Serial vessel wall enhancement pattern on high-resolution vessel wall magnetic resonance imaging and clinical implications in patients with central nervous system vasculitis

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Abstract

Objective

High-resolution vessel wall imaging (HR-VWI) often demonstrates strong and concentric vessel wall enhancement (VWE) in patients with central nervous system vasculitis (CNS-V). However, little is known about follow-up VWE characteristics and monitoring the response to treatments. The aim of this study was to investigate serial VWE patterns and its clinical practice through the management of CNS-V.

Methods

We extracted 9 patients with diagnosed of CNS-V who underwent serial HR-VWI (baseline, 1st follow-up, and 2nd follow-up) from Cleveland Clinic CNS vasculopathy registry. VWE were analysed in 17 intracranial artery segments. VWE was graded on a 3-point scale (0; none, 1; mild/eccentric, and 2; strong/concentric). VWE grade for each arterial segment was summed to create a total VWE score. We investigated the relationship between serial VWE patterns and clinical course.

Result

In unique 153 intracranial arterial segments, 39 arteries (25.5%) had strong/concentric VWE on baseline HR-VWI. The positive rates of concentric VWE have decreased to 12.4% (19/153) at 1st follow-up and (10/153) 6.5% at 2nd follow-up, respectively ($p<0.001$). Mean total VWE scores have significantly decreased over time courses ($p=0.034$). Two patients had relapse at 1st follow-up image. In relapse cases, mean total VWE scores have worsened at 1st follow-up (baseline:2.0 to 1st follow-up: 6.0). After intensive immunosuppressive treatment, mean VWE scores have improved at 2nd follow-up (1st follow-up: 6.0 to 2nd follow-up: 2.0).

Conclusion

Decreasing contrast VWE at follow-up images may indicate good response to treatment in CNS-V. By contrast, relapse patients might have temporal VWE worsening during the clinical course.

Key words
central nervous system vasculitis, MRI, follow-up study, recurrence

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Introduction

Central nervous system vasculitis (CNS-V) is a rare inflammatory brain disease affecting the medium and small vessels of the CNS (1, 2). Although diagnostic criteria were proposed by Calabrese and Mallek in 1988 (3), establishing the diagnosis of CNS-V can be a challenging due to the presence of wide mimicking conditions and the lack of a specific diagnostic marker as opposed to systematic vasculitis (4, 5). With the advance of neuroimaging modalities, high-resolution vessel walls magnetic resonance imaging (HR-VWI) has emerged as a non-invasive technique directly visualising vessel wall inflammation and oedema in patients with CNS-V (6-9). HR-VWI often demonstrates smooth, homogeneous, concentric arterial wall thickening and strong enhancement in patients with CNS-V, in comparison with the mild to no vessel enhancement of reversible cerebral vasoconstriction syndrome (RCVS) and other intracranial vasculopathies (6-10). Previous studies mainly focused on the technical aspects and utility in the differential diagnosis of intracranial artery disease, whereas only few studies described the temporal vessel wall enhancement (VWE) characteristics of CNS-V after immunosuppressive treatments (11, 12).

CNS-V has been considered as a relapsing-remitting disease with a heterogeneous disease course (13-16). Recently published long-term follow-up studies showed that favourable outcome was observed in 50-70% of CNS-V patients (13-16). By contrast, relapse affected approximately 30-50% of CNS-V patients (13-15) and the annual relapse rate was 1.4 under the immunosuppressive treatments (15). Repeated clinical, cerebral spinal fluid (CSF), and neuroimaging can be informative to assess the disease activity through the management of patients with CNS-V. We hypothesised that serial HR-VWI may be helpful for monitoring the response to the treatments of patients with CNS-V. With immunosuppressive treatments, majority of remission patients diminished the degree and extent of VWE or remained stable enhancement status on follow-up HR-VWI in the previous reports (11, 12). However, no reports in the relevant literature appear to have described serial VWE findings in the relapse cases. The aim of this study was to evaluate the serial VWE patterns on HR-VWI and its clinical implications in patients with CNS-V.

Subjects and methods

Study design and cohort

Patients were identified from Cleveland Clinic prospective CNS vasculopathy registry. This bioregistry has been set up to analyse the clinical, neuroradiographic, and laboratory features of patients with CNS-V, RCVS, and other intracranial vasculopathies seen at Cleveland Clinic. Data was collected, including history of signs and symptoms at presentation, as well as over time, diagnostic tests, including laboratory work, neuroradiographic studies (*i.e.* computed tomography (CT), magnetic resonance image (MRI), and angiography), and biopsy data. For this study, we included patients with the following 1) diagnosis of CNS-V based on pathologic findings of vasculitis on brain tissue and/or radiologic findings of cerebrovascular abnormalities with an inflammatory CSF and exclusion of other entities, 2) demonstration of serial HR-VWI (baseline, 1st follow-up, and 2nd follow-up), and 3) availability of information on treatment and outcome. Cleveland Clinic Institutional Review Board approved the protocol for this study.

Diagnosis of CNS-V and definitionof relapse

The patients with CNS-V were diagnosed on the basis of established clinical diagnostic criteria proposed by Calabrese and Mallek (3). Biopsy proven CNS-V was considered to be the presence of granulomatous, lymphocytic or necrotising vasculitis of medium to small size vessels in the brain tissue specimens. In cases without evidence of histological confirmation, the diagnosis of CNS-V was made according to the clinical pictures, neuroimaging findings, and inflammatory CSF profiles (16). Finally, the diagnosis of all CNS-V cases was confirmed

by expert rheumatologist (R.HA) and neurologist (K.U.). All patients were followed over a mean time of 15.6 month to ensure the accuracy of the final diagnosis.

