Cerebral hemodynamic disturbance in dural arteriovenous fistula with retrograde leptomeningeal venous drainage: a prospective study using $^{123}$I-iodoamphetamine single photon emission computed tomography

Kazuya Kanemaru, MD, PhD,1 Hiroyuki Kinouchi, MD, PhD,1 Hideyuki Yoshioka, MD, PhD,1 Takashi Yagi, MD, PhD,1 Takuma Wakai, MD,1 Koji Hashimoto, MD,1 Yuichiro Fukumoto, MD,1 Takako Umeda, MD,2 Hiroshi Onishi, MD, PhD,2 Yoshihisa Nishiyama, MD, PhD,1 and Toru Horikoshi, MD, PhD1

Departments of 1Neurosurgery and 2Radiology, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Chuo, Yamanashi, Japan

OBJECT The severity of cerebral hemodynamic disturbance caused by retrograde leptomeningeal venous drainage (RLVD) of a dural arteriovenous fistula (dAVF) is related to neurological morbidity and unfavorable outcome. However, the cerebral hemodynamics of this disorder have not been elucidated well. The aim of this study was to assess the relationship between the cerebral venous congestive encephalopathy represented as a high-intensity area (HIA) on T2-weighted MR images and the cerebral hemodynamics examined by $^{123}$I-iodoamphetamine (IMP) single photon emission computed tomography (SPECT), as well as the predictive value of $^{123}$I-IMP SPECT for the development and reversibility of venous congestion encephalopathy.

METHODS Based on the pre- and posttreatment T2 HIAs associated with venous congestion encephalopathy, patients were divided into 3 groups: a normal group, an edema group, and an infarction group. The regional cerebral blood flow (rCBF) at the region with RLVD was analyzed by $^{123}$I-IMP SPECT, and the results were compared among the groups.

RESULTS There were 11, 6, and 3 patients in the normal, edema, and infarction groups, respectively. No patients in the normal group showed any symptoms related to venous congestion. In contrast, all patients in the edema and infarction groups developed neurological symptoms. The rCBF in the edema group was significantly lower than that in the normal group, and significantly higher than that in the infarction group. The cerebral vascular reactivity (CVR) of the infarction group was significantly lower than that of the normal and edema groups. After treatment, the neurological signs disappeared in the edema group, but only partial improvement was seen in the infarction group. The rCBF also significantly increased in the normal and edema groups, but not in the infarction group.

CONCLUSIONS Quantitative rCBF measurement is useful for evaluating hemodynamic disturbance in dAVF with RLVD. The reduction of rCBF was strongly correlated with the severity of venous congestive encephalopathy, and loss of CVR is a reliable indicator of irreversible venous infarction caused by RLVD.

KEY WORDS dural arteriovenous fistula; endovascular treatment; retrograde leptomeningeal venous drainage; single photon emission computed tomography; venous congestion; vascular disorders
Dural arteriovenous fistula (dAVF) sometimes leads to an intracranial hemorrhage or venous congestion encephalopathy resulting in severe neurological deficits. These devastating phenomena have been considered to be associated with retrograde leptomeningeal venous drainage (RLVD). Therefore, recent classifications of dAVF proposed by Borden et al. and Cognard et al. are based on the venous drainage pattern of the shunts, revealing an increasing prevalence of aggressive neurological symptoms with advancing grade. In addition, it has been reported that dAVF patients with RLVD presenting with intracranial hemorrhage showed a 35% rebleeding rate within a mean follow-up period of 20 days. An annual neurological event rate of 15% was also reported in a dAVF case series study involving mostly symptomatic patients. Consequently, symptomatic RLVD has been considered an important factor when judging the necessity of radical treatment. In comparison, recent studies have reported a considerably lower annual event risk of 1.4%–1.5% in asymptomatic dAVF patients with RLVD. Consequently, it is important to understand the differences between symptomatic and asymptomatic dAVF with RLVD to establish predictive factors for the disastrous events. More recently, cerebral hemodynamic impairment of the dAVF with RLVD has been investigated, revealing that patients with symptomatic dAVFs are likely to be more severely hemodynamically compromised than asymptomatic patients and that the degree of hemodynamic disturbance might predict the severity and reversibility of venous congestive encephalopathy. However, the details of cerebral hemodynamics in dAVF have not been fully elucidated. The aim of the present study was to assess the cerebral hemodynamics by 123I-iodoamphetamine (IMP) single photon emission computed tomography (SPECT) before and after curative treatment and to clarify the relationship between the degree of hemodynamic disturbance and venous congestive encephalopathy and its reversibility.

