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The value of high-resolution MRI in the diagnosis, efficacy of treatment, and prognosis of central nervous system vasculitis

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Abstract

Aim of the study: *To explore the high-resolution magnetic resonance imaging (HR-MRI) characteristics of central nervous system (CNS) vasculitis and to explore the value of HR-MRI in the treatment effect and prognosis evaluation of CNS vasculitis.*

Material and methods: *During the follow-up of 24 patients diagnosed as CNS vasculitis by the Second Hospital of Hebei Medical University, 3.0T HR-MRI was used for imaging examination and HR-MRI characteristics were analysed.*

Results: *The affected vessel wall of 24 patients showed diffuse uniform centripetal thickening. The HR-MRI examination showed varying degrees of lumen stenosis, including 5 cases (20.8%) involving a single arterial segment, and 19 cases (79.2%) involving multiple arterial segments. And most cases (92.9%) showed grade 2 enhancement of the involved vessel wall. Except for one case involving the basilar artery at the same time, the remaining 23 cases involved only the anterior circulation vessels. We analysed and compared the affected vessels between the relapsed group and the non-relapsed group, and found that the average number of involved vascular segments was 6.5 ±3.4 (3-11) in the relapsed group and 3.5 ±2.1 (1-8) in the non-relapsed group, with a significant difference between the two groups (p = 0.039).*

Conclusions: *The CNS vasculitis was more likely to involve the anterior circulation vessels. The number of affected vascular segments in the relapsed group of CNS vasculitis was higher than in the non-relapsed group, suggesting that the more vascular segments involved, the more prone to recurrence.*

Key words: *high-resolution magnetic resonance imaging, central nervous system vasculitis, ischemic stroke, intracranial vascular stenosis.*

Introduction

Central nervous system (CNS) vasculitis is an inflammatory vascular disease involving the CNS. Its clinical manifestation is not very specific [7,14,16], making the diagnosis of CNS vasculitis difficult. High-resolution magnetic imaging (HR-MRI) technology can display the vessel wall and vessel lumen simultaneously, which has a high clinical value in judging the cause of intracranial artery stenosis and guiding treatment. However, few studies have reported the distribution characteristics of HR-MRI in the CNS and the relationship between these characteristics and clinical prognosis. The aim of this study was to explore the HR-MRI characteristics of CNS vasculitis and its relationship with clinical prognosis.

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Material and methods

Patients

From January 2018 to January 2020, all twenty-four patients with CNS vasculitis who were treated in the Second Hospital of Hebei Medical University were included. All the patients met the diagnostic criteria of primary angiitis of the central nervous system (PACNS) proposed by Calabrese and Mallek [3] in 1988: 1) acquired neurological or mental dysfunction that cannot be explained by other diseases after laboratory examination and clinical evaluation; 2) typical vasculitis characteristics by cerebral angiography or histopathological confirmation; 3) no systemic or systemic immune diseases, the evidence of secondary vasculitis was excluded. After admission, all patients underwent diffusion-weighted imaging (DWI), 3.0T HR-MRI plain and enhanced scans. All patients signed informed consent. The study was reviewed by the Ethics Committee of the Second Hospital of Hebei Medical University.

Instruments and methods

Philips Achieva 3.0T scanner and standard 8-channel phased-array head coil were used. DWI, 3D-TOF MRA, HR-MRI T1WI, and post-enhancement HR-MRI T1WI were performed sequentially. Scanning parameters were as follows – DWI: TR 2191 ms, TE 95 ms, slice thickness 6.5 mm, matrix 200 mm × 204 mm; MRA: 3D-TOF sequence, TR 15 ms, TE 3.5 ms, slice thickness 6 mm, matrix 320 mm × 191 mm; HR MRI T1WI VISTA scanning parameters: TR 800 ms, TE 20 ms, TE flip angle 90 degrees, Refocusing control 50 degrees, slice thickness 3 mm, matrix 200 mm × 181 mm. HR-MRI T1WI enhanced scan: the contrast agent was gadolinium diamine injection, 0.1 ml/kg body weight. Enhanced scans were performed 5 minutes after contrast injection, and the scanning parameters and locations were consistent with T1WI plain scans.