Relapse was defined as a new neurological event associated with new significant radiological abnormalities (new cerebral infarct, extension of white matter lesion, appearance of gadolinium enhancements, and worsening of arterial stenosis), leading to an intensification of treatment by the treating physician (13-15).

HR-VWI and visual VWE scores

All neuroimages were evaluated by one neurologist (T.S), blinded to clinical, laboratory, and pathological findings, and assessments were adjudicated by consensus when necessary. Brain MRI was performed using a commercially available echo planar instrument operating at 3.0 Teslas (Skyra or Trio; Siemens, Erlangen, Germany). HR-VWI protocol included 2D black-blood contrast-enhanced T1-weighted sequences and time-of-flight magnetic resonance angiography (MRA) of the circle of Willis. Detailed protocol, sequence, and acquisition of MRA and HR-VWI at Cleveland Clinic have been reported previously (11).

The following intracranial vessel segments were assessed on HR-VWI: internal carotid artery (ICA: C4-C7 segment), anterior cerebral artery (ACA: A1, A2 segment), middle cerebral artery (MCA: M1, M2 segment), posterior cerebral artery (PCA: P1, P2 segment), vertebral artery (VA: V4 segment), and basilar artery (BA: union-top).

The presence or absence of VWE was determined by comparing pre-gadolinium and post-gadolinium vessel wall imaging. VWE grade was classified on a 3-point scale: 0, none or signal equal to that of the pre-contrast image; 1, eccentric enhancement if there was clearly non-uniform and non-circumferential thin-wall artery with mild hyperintensity; 2, concentric enhancement if there was the whole wall circumference and thick-wall artery with strong hyper intensity (11). We generated the quantitative VWE score to provide a more detailed assessment of VWE in the intracranial arteries. In this modification, we assigned VWE grade (0 for none, 1 for mild/eccentric, and 2 for strong/concentric) for each arterial segments. The VWE grade assigned for each arterial segment was summed up to create a total VWE score (Fig. 1-3). MRA findings were compared with the HR-VWI findings for concordance of abnormalities. We assessed the appearance of the arterial irregularity, and the presence of segmental arterial dilatation in proximal (ICA, M1, A1, P1, VA, BA) arterial segments, middle (M2, A2, P2) arterial segments, and small distal branches (16).

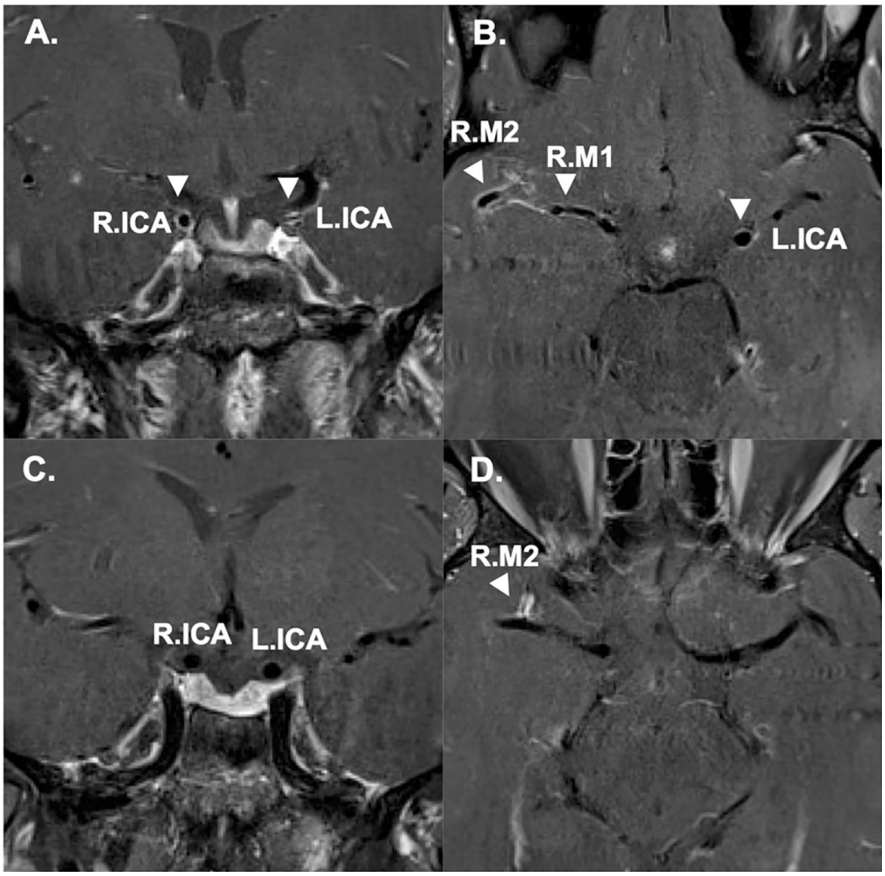

Fig. 1. Example of quantitative VWE score (Case 3: A 35-year-old woman with good clinical course). Baseline 3T-HRMRI post-gadolinium (**A**: Coronal image and **B**: Axial image).
A, B: Multiple strong smooth, concentric wall enhancements (arrow-heads) were identified in the right ICA (2 points), M1 (2points), M2 (2 points) and the left ICA (2points). Baseline total visual VWE score was 8.
Follow-up 3T-HRMRI post-gadolinium at 19 months (**C**: Coronal image and **D**: Axial image)
C, D: Strong smooth, concentric wall enhancement (arrow-head) remained in the right M2 segment (2 points). Interval resolution of vessel wall enhancement was observed in the bilateral ICA and the right M1 segments. Follow-up total visual VWE vessel score was 2.