Methods

From January 2008 until December 2012, dAVF patients with RLVD were evaluated prospectively with clinical examination, MRI, digital subtraction angiography (DSA), and 123I-IMP SPECT within 1 month before treatment. The patients were subsequently treated by endovascular therapy, surgery, stereotactic radiotherapy, or a combination of these modalities. Three months after the final treatment, the above-mentioned examinations were repeated to evaluate the effectiveness of the treatment. This study was approved by the ethics committee of the University of Yamanashi, and all patients provided written informed consent.

Clinical symptoms were divided into those related to cerebral venous congestion such as dementia, seizure, or focal neurological deficits, and other symptoms, such as tinnitus, cranial nerve palsy, or ocular symptoms, including exophthalmos, chemosis, and conjunctival injection. Outcomes of the symptoms 3 months after curative treatment were judged as disappeared, partially improved, no change, or worsened.

The diagnosis and location of dAVF were determined by DSA and the lesions were classified according to the Cognard classification. Distribution of RLVD was also assessed on DSA. MRI was performed to check the venous congestive encephalopathy. The existence of a high-intensity area (HIA) on T2-weighted MR images related to venous congestion in the affected area with RLVD was evaluated.

SPECT imaging was performed using a 3-headed γ-camera equipped with low-energy, high-resolution collimators (Toshiba GCA9300A/ID, Toshiba Medical Systems). The quantitative SPECT (QSPECT)/dual-table autoradiographic (DTARG) method was applied. Detailed procedures of the QSPECT/DTARG method are reported elsewhere. In short, IMP (111 MBq each dose) was injected intravenously twice at an interval of 32 minutes. The first and second scan continued from 0 to 30 and 32 to 62 minutes after the first IMP injection, respectively. At 20 minutes after the first IMP injection, acetazolamide (17 mg/kg) was injected intravenously to evaluate cerebral vascular reactivity (CVR). Using 3D stereotactic surface projection, quantitative image data evaluated by the QSPECT/DTARG method was standardized to the standard brain. Then, the decrease of regional cerebral blood flow (rCBF) was visually examined. To measure the mean value of radioactive counts, an elliptical region of interest (ROI) was set to the most hemodynamically impaired region with RLVD and to the same region on the contralateral side. When there was an HIA on T2-weighted images (edema or venous infarction), the ROI was set to an area almost equal to it. Then the affected-to-contralateral side asymmetry ratio (ACR) was calculated as follows: ACR = rCBF_{edema/venous infarction}/rCBF_{contra} × 100 (%). The ACR was adopted to minimize errors from individual factors and regional variations. CVR was also calculated as follows: CVR = (rCBF_{acetazolamide} − rCBF_{pre})/rCBF_{rest} × 100 (%) to estimate severity of hemodynamic compromise.

According to the MRI studies performed before and after treatment, patients were divided into 3 groups: a normal group (no HIA on T2-weighted images), an edema group (vasogenic edema; HIA on T2-weighted images disappeared after treatment), and an infarction group (venous infarction; HIA on T2-weighted images persisted after treatment) group. The results of the SPECT studies before and after treatment were compared among the 3 groups.

After the confirmation of angiographic cure, clinical and MRI follow-up was conducted once a year.

Data were expressed as mean ± standard deviation. Univariate analyses were performed using the Mann-Whitney U-test. A p value of less than 0.05 was considered significant.