Image data analysis

The results of the imaging examinations were evaluated on the PACS workstation by two associate chief physicians engaged in neuroimaging diagnosis independently. Inter-rater reliability for the imaging examinations among our investigators was assessed through evaluation of 99 images (Supplemental Tables I and II). After the stenosis and ischemic lesions were determined by TOF MRA and DWI images, the number and extent of the intracranial artery segments involved by the stenosis were further determined: internal carotid artery (ICA) petrous segment (C2), ruptured foramen segment (C3), cavernous sinus segment (C4), bed segment (C5), ocular and communicating segment (C6-7), middle cerebral artery (MCA) sphenoidal segment (M1), insula segment (M2) [1]. Horizontal segment of anterior cerebral artery (A1), basilar artery (BA), posterior cerebral artery (PA), and intracranial segment of vertebral artery (VA). The Philips extended Mr workspace 2.6 workstation was used to process the images and get MRA MIP images. The degree of stenosis was measured on HR-MRI Tiwi axis map, and the image was magnified to 400%. We then found the maximum lumen narrowing (MLN) vascular lumen as the target vascular lumen. The normal vascular lumen nearby was taken as control. The lumen area (LA) of the MCA according to the blood intima boundary was measured and compared between the target (MLN) and the control vascular lumen. The ratio of the LA of the target (MLN) and the control vascular lumen was calculated. The degree of stenosis was determined according to the ratio (luminal stenosis: < 50% was mild stenosis; 50-69% was moderate stenosis; > 70-99% was severe stenosis, and > 99% was occlusion). According to previous literature [13], the degree of enhancement of the affected vessel wall was divided into three grades: grade 0 enhancement without enhancement or near the normal arterial wall; grade 1 enhancement above grade 0 but less than the pituitary funnel; and grade 2 enhancement equal to or higher than the pituitary funnel [13]. Our investigators assessed the reliability for the degree of enhancement of the affected vessel wall by interpreting 99 images (Supplemental Tables III and IV).

Treatment

On the basis of promoting blood circulation and removing blood stasis, nourishing nerves and scavenging oxygen free radicals, glucocorticoid therapy (dexamethasone, intravenous drip 5 mg/d) were added. Then prednisone acetate tablets were taken orally 20 mg/d after 3 days of hormone therapy. After one week, the dose was reduced by 5 mg every week until 5 mg/d. After 3 months of maintenance treatment, HR-MRI was re-examined to observe the dynamic changes of the affected vessels and record

the treatment response. Radiographic remission was defined as a reduction in the degree of vessel wall enhancement and luminal stenosis.

Follow-up

The follow-up period of the patients is from the beginning of therapy to the last medical visit or death. Follow-up was at least 6 months. Recurrence is defined as the recurrence or deterioration of the existing symptoms of vasculitis, or the discovery of new vascular lesions, new cerebral infraction or the enlargement of the scope of the original vascular lesions, enhancement of the wall and progression of the degree of stenosis of the lumen in MRI examination. Imaging remission was defined as the reduction of vascular wall enhancement and luminal stenosis. No response was defined as no change in the affected vessel after 6 months of treatment [4].

Statistical analysis

All the data collected in this study were analysed using SPSS 25.0 software. Measurement data were expressed as mean ± standard deviation (mean ±SD). The differences between two groups were examined using independent sample *t* test. $P < 0.05$ was considered statistically significant.

Results

Twenty-four patients were diagnosed by HR-MRI without brain biopsy. The 24 patients with CNS vasculitis were diagnosed as cerebral ischemic events. Eight patients (42.1%) had bilateral multiple cerebral infarctions, eight patients (42.1%) had unilateral multiple cerebral infarctions, three patients (15.8%) had single cerebral infarction, and five patients (20.8%) had a transient ischemic attack (TIA). The average age of the patients was 32.5 years, with a median age of 32.5 years. There were 16 males (67.0%) and 8 females (33.0%).