Statistical analysis

We evaluated following findings on serial HR-VWI (Baseline, 1st follow-up, and 2nd follow-up); 1) the positive rates of concentric intraluminal enhancement, 2) visual VWE score, and 3) serial VWE patterns according to clinical course (relapse and without relapse). The changes of serial VWE were assessed on the basis of the previous report by Kwee *et al*. (Fig. 5) (18). Continuous variables are expressed as mean ± standard deviation (SD) in the text and tables. The significance of intergroup differences was assessed using a χ^2 test for categorical variables and a Mann-Whitney and Kruskal-Wallis U-test for continuous variables in univariate analysis. Values of $p<0.05$ were considered to indicate statistically significant differences. All statistical analyses were performed using Statistical Package for the Social Sciences software for Windows (SPSS v. 26.0, Chicago, IL).

Table I. Clinical characteristics and baseline MRI findings.

	All (n=9)
Age, (y)	40.2±11.6
Male, n (%)	4 (44.4)
Biopsy-proven, n (%)	5 (55.6)
Interval from onset to initial HR-VWI, (months)	5.6±7.9
Immunosuppressive treatment before baseline HR-VWI, n (%)	3 (33.3)
Glucocorticoid	3 (33.3)
Cyclophosphamide	2 (22.2)
Azathioprine	1 (11.1)
Mean follow-up period, n (months)	15.6±7.4
Relapse cases during follow-up, (%)	2 (22.2)
Arterial involvement on baseline MRA, n (%)	
Proximal segment (ICA, M1, A1, P1, VA, BA)	3 (33.3)
Middle segment (M2. A2, P2)	6 (66.6)
Small distal branch	2 (22.2)
No arterial stenosis	3 (33.3)
VWE patterns on baseline HR-VWI, n (%)	
Concentric VWE (Grade 2)	7 (77.8)
Eccentric VWE (Grade 1)	2 (22.2)
None (Grade 0)	1 (11.1)
Mean numbers of arterial segments with concentric VWE	5.2±4.7
Mean total visual VWE scores	9.3±9.1

MRI: magnetic resonance imaging: HR-VWI: high-resolution vessel wall image; MRA: magnetic resonance angiography; ICA: internal carotid artery; VA: vertebral artery; BA: basilar artery; VWE: vessel wall enhancement.

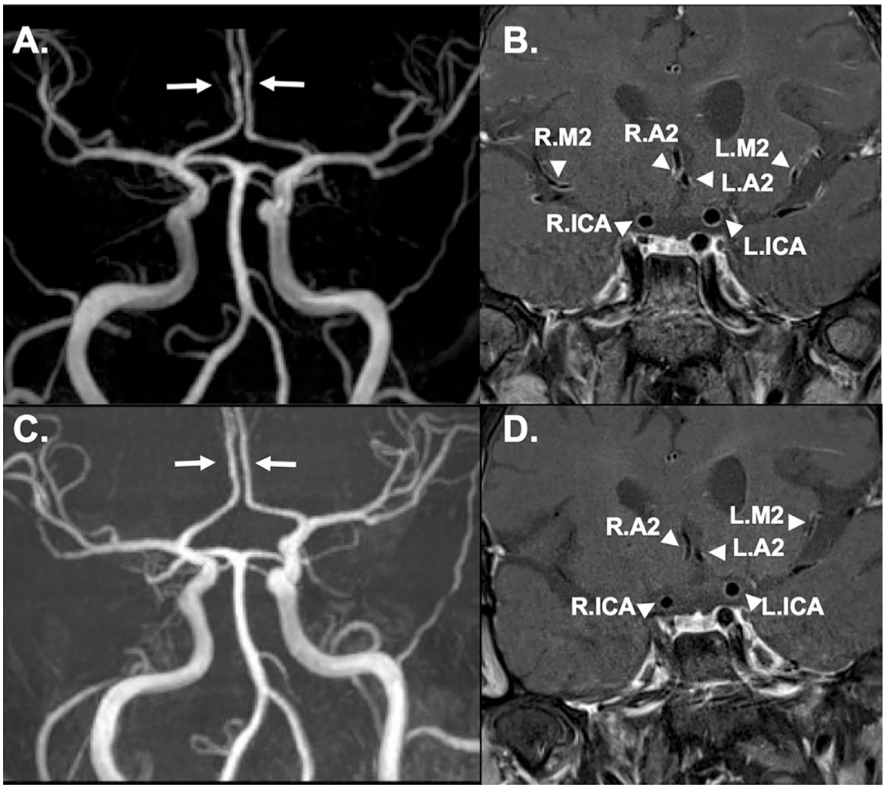

Fig. 2. Numerous strong/concentric VWE with mild vessel narrowing. (Case 5: A 46-year-old man with good clinical course).
Baseline MRA (**A**) and 3T-HRMRI post-gadolinium (**B**).
A: MRA shows the mild irregularities in the bilateral A2 segments(arrows).
B: Strong smooth, concentric wall enhancements (arrow-heads) were identified in the bilateral ICA, bilateral M2, and bilateral A2 segments.Baseline total visual VWE score was 20.
Follow-up MRA (**C**) and 3T-HRMRI post-gadolinium (**D**) at 4 months.
C: Follow-up MRA revealed the improvement of vessel irregularities in the bilateral A2 segments (arrows).
D: Although the left ICA remained concentric VWE, most affected segments decreased the degree of intraluminal enhancements (arrows). Follow-up total visual VWE score was 11.