Results

Patient Characteristics

Twenty-seven patients with dAVFs were treated from January 2008 to December 2012. Four patients without RLVD were excluded. One patient with a massive hemorrhage requiring emergency treatment was also excluded. Two patients with venous congestion in both hemispheres were also excluded because of difficulty of assessment us-
ing the asymmetry ratio. As a result, 20 dAVF patients were included in this study. The clinical and radiological findings of the patients are summarized in Table 1. There were 9 men and 11 women, with a mean age of 67 ± 11 years (range 42–84 years). The dAVFs were located in the transverse-sigmoid sinus in 15 cases, the cavernous sinus in 3, the anterior fossa in 1, and the superior sagittal sinus in 1. According to the Cognard classification, 12 cases were classified as Type IIa+b, 7 as Type IIb, and 1 as Type III. Three patients were asymptomatic, and 8 patients showed only symptoms not related to cerebral venous congestion, such as tinnitus and ocular symptoms. Nine patients suffered from symptoms related to cerebral venous congestion, such as seizure, dementia, and focal neurological signs. The curative treatment was transvenous embolization (TVE) with platinum coils in 15, surgery in 3, transarterial embolization with n-butyl-cyanoacrylate in 1, and stereotactic radiotherapy in 1. In all cases, complete occlusion of dAVF was confirmed by DSA except for the one case treated with stereotactic radiosurgery who exhibited a tendency of improved symptoms. Three months after the final treatment, symptoms had disappeared in 13 patients, had partially improved in 3, were unchanged in 1, and had worsened due to hemorrhage in 1. HIA on T2-weighted images was observed in 9 cases before treatment, disappeared after treatment in 6, and remained in 3. Accordingly, 11 patients were classified into the normal group (cases 1–11), 6 patients into the edema group (cases 12–17), and 3 patients into the infarction group (cases 18–20). The normal group had no symptoms related to venous congestion. Three months after the curative treatment, the symptoms related to venous congestion had disappeared in all cases in the edema group; however, the symptoms persisted with partial improvement in the infarction group.

Comparison of SPECT Findings Among the 3 Groups

The overall pretreatment values for ACR and CVR were 73.8% ± 17.3% and 29.4% ± 24.1%, respectively. A follow-up SPECT study was not performed in 5 cases because of the patients’ refusal in 2 cases, no abnormalities in the pretreatment SPECT study in 1 case, intracerebral hemorrhage after treatment in 1 case, and persistent RLVD after stereotactic radiotherapy in 1 case. Consequently, the comparison of pre- and posttreatment studies was made in the remaining 15 patients, and the ACR was found to have increased significantly to 83.9% ± 18.0%, and the CVR improved to 32.1% ± 19.7% in total.

Before treatment, the ACR of the normal, edema, and infarction groups according to the MRI studies was 87% ± 8.7%, 63% ± 7.6%, and 47% ± 1.1%, respectively, and the CVR of these 3 groups was 42% ± 18%, 27% ± 15%, and 12% ± 15%, respectively. The ACR and CVR of each case in the 3 groups were plotted in a scatter diagram (Fig. 1). Values for the cases in the normal group were distributed in the upper-right part, values for the infarction group showed lower ACR and CVR and were distributed in the lower-left part, and those for the edema group were distributed between those of the 2 other groups. The ACRs of these 3 groups and their statistical relationships are shown in Fig. 2 (left). The ACR of the edema group was significantly lower than that of the normal group (p < 0.001) and significantly higher than that of the infarction group (p = 0.003). The CVR values for the 3 groups and their statistical relationships are shown in Fig. 2 (right). Only the infarction group showed loss of CVR, and 2 patients in this group had a steal phenomenon preoperatively. The CVR of the infarction group was significantly lower than that of the edema group (p = 0.02) and the normal group (p = 0.006). There was no significant difference between the edema and normal groups.

The posttreatment ACRs of the normal, edema, and infarction groups were 93% ± 2.9%, 86% ± 5.1%, and 54% ± 11%, respectively (Fig. 2 left). The increase of ACR was prominent in the edema group (p < 0.001) and the normal group (p = 0.04), but not significant in the infarction group. The posttreatment CVRs of these 3 groups were 44% ± 26%, 35% ± 18%, and 12% ± 6.9%, respectively (Fig. 2 right). Although the CVR increased after treatment, there were no significant differences between pre- and posttreatment CVR in any of the 3 groups.

Clinical and Radiological Follow-Up

After the confirmation of angiographic cure, clinical and MRI follow-up was conducted once a year. During the follow-up period (mean 2.9 ± 1.4 years) no patient was found to have recurrence of the dAVF on imaging studies or clinical deterioration that might be related to dAVF recurrence.

