.786	16 (20)
M1 portion	1 (5)	7 (12)	0.674	7 (18)	1 (2)	0.020	8 (10)
M2–3 portion	19 (90)	51 (86)	1.000	36 (95)	34 (81)	0.092	70 (88)
P1 portion	3 (14)	5 (8)	0.350	7 (18)	1 (2)	0.020	8 (10)
P2–3 portion	20 (95)	52 (88)	0.674	33 (87)	39 (93)	0.467	72 (90)
Basilar artery	2 (9)	0	0.066	1 (3)	1 (2)	1.000	2 (3)
Vertebral artery	3 (14)	2 (3)	0.110	3 (8)	2 (5)	0.664	5 (6)
Associated lesions on MRI							
Cerebral lesion (SAH, PRES, infarction, ICH)	4 (19)	13 (22)	1.000	11 (29)	6 (14)	0.170	17 (21)
Cortical SAH	1 (5)	9 (15)	0.278	7 (18)	3 (7)	0.180	10 (13)
PRES	1 (5)	3 (5)	1.000	2 (5)	2 (5)	1.000	4 (5)
Infarction	1 (5)	2 (3)	1.000	2 (5)	1 (2)	0.602	3 (4)
ICH	1 (5)	0	0.262	1 (3)	0	0.475	1 (1)
DSWMH							
Initial MRI	10 (48)	18 (31)	0.188	18 (47)	10 (24)	0.036	28 (35)
Progression at time of chronic stage	11 (52)	19 (32)	0.121	19 (50)	11 (26)	0.038	30 (38)
Follow-up MRI (%)							
CPV*	12 (57)	25 (45)	0.445	21 (57)	16 (41)	0.251	37 (49)
Hyperintense vessel sign (%)							
Clarification of findings	2 (10)	–	–	5 (13)	–	–	8 (10)
Disappearance of findings	8 (38)	–	–	15 (39)	–	–	23 (29)
New appearance	0	6 (10)	0.332	1 (3)	2 (5)	1.000	9 (11)

PCA: Posterior cerebral artery, hyperintense PCA sign, hyperintense vessel sign in the P1 and/or P2 portion of a posterior cerebral artery, ACA: Anterior cerebral artery, SD: Standard deviation, PRES: Posterior reversible encephalopathy syndrome, ICH: Intracerebral hemorrhage, DSWMH: Deep and subcortical white matter hyperintensity, CPV: Centripetal propagation of vasoconstriction. Values represent n (%) unless otherwise stated. Percentages in the "Number of patients" row show percentages of the total number of patients, whereas percentages in the "Present" and "Absent" columns indicate percentages of patients with presence or absence of hyperintense vessel sign in P1 and/or P2 (or hyperintense vessel sign findings in a cortical branch), respectively. *CPV at the time of TCH remission was not confirmed in four cases, and population parameters of this item differ, MRA: Magnetic resonance angiography

Since severe vasoconstriction of the ICA is rarely associated with patients with RCVS, obtaining HVS findings in M1 and A1 seemed rare in this study.

On the other hand, when performing endovascular surgery for aneurysms of a PCA, the low incidence of complications due to parent artery occlusion is related to the rich anastomotic collaterals that exist between the area of the PCA and the areas of other arteries, which include: (1) collateral circulation between the lateral posterior choroidal artery (branch of the P2 segment) and the anterior choroidal arteries (branches of the ICA); (2) collateral circulation between the long circumflex arteries (branches of the P1 segment) and the superior cerebellar artery territory at the level of the quadrigeminal plate; (3) collateral circulation between the splenial artery (branch of the P3–P4 segments) and posterior pericallosal artery (branch of the ACA); and (4) collateral circulation between the inferior temporal branches of PCAs and the superior temporal branches of the MCA.[4] That is, PCAs show collateral circulation to many cerebral arteries such as the ICA, superior cerebellar artery, ACA, and MCA.

Therefore, due to the usual presence of rich collateral flows around PCAs, HPS rarely appears because blood flow through the proximal PCA (P1–2) would be expected to be

Table 4: Results of multivariate logistic regression analysis for the presence of hyperintense PCA sign and hyperintense vessel sign in a cortical artery.

	Odds ratio	95%CI	*P*-value
Hyperintense PCA sign			
Vasoconstriction of A2-3 portion on initial MRA	4.630	1.429–15.152	0.011
Hyperintense vessel sign in a cortical artery			
Vasoconstriction of M1 portion on initial MRA	9.259	1.082–76.923	0.042
Vasoconstriction of P1 portion on initial MRA	20.4	1.453–250	0.025
DSWMH on initial MRI	2.882	1.110–7.463	0.030
Progression of DSWMH at the time of chronic stage	2.817	1.105–7.194	0.030