Results

Total of the 201 patients were enrolled in Cleveland Clinic prospective CNS vasculopathy registry from March 2012 to December 2019. Among them, 37 patients (22 males; mean age 48.2±12.8 years) met the diagnostic criteria of CNS-V. Of these, we excluded 14 CNS-V patients without HR-VWI and 14 CNS-V patients with incomplete follow-up HR-VWI. The remaining 9 patients were analysed in the present study.

Clinical characteristics

Table I shows the baseline clinical characteristics of this study. Patient mean age at registration was 40.2±11.6 years, with 5 females and 4 males. Diagnosis of CNS-V was confirmed by histopathologic examination in 5 patients; and the remaining 4 patients were diagnosed by the clinical pictures, abnormal cerebral angiography, and inflammatory CSF findings. Mean interval from onset to initial HR-VWI was 5.6 months. Total of three patients received immunosuppressant therapy at the baseline HR-VWI; glucocorticoid in 3 cases, cyclophosphamide in 2 cases, and azathioprine in 1case. Mean follow-up period was 15.6 months and 2 patients had relapse during follow-up period.

Baseline MRA and HR-VWI findings

Table I summarises the baseline brain MRA and HR-VWI findings. Arterial involvements were observed in 6 of 9 patients (66.6%; all vascular segments: 1 case, both proximal and middle segment: 2 cases, only middle segment: 2cases, middle segment and small distal branch: 1 cases). On the baseline HR-VWI, strong/concentric VWE was identified in 7 of 9 patients (77.8%) and only one patient (11.1%) had no VWE. Mean numbers of arterial segments with concentric VWE were 5.2±4.7 and mean total VWE scores were 9.3±9.1. Table II showed detailed brain images findings and clinical data in the 9 CNS-V patients.

Serial HR-VWI findings

We assessed the unique 153 intracranial arterial segments of 9 patients on each image (baseline, 1st follow-up, and 2nd follow-up). Mean intervals from baseline to follow-up HR-VWI was 4.7±5.4 months for 1st follow-up and 10.0±5.6 months for 2nd follow-up. On the baseline HR-VWI, 39 of 153 (25.5%) arterial segments had strong/concentric VWE. The positive rates of strong/concentric VWE have decreased to 12.4% (19 of 153 arteries) at 1st follow-up image and 6.5% (10 of 153 arteries) at 2nd follow-up image, respec-