There was a good consistency between the two diagnostic doctors on the degree of stenosis (K = 0.910) and the degree of enhancement (K = 0.918). HR-MRI images of 24 patients with CNS vasculitis showed uniform annular centripetal thickening of the involved vessel wall, and 5 patients (20.8%) had a single arterial segment involved while 19 cases (79.2%) had multiple arterial segments involved. A total of 99 arterial segments were involved, 7 (7.1%) had grade 1 enhancement and 92 (92.9%) had grade 2 enhancement. 30 (30.3%) arterial segments had mild stenosis, 43 (43.4%) arterial segments had moderate stenosis, 21 (21.2%) arterial segments had severe stenosis or occlusion, and 5 (5.1%) arterial segments had no significant stenosis in the lumen. Except for one case involving the basilar artery at the same time, the remaining 23 cases had only the anterior circulation vessels involved.

Among the patients with CNS vasculitis, 5 patients only received conventional treatment, and 19 patients received glucocorticoid therapy on the basis of conventional treatment. The median follow-up time was 9 months (9-12 months). Of the 19 patients treated with hormones, 11 had a remission after 9 months of treatment (Fig. 1), 4 had a relapse, and 4 had no response. They were divided into the relapsed group and the non-relapsed group. There were no significant differences between the two groups in the side and type of the affected vessel (only involving MCA, only involving ICA, involving MCA and ICA) (Table I; $p \geq 0.05$).

The mean number of vascular segments involved in the relapsed group was 6.5 ±3.4 (3-11), with a median of 9, and the mean number of vascular segments involved in the non-relapsed group was 3.5 ±2.1 (1-8), with a median of 3. The difference between the two groups was statistically significant (Table I; $p < 0.05$).

Discussion

Central nervous system is an inflammatory vascular disease involving the central nervous system. The damage to the surrounding brain tissue includes direct damage to blood vessels caused by inflammation, as well as brain infarction and bleeding caused by damage to blood vessel walls. PACNS was previously reported as a rare disease with an average annual incidence of 2.4/1 million. Recent studies [8] have pointed out that CNS vasculitis has become the second leading cause of stroke after arteriosclerosis. Brain histopathological biopsy is the gold standard for the diagnosis of CNS vasculitis. Pathological changes include transmural damage and transmural inflammatory infiltration. But because of its risk and limited sensitivity [2], it is rarely applied. HR-MRI can clearly show the characteristics of the affected vessel wall of CNS vasculitis [18]. In recent years, many studies have shown that HR-MRI is more and more important and practical for the diagnosis of CNS vasculitis, which largely avoids the risks and adverse