PCA: Posterior cerebral artery, hyperintense PCA sign, hyperintense vessel sign in the P1 and/or P2 portion of a posterior cerebral artery, DSWMH: Deep and subcortical white matter hyperintensity, MRA: Magnetic resonance angiography

maintained through these rich collaterals even if peripheral PCA flow is decrease. Furthermore, this study found no significant association between the development of HPS and vasoconstriction of the basilar artery or vertebral artery as arteries proximal to the PCA. In addition, vasoconstriction of the P1 and P2–3 portions was not significantly associated with the development of HPS. We, therefore, speculated that HPS may be caused by the coexistence of not only decreased flow due to vasoconstriction in PCA peripherals, but also decreased flow due to vasoconstriction of multiple other arteries associated with the collateral circulation of the PCAs. Because HPS comprehensively evaluate flow decreases due to vasoconstriction of not only PCAs, but also multiple vessels associated with the network of collateral circulation of the PCAs, we think that HPS represent a neuroradiological finding suitable for diagnosing RCVS in the acute phase. We believe that absence of HPS is unsuitable for excluding the diagnosis due to the relatively low frequency of this sign (low sensitivity), but their presence is extremely useful for definitive diagnosis of RCVS. Because vasoconstriction vessels are located peripherally during the acute phase,[17,18] the diagnosis of RCVS appears to be missed frequently.[3,5] We, therefore, emphasize that this HPS finding is extremely useful when clinicians encounter cases in which they are confused about the acute diagnosis of RCVS.

In this study, the vasoconstriction that occurred in A2–3, which was associated with the collateral circulation of PCAs, was significantly associated with the development of HPS. Although M2–3 and P2–3 are similarly associated

with the collateral circulations of the PCA and PCAs, no significant association was evident between M2–3 and P2–3 vasoconstriction and HPS findings. In this study, the incidences of M2–3 and P2–3 vasoconstrictions were as high as ≥85% with or without findings of HPS. We, therefore, speculate that whether M2–3 and P2–3 vasoconstriction results in HPS depends on individual differences in the degree or location of the collateral circulation associated with the PCAs.

Besides RCVS, other disorders that may show HPS findings include PCA atherosclerosis. This can be easily distinguished from RCVS by the presence or absence of TCH as a symptom and vasoconstrictions of multiple other arteries.

Clinical factors related to HVS in a cortical artery

In our study, MCA was the most frequent site of HVS of cortical arteries, but the cause remains unknown. One possible reason is that HVS of the insular-opercular segment of the MCA around the sylvian fissure are easily identified. In this study, because M1 and P1 are vessels proximal to the cortical artery, vasoconstrictions of the M1 and P1 were significantly associated with findings of HVS in a cortical artery on initial MRI of RCVS patients. HVS in a cortical artery also correlated significantly with the presence of DSWMH on initial MRI, and progression of DSWHM on MRI in the chronic phase. We interpret DSWMH on the initial MRI as a lesion caused by microcirculatory dysfunction due to some previous cerebral small vessel disease.[14] Maintenance of cerebral arteriolar function, especially vascular endothelial function, is known to be required for the development of collateral circulation through cerebral pial artery anastomosis.[8,13] Given this situation, when DSWMH was caused by some cerebral small vessel disease in the past, collateral circulation may have been impaired by the vascular endothelial dysfunction. In addition, vascular endothelial dysfunction is a central pathological condition in RCVS[2] and is also potentially present in migraine patients,[19] who often have a history of RCVS. Based on these findings, RCVS patients with DSWMH on initial MRI may be more likely to have impaired collateral circulation. We also speculate that because HVS in a cortical artery indicates a decrease in antegrade circulation due to vasoconstriction of both peripheral vessel and major trunk, it would be significantly associated with the progression of DSWMH in the chronic phase of RCVS. From the above, even with the same HVS findings, the pathological conditions underlying HPS and HVS in cortical arteries differ.

Changes to findings of HPS and HVS in a cortical artery

We reported that, from findings of sequential MRA before and after TCH remission, CPV gradually progresses after the onset of RCVS, peaks at the time of TCH remission, and does

not progress further upon TCH remission.[18] That is, at the time of TCH remission, the vasoconstriction of the major trunks, which are vessels proximal to the cortical artery, has bottomed out. Therefore, on MRI performed at the time of TCH remission in our study, the probability of a new appearance of HPS or HVS findings in cortical arteries was extremely low, and the probability of disappearance reached about 40%. Although HPS and HVS findings in cortical arteries may be clarified by follow-up MRI, we believe that these findings are more suitable for diagnosing of RCVS on initial MRI in the acute phase.

Limitations

In this study, MRI findings were interpreted by senior stroke neurosurgeons, but blinding to the timing of imaging was not performed. Because nimodipine has not been approved for use in Japan as a calcium channel antagonist for preventing vasoconstriction, we could not administer this drug. Our results thus may not be generalizable to hospital facilities using nimodipine. This was a retrospective study of a small group of patients, and prospective studies with a greater number of cases are necessary in the future.

CONCLUSION

Because rich collateral flows exist around the PCAs, HPS rarely appear; that is, flow through proximal PCAs would be expected to be maintained through the rich collateral vasculature even if peripheral PCA flow is decreased. An absence of HPS is therefore unsuitable for excluding the diagnosis of RCVS. However, HPS findings obtained from patients with suspected RCVS offer clinicians credible evidence of extreme flow decreases due to vasoconstriction in peripheral PCAs and other arteries associated with the collateral circulation of PCAs. Conversely, HVS in a cortical artery tend to reflect slow antegrade circulation due to vasoconstriction of peripheral vessels and major trunks and were significantly associated with progression of DSWMH in the chronic phase of RCVS. Although the diagnosis of RCVS is frequently missed because the vasoconstriction vessels are located peripherally during the acute phase, we emphasize that both HPS and HVS in a cortical artery are extremely useful when clinicians encounter cases in which they are confused about the acute diagnosis of RCVS.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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