Illustrative Cases

Case 16

A 75-year-old woman presented with a history of epilepsy who had developed gait disturbance and was referred to our hospital. MRI revealed an HIA in the right temporal lobe on T2-weighted images as well as scattered flow voids representing dilated varicose cortical veins (Fig. 3A). Right external carotid angiography delineated a dAVF at the right transverse-sigmoid sinus. The right occipital and middle meningeal arteries were feeders shunting into the isolated right transverse-sigmoid sinus. The right occipital and middle meningeal arteries were feeders shunting into the isolated right transverse-sigmoid sinus (Fig. 3B), and RLVD was found extensively in the right temporal, parietal, and occipital lobes (Fig. 3C). 123I-IMP SPECT showed a wide area of hypoperfusion in the same region with RLVD. Although the resting rCBF (ACR 69%) was decreased (Fig. 3D), CVR (12%) was not completely lost (Fig. 3E). The patient’s neurological symptoms were considered to be due to venous congestion in the right temporal lobe. TVE was performed through the obstructed right sigmoid sinus. Coils were delivered into the sinus, and complete occlusion of the dAVF was achieved. The patient’s posttreatment course was uneventful and her symptoms gradually resolved within a month. An MRI study performed 3 months after the treatment showed disappearance of the T2 HIA in the right temporal lobe, and therefore the HIA on the initial MRI was diagnosed as reversible vasogenic edema (Fig. 3F). 123I-IMP SPECT at the same time showed improvement in both resting rCBF (ACR 88%) and CVR (35%) (Fig. 3G and H).

Case 18

A 79-year-old woman presented with truncal ataxia and
### TABLE 1: Clinical and radiological characteristics of the patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Location</th>
<th>Cognard Class</th>
<th>Region w/ RLVD</th>
<th>Tx</th>
<th>Angiography</th>
<th>Symptoms</th>
<th>MRI</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PreTx</td>
<td>Related to VC</td>
<td>PostTx</td>
<td>Group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PreTx PostTx</td>
<td>ROI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ACR CVR</td>
<td>ACR CVR</td>
</tr>
<tr>
<td>1</td>
<td>65, M</td>
<td>AF</td>
<td>III</td>
<td>Fr</td>
<td>Surgery</td>
<td>None</td>
<td>No</td>
<td>PreTx</td>
<td>PostTx</td>
</tr>
<tr>
<td>2</td>
<td>67, F</td>
<td>CS</td>
<td>Ila+b</td>
<td>Fr, C</td>
<td>TVE</td>
<td>Ocular, CN palsy</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>72, F</td>
<td>CS</td>
<td>Ila+b</td>
<td>Fr</td>
<td>TVE</td>
<td>Ocular, CN palsy</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>50, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T</td>
<td>TAE + TVE</td>
<td>Tinnitus</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>54, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TAE + TVE</td>
<td>Tinnitus</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>77, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O</td>
<td>TVE</td>
<td>None</td>
<td>No</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>75, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O</td>
<td>TVE, TAE, SRT</td>
<td>Tinnitus</td>
<td>No No changes</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>84, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TVE, TAE, SRT</td>
<td>Tinnitus</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>42, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O</td>
<td>TVE, TAE + surgery</td>
<td>None</td>
<td>No Worsened*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>65, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T</td>
<td>TVE</td>
<td>Tinnitus</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>63, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TAE + TVE</td>
<td>Tinnitus</td>
<td>No Disappeared</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>53, F</td>
<td>CS</td>
<td>Ila+b</td>
<td>T, O</td>
<td>TVE</td>
<td>Seizure, ocular</td>
<td>Yes Disappeared</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>62, M</td>
<td>SSS</td>
<td>Ila+b</td>
<td>Fr, T</td>
<td>TAE</td>
<td>Seizure</td>
<td>Yes Disappeared</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>14</td>
<td>71, M</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TVE</td>
<td>Hemianopsia</td>
<td>Yes Disappeared</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>74, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TVE</td>
<td>Ataxia</td>
<td>Yes Disappeared</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>75, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, Pa, O, C</td>
<td>TVE</td>
<td>Seizure, gait disturbance</td>
<td>Yes Disappeared</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>64, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TVE</td>
<td>DOC</td>
<td>Yes Disappeared</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>79, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>T, O, C</td>
<td>TAE + TVE</td>
<td>Ataxia</td>
<td>Yes Partially improved</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>19</td>
<td>74, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>O, C, Th</td>
<td>TVE</td>
<td>Dementia, hemianopsia</td>
<td>Yes Partially improved</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>20</td>
<td>79, F</td>
<td>TSS</td>
<td>Ila+b</td>
<td>O, C</td>
<td>TVE, TAE + surgery</td>
<td>Aphasia, dementia</td>
<td>Yes Partially improved</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

AF = anterior fossa; C = cerebellum; CN = cranial nerve; CS = cavernous sinus; DOC = disturbance of consciousness; E = edema; Fr = frontal lobe; I = infarction; N = normal; NA = not applicable; O = occipital lobe; Ocular = ocular symptoms; Pa = parietal lobe; SRT = stereotactic radiotherapy; SSS = superior sagittal sinus; T = temporal lobe; T2WI = T2-weighted imaging; Th = thalamus; TSS = transverse-sigmoid sinus; Tx = treatment; VC = venous congestion.