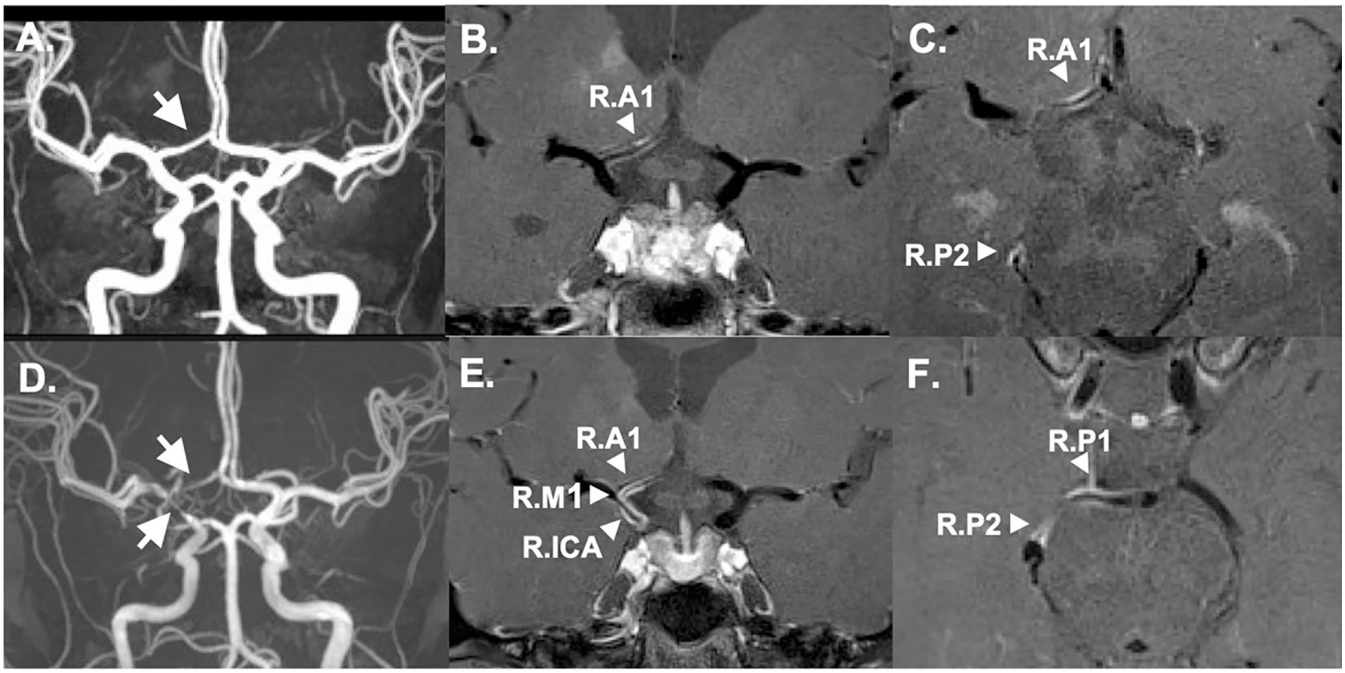

Fig. 3. Example of quantitative VWE score (Case 9: A 53-year-old woman with relapse).
Baseline MRA (**A**) and 3T-HRMRI post-gadolinium (**B**) Coronal image and (**C**) Axial image).
A: MRA shows the mild irregularity in the right A1 segment (arrow).
B, C: Strong smooth, concentric wall enhancements (arrow-heads) were identified in the right A1 (2 points) and P2 (2points). Baseline total visual VWE score was 4.
Follow-up MRA (**D**) and 3T-HRMRI post-gadolinium (**E**) Coronal image and (**F**) Axial image) at 7 months.
D: Follow-up MRA revealed progressive severe narrowing at the junction of the right terminal ICA, MCA, and ACA origin (arrows).
E, F: New strong smooth, concentric wall enhancements (arrow-heads) appeared in the right ICA (2 points), M1 (2 points), and P1 (2 points). Follow-up total visual VWE score was 10.

tively (p<0.001; Fig. 4a). Moreover, total VWE scores have significantly decreased over time courses (Baseline: 9.3±8.3, 1st follow-up: 6.0±6.3, 2nd follow-up: 3.2±6.7, p=0.034; Fig. 4b).

Serial VWE patterns and clinical course

Fig. 5 showed the changes of VWE patterns according to clinical status. In 7 patients without relapse, the numbers of arterial segments with strong/concentric VWE decreased over time course (baseline: 37 arteries (24.2%), 1st follow-up: 14 arteries (9.2%), and 2nd follow-up: 9 arteries (5.9%), Fig.5), as well as mean total VWE scores (baseline: 11.1, 1st follow-up: 6.0, and 2nd follow-up: 3.6, Fig. 5). Two patients (Case 6 and 7: Table II) remained stable degrees and extent of VWE on follow-up images (Case 6: Total VWE score; baseline: 26, 1st follow-up: 20, and 2nd follow-up: 21, Case 7: Total VWE score; baseline: 3, 1st follow-up: 2, and 2nd follow-up: 2).

Two patients (Case 8 and 9: Table II) had relapse at 1st follow-up image. The numbers of arterial segments with strong/concentric VWE increased at 1st follow-up HR-VWI (baseline: 2 to 1st follow-up: 5, Fig. 5), as well as mild/eccentric VWE (baseline: 0 to 1st follow-up: 2, Fig. 5). Mean total VWE scores have temporarily worsened at 1st follow-up (baseline:2.0 to 1st follow-up: 6.0, Fig. 5). All of 2 cases were treated with intravenous high dose methylprednisolone followed by cyclophosphamide and improved clinically stable. The numbers of arterial segments with strong/concentric VWE (1st follow-up: 5 to 2nd follow up: 1, Fig. 5) and mean total VWE scores (1st follow-up: 6.0 to 2nd follow-up: 2.0, Fig. 5) have decreased on 2nd follow-up HR-VWI.

Discussion

We investigated the serial VWE patterns on HR-VWI and its implications regarding the clinical status in patients with CNS-V. The numbers of arterial segments with strong/concentric VWE gradually decreased over time course [baseline: 37 arteries (24.2%), 1st follow-up: 14 arteries (9.2%), and 2nd follow-up: 9 arteries (5.9%)], as well as mean total VWE scores (baseline: 11.1, 1st follow-up: 6.0, and 2nd follow-up: 3.6) in patients without relapse. A case report by Saam *et al*. reported strong vessel wall enhancement in multiple arteries of a patient with intracranial arteritis (19). Follow-up imaging at 3 months showed a slight decrease in enhancement, and at 6 months, there was further substantial decrease with some persistent enhancement (19). Tsivgoulis *et al*. reported the case of a 45-year-old with CNS-V (20). Repeat follow-up HR-VWI at 3 and 9 months showed reduction and final resolution of vessel wall enhancement without relapse (20). Therefore, decreasing contrast VWE at follow-up images may indicate good response to treatment in patients with CNS-V.

By contrast, two of seven patients without relapse remained stable enhancements on repeat follow-up images (Case 6, 7). Obsez *et al*. showed the concentric VWE enhancement remained stable

Table II. Detailed serial neuroimage changes and clinical status.