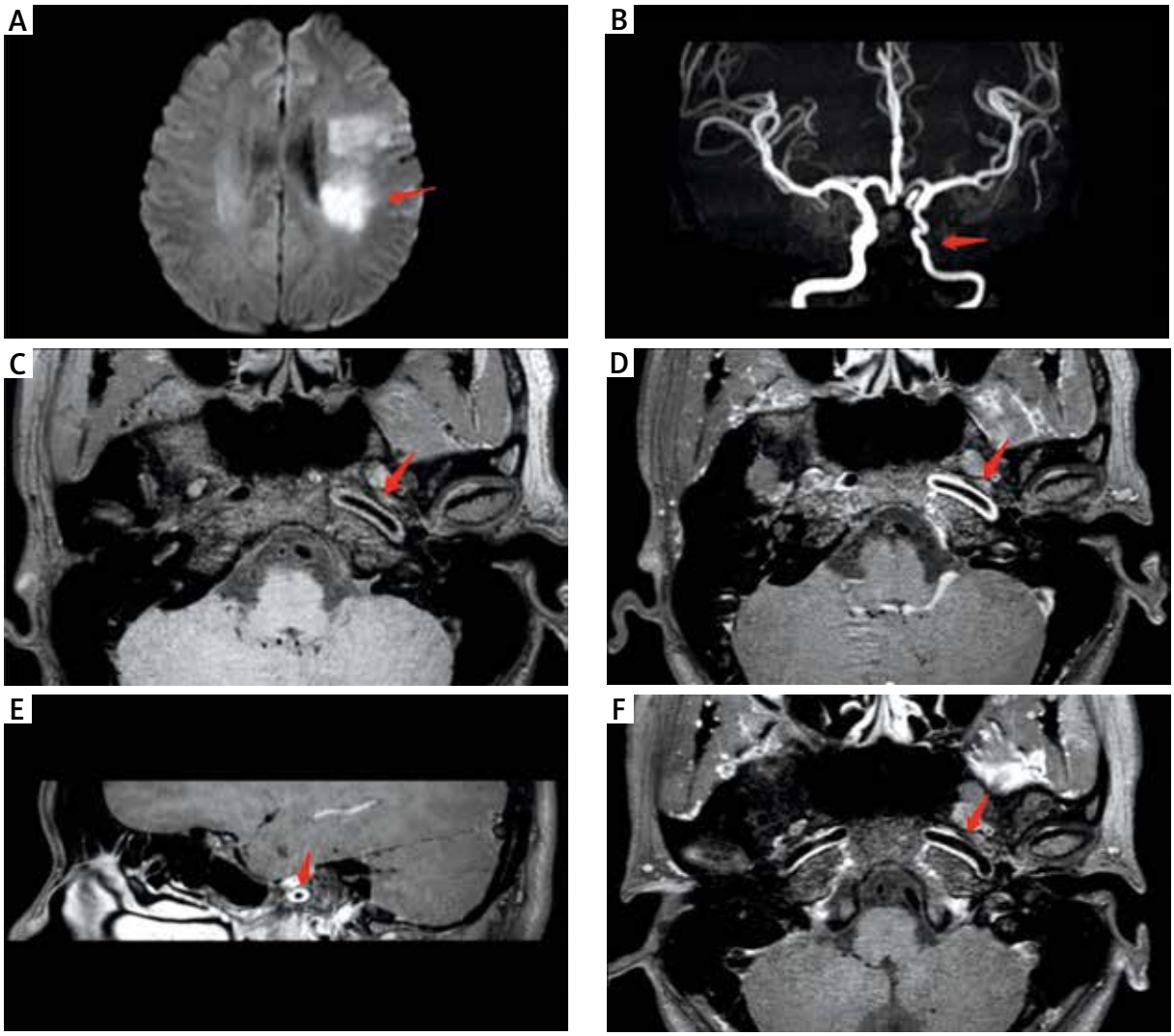

Fig. 1. Typical cases of remission after treatment of CNS vasculitis. The patient is a 36-year-old female. **A**) DWI showing acute infarction of the left radiation coronary artery; **B**) 3D-TOF MRA showing the thin left internal carotid artery; **C-E**) HR-MRI showing uniform centripetal thickening of the wall of C2-3 segment of the left internal carotid artery with grade 2 enhancement, corresponding to mild stenosis of the lumen; **F**) HR-MRI T1WI enhanced image after hormone treatment showing reduced wall enhancement and thickening.

reactions brought by brain biopsy and digital subtraction angiography (DSA) for patients.

A previous study reported that the incidence of CNS vasculitis in men was higher than that in women, and the peak age of onset is 50 years old [7]. Among the 24 cases of CNS vasculitis in this study, 16 cases were male (67.0%) and 8 cases were female (33.0%). The proportion of male patients was higher than that of female patients, which was consistent with literature reports. From the perspective of onset age, the average age and median age of the patients in this group were 32.5 years old and 32.5 years old, which were close to the median age of PACNS onset in the study by Sundaram *et al*. [17]. The discrepancy with the age of 50 reported in previous studies may be due to racial differences. Hence, when cerebral infarction occurs in a young population lacking cerebrovascular risk factors, CNS vasculitis should be considered in the differential diagnosis of aetiology.

The clinical manifestations of CNS vasculitis do not have its typical unique characteristics, with focal neurological deficits secondary to cerebral infarction being

Table I. Comparison of HR-MRI imaging differences between relapsed and non-relapsed patients

Parameter	Prognosis		*P*
	Relapsed *n* (%)	Non-relapsed *n* (%)	
Vascular side involved			0.303
Unilateral	1 (25.0)	9 (60.0)	
Bilateral	3 (75.0)	6 (40.0)	
Vascular types involved			0.505
Only involving MCA	2 (50.0)	6 (40.0)	
Only involving ICA	0	5 (33.3)	
Involving MCA and ICA	2 (50.0)	4 (26.7)	
Number of vascular segments involved	6.5	3.5	0.039

MCA – middle cerebral artery, ICA – internal carotid artery

the most common, followed by headache and other symptoms (such as seizures, cognitive, or vigilance impairment). Salvarani *et al*. [15] found that cerebral infarction in patients with CNS vasculitis tended to be multiple infarcts (89%), a few were single infarcts; in multiple infarctions, it tended to be bilateral. Intracranial haemorrhage is rare. In this study, 24 patients were treated with cerebral ischemic events and no cases of cerebral haemorrhage occurred, which is consistent with the literature reports, but unilateral infarction is more common than bilateral infarction, the reason may be related to the small sample size.

