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PICTORIAL REVIEW

Clinical interpretation of high-resolution vessel wall MRI of intracranial arterial diseases

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ABSTRACT

Intracranial arterial pathology has traditionally been evaluated with luminal imaging. Recently, high-resolution vessel wall imaging (HR-VWI) with MRI has facilitated submillimetre evaluation of the arterial walls. This technique can help differentiate various causes of intracranial steno-occlusive disease, identify culprit atherosclerotic plaques with a recent cerebral infarct, locate vessel wall pathology in areas with minimal or no narrowing on luminal imaging, predict aneurysm stability and identify a ruptured aneurysm when multiple aneurysms are present. Interpretation of HR-VWI examinations requires a solid understanding of the pathophysiology, clinical features, serum and cerebrospinal fluid laboratory findings, treatment administered and fundamental patterns of VWI abnormalities that may be encountered with the intracranial vasculopathies. This pictorial essay aimed to illustrate the essential findings of common conditions encountered with HR-VWI including intracranial atherosclerosis, moyamoya disease, intracranial vasculitis, varicella zoster vasculopathy, reversible cerebral vasoconstriction syndrome and aneurysms.

INTRODUCTION

Intracranial arterial pathology has traditionally been evaluated with luminal imaging such as MR angiography, CT angiography or conventional angiography. In recent years, the development of high-resolution vessel wall imaging (HR-VWI) with MRI has enabled submillimetre MR evaluation of the arterial wall. HR-VWI complements luminal imaging and can facilitate discrimination of the many potential causes of luminal narrowing and characterize cerebral aneurysms.

BASIC IMAGING TECHNIQUES AND INTERPRETATION

HR-VWI can be performed as T_1 weighted, T_2 weighted or proton density (PD)-weighted sequences. Many radiologists prefer PD for the evaluation of contrast enhancement, given the favourable signal-to-noise ratio and sharp delineation of the arterial walls interposed between flowing blood and cerebrospinal fluid (CSF). For evaluation of contrast enhancement, images with and without gadolinium are useful, since many pathologies may demonstrate increased PD signal.

Pathologic involvement of the vessel wall can be characterized by the pattern and distribution. These features may be identified on HR-VWI prior to gadolinium administration. The pattern may be concentric, eccentric or focal and nodular. The distribution may also be solitary or multifocal. In addition, the outer diameter of the afflicted artery can decrease in size (negative remodelling) or increase in size (positive remodelling).

Currently, evaluation of vessel wall contrast enhancement is the cornerstone of the clinical use of HR-VWI. Enhancement may be pencil thin or thick and shaggy extending into the adjacent parenchyma. Multiple schemes to describe the degree of enhancement have been used for research purposes, including dichotomous characterization as simply present or absent. One useful scale with an internal reference standard has characterized enhancement as absent (Grade 0), less than the pituitary stalk (Grade 1) or equal or greater than the pituitary stalk (Grade 2: marked).¹ In clinical practice, Grade 1 enhancement ranges from minimal to moderate. Although histopathologic correlation is scant, this

Figure 1. An artist rendition of arterial wall changes with different causes of intracranial steno-occlusive disease: (a) normal proximal intracranial arterial walls consist of an intima, internal elastic lamina, tunica media and adventitia with scant *vasa vasorum*. The adventitia and *vasa vasorum* are absent in more distal intracranial arteries. (b) Atherosclerotic plaque commonly narrows the lumen, but can also eccentrically increase the total diameter of the artery (positive remodelling). Inflammatory cells and an area of haemorrhage are depicted within the plaque. There is proliferation of the *vasa vasorum*. (c) Moyamoya disease results in a markedly atrophic tunica media and intimal proliferation resulting in a small outer vessel diameter (negative remodelling) and a narrowed lumen. Although recent evidence indicates an aetiological role for inflammation, evidence of inflammation is scant on histopathology. (d) Vasculitis manifests as circumferential transmural inflammatory change and areas of wall destruction such as interrupted internal elastic lamina. The lumen is narrowed. (e) Reversible cerebral vasoconstriction syndrome (RCVS) results in a constricted tunica media with a narrowed lumen and absent inflammatory cells.

enhancement usually corresponds to expected patterns of vessel wall inflammation and/or increased *vasa vasorum* density that is known to develop with various vascular pathologies.

Interpretation of HR-VWI studies requires a solid foundation of knowledge of the clinical presentation, serologic and CSF findings and histopathology (Figures 1 and 2) of vascular diseases. The radiologist must factor in any medical treatment provided such as anti-inflammatory medication (glucocorticoids and immunosuppressants among others), antiviral medication or calcium channel blockers, since these can affect the imaging findings and their interpretation.

ATHEROSCLEROSIS

Intracranial atherosclerosis (ICAS) is one potential cause of luminal stenosis and possibly an underrecognized cause of cerebral infarction. The focus of atherosclerotic plaque characterization is shifting from a strong emphasis on the degree of stenosis to an evaluation of plaque composition and inflammation because inflammation is important for plaque development and vulnerability for rupture. On HR-VWI, ICAS typically affects the artery eccentrically along one surface and is less commonly circumferential (Figures 3 and 4). Often, there is a discrete atherosclerotic plaque that results in positive remodelling or unchanged vessel diameter and less commonly negative remodelling. ICAS plaques with recent symptomatic emboli enhance and the degree of enhancement can wane over months.¹ Asymptomatic ICAS plaques variably enhance. One advantage of HR-VWI over standard luminal imaging techniques is its ability to identify ICAS with positive remodelling and no substantial associated luminal narrowing. The length of involvement is variable, but often focal.²

In the setting of acute atherosclerotic embolic infarct, the walls of the arteries just proximal to the infarcts often demonstrate circumferential enhancement, resulting in a multifocal appearance that could be confused with vasculitis.³ In addition, an intraluminal

thrombus itself can enhance and wall enhancement just proximal to the site of embolism may be present (Figure 3).³

MOYAMOKA DISEASE

Moyamoya disease (MMD) is an intracranial steno-occlusive disease, classically involving both the distal internal carotid arteries (ICAs) and proximal middle cerebral arteries. In some

Figure 2. An artist rendition of saccular aneurysm is demonstrating a focally disrupted internal elastic lamina at the aneurysm neck. The intima, medial and adventitia are present throughout the aneurysm wall. There is proliferation of the *vasa vasorum* within the wall of the aneurysm. Increased inflammatory cells, which may be present within the aneurysm wall, are depicted.