Case no, Age (y), Sex	Biopsy proven	Treatments before initial HR-VWI	Arterial stenosis			Concentric VWE			Eccentric VWE			Visual VWE score			Relapse
			Initial	1st F/U	2nd F/U	Initial	1st F/U	2nd F/U	Initial	1st F/U	2nd F/U	Initial	1st F/U	2nd F/U	
1/27/M	Yes	None	R.M2-3, L.A2,Bil.P2	Improvement	Improvement	L.A2	None	None	None	None	None	2	0	0	No
2/19/M	Yes	None	None	No-change	No-change	Bil.P2	None	None	R. M2	R.M2	None	5	1	0	No
3/35/F	No	None	R.M1-2	Improvement	Improvement	Bil.ICA, Rt.M1-2	R.M2	None	None	None	None	8	2	0	No
4/53/F	Yes	GC	Bil.ICA, Bil.M1-2, Bil.A1-3, Bil.P1-3	Improvement	Improvement	Bil.ICA, Bil.M1-2, Bil.A1-2	L.ICA, L.M1	None	None	R.M1, LA2	None	16	6	0	No
5/46/M	Yes	None	Bil.A2	Improvement	Complete resolution	Bil.ICA, Bil.M1-2, Bil.A1-2	L.ICA, R.P2	None	None	R.ICA, Bil.M1-2, Bil.A1-2	R.M2, LA2	20	11	2	No
6/47/F	No	GC, CPA, AZP	R.M2, Bil.A2 Bil.P2	No-change	No-change	Bil.ICA, Bil.M1-2, Bil.A2, Bil.P2, BA, Bil.VA	Bil.ICA, R.M2, Bil.P2, L.M1-2, R.VA, BA	Bil.ICA, R.M2, Bil.P2, L.M1-2, R.VA, BA	None	R.M1, LA2	R.M1, Bil.A2	26	20	21	No
7/50/F	No	None	None	No-change	None	None	None	None	L.A2, BA, L.VA	BA, L. VA	BA, L.VA	3	2	2	No
8/36/M	Yes	GC, CPA	None	Worsening	Complete resolution	None	None	None	None	Bil.M2	None	0	2	0	Yes
9/49/F	No	None	R.A1, R.P2	Worsening	Improvement	R.A1, R.P2	R.ICA, R.A1, R.M1, R.P1-2	R.A1	None	None	R.ICA, R.P1	4	10	4	Yes

HR-VWI: high-resolution vessel wall image; VWE: vessel wall enhancement; F/U: follow-up; GC: glucocorticoid; CPA: cyclophosphamide; AZP: azathioprine

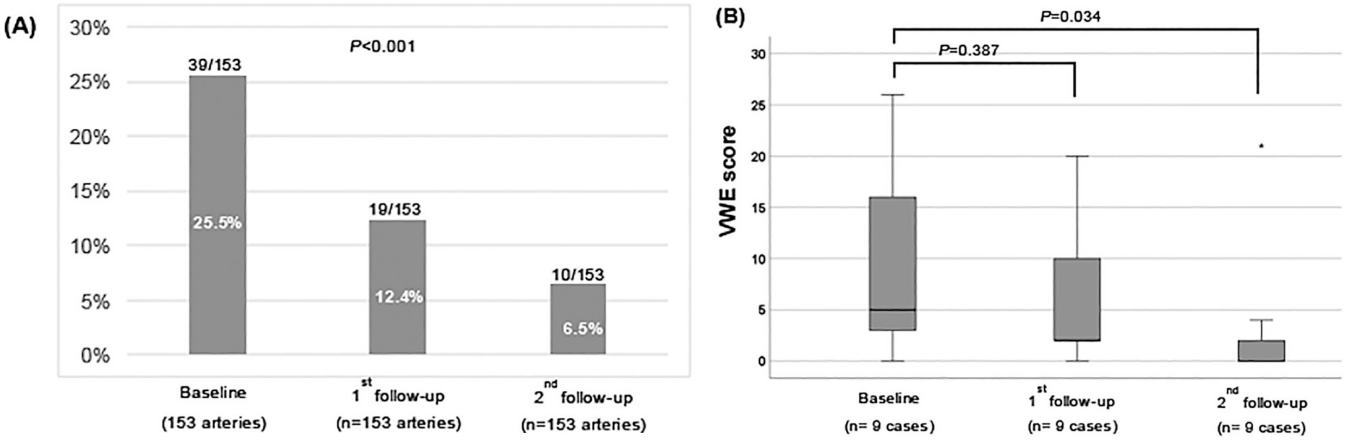

Fig. 4. Serial VWE patterns in patients with CNS-V.
A: Positive rates of concentric VWE in the 153 artery segments. **B:** Serial changes of VWE score in 9 cases.

for a follow-up median of 13.5 months in 4 patients (11). Pfefferkorn *et al*. reported the changes of HR-VWI findings in 4 patients with stable clinical course. After immunosuppressive therapy, follow-up HR-VWI showed that 2 patients had stable enhancement for 2 months and 2 patients had resolution of enhancement by 6 months (12). Although the degrees and extent of VWE on follow-up may be influenced by treatment duration and timing of evaluation, these findings suggest that persistent VWE may be common and not indicate worsening of the disease activity in patients with CNS-V.