In this study, HR-MRI of CNS vasculitis patients showed uniform centripetal thickening of the involved vessel wall with varying degrees of stenosis of the lumen, which was consistent with the literature reports. Gomes [6] found that the characteristics of concentric wall thickening were related to wall media oedema caused by an inflammatory reaction. In this study, most of the involved vessel walls were grade 2 enhancement, only a few were grade 1 enhancement, and the degree of wall enhancement was reduced after hormone treatment (Fig. 1), so the degree of wall enhancement may be related to inflammatory activity or the density of nourishing vessels. Enhancement was more pronounced when inflammation was active. Most of the cases in this study were multivessel and multiarterial segmental involvement, which was consistent with the characteristics reported in the literature that CNS vasculitis was often multiarterial segmental involvement.

In this study, 24 patients with CNS vasculitis had anterior circulation vessels involved, mainly internal carotid artery and middle cerebral artery, of which only 1 had basilar artery involved at the same time. In the cases studied by Pfefferkorn *et al*. [12] and Perez *et al*. [11], most CNS vasculitis involved anterior circulation vessels and only a few invaded posterior circulation vessels. Obusez *et al*. [10] also proposed that the affected vessels of CNS vasculitis were unilateral and often located in the anterior cerebral artery, middle cerebral artery, and internal carotid artery, while the posterior cerebral artery, basilar artery and vertebral artery were rare. This suggests that CNS vasculitis is more likely to invade anterior circulation vessels, especially the internal carotid artery and middle cerebral artery, than posterior circulation vessels.

Glucocorticoids alone or in combination with immunosuppressive agents are the main treatment for CNS vasculitis, and the degree of enhancement of the vessel wall on HR-MRI decreases after anti-inflammatory treatment. In this study, the HR-MRI of patients with remission after hormone therapy revealed different degrees of alleviation of involved vascular wall enhancement and lumen stenosis, indicating that hormone therapy is effective for CNS vasculitis, and HR-MRI is helpful to evaluate the efficacy of CNS vasculitis. For the other 8 patients with poor hormone therapy effect in this study, the main reason may be that the follow-up period is not long enough. Obusez *et al*. [10] studied 6 patients with CNS vasculitis after hormone therapy, of which 4 patients still had stable enhancement of the vessel wall after a median follow-up period of 13.5 months (11-16 months). The longest follow-up time of this study is only 12 months, and a longer period of follow-up observa-

tion is needed in the future. In addition, the absence of combined immunosuppressive therapy may also be responsible for the persistent enhancement of the vessel wall.

Central nervous system vasculitis is a disease potentially associated with morbidity and mortality, which requires early diagnosis and treatment. Severe neurological deficits and cognitive impairment at the onset, as well as abnormal EEG, have been shown to be associated with poor prognosis at 6 months [5]. This study analysed the difference of imaging data between the relapsed group and the non-relapsed group, and the results showed that relapse was not related to the unilateral or bilateral disease. Comparing the two groups of affected vessels (only involving MCA, only involving ICA, MCA, and ICA at the same time) there was no significant difference, so the involvement of different arterial segments could not be used as a prognostic indicator of CNS vasculitis. Referring to the studies of Li *et al*. [9] and Eiden *et al*. [5], the number of affected vascular segments was statistically higher in the relapsed group (mean 6.5 arterial segments involved) than in the non-relapsed group (mean 3.5 arterial segments involved). The results were statistically significant, indicating that the more vascular segments involved in CNS vasculitis, the more prone to recurrence.

Supplemental tables are available on the journal's website.

Disclosure

The authors report no conflict of interest.

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