* Newly developed hemianopsia due to intracerebral hemorrhage after treatment.
K. Kanemaru et al.

was admitted to our hospital. MRI revealed an HIA on T2-weighted images in the left cerebellar hemisphere (Fig. 4A). Left external carotid angiography revealed a dA VF at the left transverse-sigmoid sinus with RLVD in the left cerebellar hemisphere and the left occipital lobe (Fig. 4B and C). 123I-IMP SPECT revealed a hypoperfusion area in the same region with RLVD. Both resting rCBF (ACR 45%) and CVR (−27%) were severely decreased with a steal phenomenon (Fig. 4D and E). TVE combined with transarterial embolization (TAE) was performed through the contralateral side. Coils were delivered into the affected sinus and the dAVF was completely occluded. The patient's symptoms resolved gradually, but mild truncal ataxia persisted. An MRI study obtained 3 months after the treatment showed a persistent HIA on T2-weighted images, suggesting an irreversible venous infarction and atrophy of the left cerebellar hemisphere (Fig. 4F). 123I-IMP SPECT at the same time showed only minimal recovery of both resting rCBF (ACR 65%) and CVR (4%) (Fig. 4G and H).

Discussion

Using 123I-IMP SPECT, we showed that the reduction of rCBF represented by ACR was strongly correlated with the pathological findings of venous congestive encephalopathy on MRI and the loss of CVR was closely correlated with the irreversibility of the lesion. Previously, cerebral hemodynamic disturbance in dAVF was examined qualitatively by means of SPECT or PET.7,8,11,12 It has been shown that rCBF is decreased in patients with RLVD compared with those without it.6 In addition, rCBF of the dAVF with RLVD was more severely compromised in symptomatic patients than in asymptomatic patients.4,10 However, the cerebral hemodynamic disturbance of the lesion due to venous congestion caused by RLVD with or without symptoms as well as reversibility on MRI (edema vs infarction) have not been elucidated. In this study, quantitative evaluation of hemodynamic disturbance in dAVF patients with RLVD was performed, and widespread compromise of rCBF and CVR was clearly demonstrated. Based on the present results, ACR can predict the severity of venous congestion–related neurological and radiological findings, as follows. If the ACR was more than approximately 75%, there was no HIA on T2-weighted sequences and venous congestion–related neurological symptoms were not evident. In the patients presenting with HIAs on T2-weighted

![Fig. 1. Scatter plot for rCBF represented with ACR (y-axis) and CVR (x-axis). Triangles represent the infarction group distributed in the lower left. Circles indicate the normal group distributed in the upper right. Squares show the edema group distributed between aforementioned 2 groups.](image)

![Fig. 2. Box-plot representations of ACR (left) and CVR (right) in the normal, edema, and infarction group before and after treatment, depicting the 5-number summaries, the minimum and maximum, the upper and lower quartiles, and the median value. The ACR in the edema group was significantly lower than in the normal group and significantly higher than in the infarction group. The mean ACR of each of the 3 groups increased after treatment. The increase was most prominent in the edema group, followed by the normal group, but the increase was less marked in the infarction group. The CVR in the infarction group was significantly lower than in the edema group and the normal group. Although the mean CVR increased after treatment, comparison of pre- and post-treatment values within groups showed no statistically significant differences.](image)
MRI, if the ACR was between 50% and 70%, the HIA and venous congestion–related neurological symptoms were reversible and the condition could be cured by the treatment. If the ACR was decreased to less than 50%, the HIA presumably contained irreversible venous infarction, and a good outcome might not be expected. Although further investigation is necessary, these ACR values may be important indexes for the reversibility of venous congestive encephalopathy due to dAVF with RLVD.