In the relapse patients, the numbers of arterial segments with VWE and mean total VWE have temporarily worsened at 1st follow-up image. Prolonged remission rate (≥12 months after diagnosis) and good functional outcome were seen in approximately 60–70% of CNS-V patients in the previous long term follow-up studies (13-16). By contrast, relapses may occur 30% to 50% of CNS-V patients, leading to the risk of progressive neurological deterioration with severe disability (13-15). To our knowledge, on review of the literature, there are no studies that describe the serial vessel wall imaging characteristics in the relapse patients. In our study, HR-VWI of the relapse cases showed substantial decrease in the contrast enhancement of the arterial wall at 2nd follow-up image after intensive immunosuppressive therapy. Salvarani *et al*. reported that 25 (13 %) of the

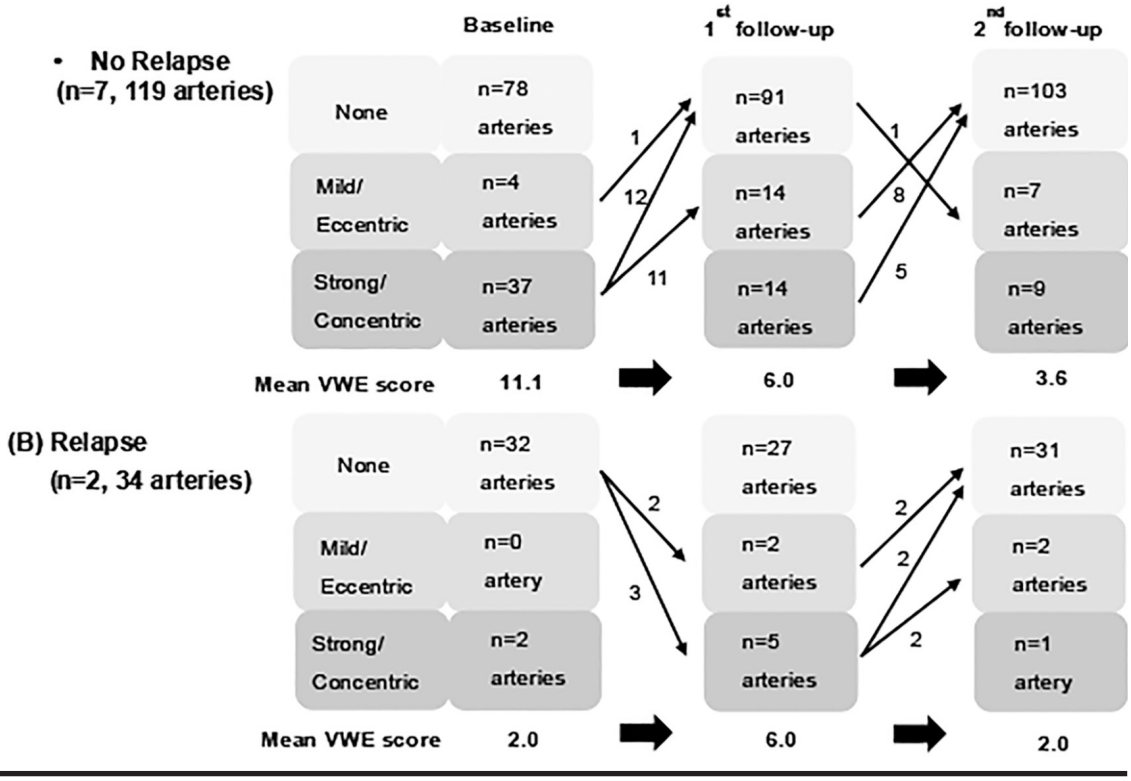

Fig. 5. Serial VWE patterns and clinical course.

191 CNS-V patients had 2 or more relapses during a median follow-up of 19 months (14). Therefore, repeat follow-up HR-VWI may be helpful for assessing disease activity and tracking treatment response especially in the relapse patients.

We found that concentric VWE in multi-vessel segments were frequently observed in patients with CNS-V on HR-VWI. This technique has already been used to distinguish CNS-V from other intracranial vasculopathies and directly visualises vessel wall inflammation and oedema (6-10). Vasculitis typically shows smooth, concentric, and long-segment wall thickening with strong enhancement of the vessel wall (6-10). By contrast, the vessel wall in RCVS is typically non-enhancing (or mildly enhancing) compared with the typical intense wall enhancement in active vasculitis (6-8). Intracranial atherosclerotic plaque typically demonstrates arterial wall thickening, which eccentrically involves the circumference of the arterial wall (6-8). Eiden *et al*. reported that vasculitic patients had significantly more numbers of arterial segments with VWE compared to non-vasculitic patients (21). Intracranial ICA, M1, M2, and V4 segments showed a higher involvement in patients with cerebral vasculitis (21). We generated the simple quantitative VWE scores on the basis of VWE grade and the numbers of arterial involved segments. This scoring system might be a useful method in the differential diagnosis of CNS-V and monitoring the post-treatment follow-up. Larger samples are needed to confirm the accuracy and reliability of the quantitative assessments on HR-VWI in patients with intracranial vasculopathies.

The present study has several limitations. First, this study conducted at a single center, and the number of the CNS-V was relatively small. Second, complete follow-up HR-VWI were available in only 25% of CNS-V patients from our cohort. Therefore, there have been missing data, and selection and referral bias that we cannot control. Third, three on nine patients already received immunosuppressant therapy at baseline HR-VWI. In our study, mean interval from onset to registration was 5.6 months. Obsez *et al*. reported that there was stable enhancement for many months in some CNS-V patients under immunosuppressive therapy (11). However, our results suggested that HR-VWI should be examined as soon as possible to assess the disease activity in CNS-V patients if immunosuppressive treatment was initiated. Finally, the management of immunosuppressive treatment and the timing for follow-up HR-VWI were conducted on the basis of the attending physician judgments. These differences may have had potentially significant confounding effects on the relationship between serial VWE patterns and clinical status. To reach more definitive conclusions, further prospective studies with some other centres are needed.

In conclusion, decreasing contrast VWE at follow-up images were frequently observed in CNS-V patients with good correlation to the clinical status of the patient. By contrast, some patients might have temporal VWE worsening at the relapse. Serial VWE patterns on HR-VWI may be useful for monitoring the response to treatment in patients with CNS-V.

References

1. SALVARANI C, BROWN RD JR, HUNDER GG: Adult primary central nervous system vasculitis. *Lancet* 2012; 380: 767-77.
2. HAJJ-ALI RA, SINGHAL AB, BENSELER S, MOLLOY E, CALABRESE LH: Primary angiitis of the CNS. *Lancet Neurol* 2011; 10: 561-72.
3. CALABRESE LH, MALLEK JA: Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and

proposal for diagnostic criteria. *Medicine* (Baltimore) 1988; 67: 20-39.
4. HAJJ-ALI RA, CALABRESE LH: Central nervous system vasculitis: advances in diagnosis. *Curr Opin Rheumatol* 2020; 32: 41-6.
5. FERRO F, QUARTUCCIO L, MONTI S *et al*.: One year in review 2021: systematic vasculitis. *Clin Exp Rheumatol* 2021; 39 (Suppl. 129): S3-12.
6. ALEXANDER MD, YUAN C, RUTMAN A *et al*.: High-resolution intracranial vessel wall imaging: imaging beyond the lumen. *J Neurol Neurosurg Psychiatry* 2016; 87: 589-97.
7. MANDELL DM, MOSSA-BASHA M, QIAO Y *et al*.: Intracranial vessel wall MRI: principles and expert consensus recommendations of the American Society of Neuroradiology. *Am J Neuroradiol* 2017; 38: 218-29.
8. ARENILLAS JF, DIELEMAN N, BOS D: Intracranial arterial wall imaging: techniques, clinical applicability, and future perspectives. *Int J Stroke* 2019; 14: 564-73.
9. ZEILER SR, QIAO Y, PARDO CA, LIM M, WASSERMAN BA: Vessel wall MRI for targeting biopsies of intracranial vasculitis. *AJNR Am J Neuroradiol* 2018; 39: 2034-6.
10. VAN ROOIJ JL, RUTGERS DR, SPLIET WG, FRIJNS CJ: Vessel wall enhancement on MRI in the diagnosis of primary central nervous system vasculitis. *Int J Stroke* 2018; 13: NP24-7.
11. OBUSEZ E C, FERDINAND H, HAJJ-ALI RA *et al*.: High resolution MRI vessel wall imaging: spatial and temporal patterns of reversible cerebral vasoconstriction syndrome and central nervous system vasculitis. *Am J Neuroradiol* 2014; 35: 1527-32.
12. PFEFFERKORN T, LINN J, HABS M *et al*.: Black blood MRI in suspected large artery primary angiitis of the central nervous system. *J Neuroimaging* 2013; 23: 379-83.
13. DE BOYSSON H, ARQUIZAN C, TOUZE E *et al*.: Treatment and long-term outcomes of primary central nervous system vasculitis. *Stroke* 2018; 49: 1946-52.
14. SALVARANI C, BROWN RD, CHRISTIANSON TJH *et al*.: Long-term remission, relapses and maintenance therapy in adult primary central nervous system vasculitis: a single-center 35-year experience. *Autoimmun Rev* 2020; 19: 102497.
15. SCHUSTER S, OZGA AK, STELLMANN JP *et al*.: Relapse rates and long-term outcome in primary angiitis of the central nervous system. *J Neurol* 2019; 266: 1481-9.
16. HAJJ-ALI RA, SAVGIN D, RAY E *et al*.: Long-term outcomes of patients with primary angiitis of the central nervous system. *Clin Exp Rheumatol* 2019; 37 (Suppl. 117): S45-51.
17. DE BOYSSON H, BOULOUIS G, AOUBA A *et al*.: Adult primary angiitis of the central nervous system: Isolated small-vasculitis represents distinct disease pattern. *Rheumatology* (Oxford) 2017; 56: 439-44.
18. KWEE RM, QIAO Y, LIU L, ZEILER SR, WASSERMAN BA: Temporal course and implications of intracranial atherosclerotic plaque enhancement on high-resolution vessel wall MRI. *Neuroradiology* 2019; 61: 651-7.
19. SAAM T, HABS M, POLLATO O *et al*.: High-resolution black-blood contrast-enhanced T1 weighted images for the diagnosis and follow-up of intracranial arteritis. *Br J Radiol* 2010; 83: e182-4.
20. TSIVGOULIS G, PAPADIMITROPOULOS GN, LACHANIS S *et al*.: High-resolution Intracranial Vessel Wall Imaging in Monitoring Treatment Response in Primary CNS Angiitis. *Neurologist* 2018; 23: 188-90.
21. EIDEN S, BECK C, VENHOFF N *et al*.: High-resolution contrast-enhanced vessel wall imaging in patients with suspected cerebral vasculitis: Prospective comparison of whole-brain 3D T1 SPACE versus 2D T1 black blood MRI at 3 Tesla. *PLoS One* 2019; 14: e0213514.