The CVR values of the infarction group were significantly lower than those of the edema group and the normal group. Only the infarction group showed loss of CVR below 2%, and 2 patients in this group demonstrated the so-called steal phenomenon. In contrast to the situation in arterial cerebral ischemia, the meaning of changes in CVR in venous ischemia is not understood. However, based on the present results, loss of CVR suggests that an HIA on T2-weighted images will contain venous infarction, consistent with the results of a previous qualitative study using 123I-IMP SPECT. As the edema group showed a wide distribution of CVR, from 12% to 51%, patients whose CVR was relatively low in this group might face progression to venous infarction, which would require immediate treatment.

Comparing the pre- and posttreatment rCBF, the edema group showed the largest increase of ACR among the 3 groups. This means that hemodynamic disturbance due to vasogenic edema could be reversible with treatment. In contrast, ACR in the infarction group did not show recovery, consistent with histological irreversibility of the damage. However, the HIs on T2-weighted MRI in the infarction group decreased to some extent with some neurological improvement. Therefore, HIs on T2-weighted MRI of the venous infarction contain both vasogenic edema and venous infarction, and the peripheral part, which contains vasogenic edema, would resolve while the core, which contains venous infarction, would persist after treatment. The above-mentioned study also showed that in 1 patient both symptoms and the HIA on T2-weighted MRI disappeared. However, the remaining 3 patients showed persistent T2 HIs and partial improvement of the symptoms after treatment.

On the other hand, the ACR of the normal group showed a significant improvement after curative treatment, indicating the benefits of the treatment even for patients with RLVD presenting with neither neurological symptoms nor HIs on T2-weighted MRI.

The CVR of the normal group and the edema group was not decreased before treatment and did not change after treatment. Although the CVR in the infarction group tended to show a recovery after treatment, the change was

---

**FIG. 3.** Case 16. This case involved a 75-year-old woman with a reversible HIA on T2-weighted MRI. Pretreatment MRI revealed an T2 HIA in the right temporal lobe and flow voids representing dilated varicose cortical veins (A). Right external carotid angiography demonstrated a dAVF at the right transverse-sigmoid sinus (lateral view, B) and extensive RLVD in the right temporal, parietal, and occipital lobes (lateral view, C). 123I-IMP SPECT showed global hypoperfusion in the same region with RLVD (D). Although the resting rCBF was decreased, CVR was not completely lost (E). An MRI study performed 3 months after treatment showed disappearance of the HIA on T2-weighted sequences (F). 123I-IMP SPECT at the same time showed an improvement of both resting rCBF (G) and CVR (H). Figure is available in color online only.
K. Kanemaru et al.

not statistically significant, and the values still showed low reactivity, indicating irreversible damage. Therefore, CVR probably reflects the viability of brain tissue in patients with venous congestive encephalopathy. This is consistent with a previous SPECT study that assessed CVR.

With recent advances in neuroradiological examinations, dAVF with RLVD is being detected with increasing frequency in patients without symptoms of this condition. Indeed, dAVF was diagnosed incidentally in 3 of our patients on the basis of brain MRI studies. Therefore, it is important to elucidate the natural history of asymptomatic dAVF and risk factors for progression. A prospective study with a large number of samples is warranted to confirm our observation.

Our study has several limitations. First, rCBF was assessed using an asymmetry ratio instead of the absolute value to minimize errors from individual factors and regional variations. Therefore, cases with venous congestion affecting both hemispheres could not be assessed by this method. Second, although the loss of CVR appeared to indicate irreversible venous infarction, the precise mechanism remains to be elucidated. Third, the result of this study cannot be applied to the prediction of intracranial hemorrhage from a dAVF with RLVD, a poor prognostic factor along with venous congestion encephalopathy. Fourth, the sample size of this study was relatively small to obtain firm conclusions. A prospective study with a large number of patients is needed.

Conclusions
The reduction of rCBF was strongly correlated with the severity of venous congestive encephalopathy in dAVF with RLVD. Loss of CVR is a reliable indicator of irreversible venous infarction caused by RLVD.

References

**Author Contributions**
Conception and design: Kinouchi, Kanemaru. Acquisition of data: Kanemaru, Umeda. Analysis and interpretation of data: Kanemaru. Drafting the article: Kanemaru. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kinouchi. Statistical analysis: Kanemaru. Administrative/technical/material support: Kinouchi, Onishi, Horikoshi. Study supervision: Kinouchi, Onishi, Horikoshi.

**Correspondence**
Hiroyuki Kinouchi, Department of Neurosurgery, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, 1110 Shimokato, Chuo, Yamanashi 409-3898, Japan. email: hkinouchi@yamanashi.ac.jp.