Figure 3. An 80-year-old female with hyperlipidaemia and hypertension: (a) coronal proton density high-resolution vessel wall imaging with gadolinium is demonstrating simultaneously mildly enhancing (Grade 1) (arrow) and non-enhancing (Grade 0) (arrowhead) atherosclerotic plaque in an M2 branch. (b) There is a more avidly enhancing atherosclerotic plaque in another M2 branch (Grade 2) (arrow); (c) just distal to this, an enhancing presumed embolic atherosclerotic plaque is present within the vessel lumen (arrow) with wall enhancement proximally (arrowhead). (d) There is also smooth concentric wall enhancement of a distal middle cerebral artery branch (arrow) proximal to an area of acute infarct (the concentric distribution was more fully depicted on the complete data set). An asymptomatic mildly enhancing plaque was also present on the left (not shown).

cases, MMD can be unilateral.² Involvement of the entire M1 segment can occur. Early MMD does not always demonstrate the classic basal “puff of smoke” collateralization and may not be distinguishable from other causes of steno-occlusive disease on luminal evaluation. It is important to identify MMD, since it is generally treated surgically rather than with anti-inflammatory medications.

Most reports to date indicate that MMD demonstrates negative remodelling associated with either no enhancement or mild thin circumferential enhancement on HR-VWI (Figure 5). This enhancement potentially corresponds to intimal hyperplasia or inflammation, but the cause and clinical significance of such enhancement is still not definitively established. Simultaneous areas of enhancing and non-enhancing walls of the involved arteries may be seen. Interestingly, segments of moderate circumferential enhancement have been reported in Asian populations,⁴ but this degree of enhancement has not been widely reported in patients in Europe or North America. Some patients have areas of apparently complete arterial obliteration with no identifiable arterial wall or lumen on HR-VWI.

VASCULITIS

The intracranial arteries can be affected by either primary angiitis of the central nervous system (PACNS) or involvement from a systemic vasculitis. PACNS is notoriously difficult to diagnose clinically. While erythrocyte sedimentation rate and C-reactive protein may be elevated in systemic vasculitides, these are usually normal with PACNS. Furthermore, CSF studies generally reveal only mildly elevated total protein concentration or white blood cell counts. The sensitivity and specificity of conventional angiograms and biopsies are also limited and have procedure-related risk. Because of the general lack of sensitivity and specificity of traditional imaging techniques and laboratory values, HR-VWI has emerged as a useful tool for the diagnosis of vasculitis. HR-VWI typically demonstrates multifocal areas of marked vessel wall enhancement.⁵ This enhancement is usually concentric, but can also be eccentric (Figure 6). The enhancement can be either pencil thin or thick, extending beyond the margin of the vessel wall.

HR-VWI has also been shown to demonstrate wall enhancement of the intracranial ICAs and in some cases, the

Figure 4. A 51-year-old female with a 60 pack-year history smoking, Sjogren's syndrome and normal sedimentation rate: MRI demonstrated changes consistent with chronic anterior cerebral artery-middle cerebral artery (MCA) border zone infarcts (not shown). Conventional angiography demonstrated approximately 80 % short-segment left MCA stenosis. (a, b) High-resolution vessel wall imaging without gadolinium (a) and with gadolinium (b) demonstrating findings most consistent with eccentric enhancing (Grade 2) atherosclerotic plaque most marked along the anterior wall (arrows), but also involving the posterior wall (arrowheads).

intracranial vertebral bodies with intracranial involvement of giant-cell arteritis (Figure 7). Close examination of the external carotid artery (ECA) branches including the superficial temporal artery is generally recommended, as it can aid in the diagnosis of temporal arteritis.⁶ In addition, findings on HR-VWI could potentially be indistinguishable from varicella zoster vasculopathy; CSF tests to exclude varicella zoster in suspected cases of PACNS are routinely performed at our institution.

HR-VWI has also emerged as a useful tool for assessing response to therapy. Enhancement can substantially decrease after institution of anti-inflammatory agents. In our experience, marked reduction in enhancement has been demonstrated within weeks.

VARICELLA ZOSTER VASCULOPATHY

Varicella zoster vasculopathy is the most common viral vasculopathy of the CNS. This can occur after primary or reactivated varicella zoster virus (VZV) infection and in patients who are immunocompetent or immunosuppressed.⁷ Onset of neurologic symptoms after cutaneous eruption ranges from days to years.

VZV can result in steno-occlusive disease or aneurysmal dilatation on luminal imaging. Luminal imaging findings include areas of narrowing and occasionally aneurysm. However, false-negative results occur with conventional angiography.⁷ On CSF examination, anti-VZV immunoglobulin G (IgG) testing is more sensitive than polymerase chain reaction (PCR) for VZV DNA, which may become undetectable after 2 weeks of CNS vasculopathy.⁷

Figure 5. A 32-year-old male with history of tobacco use presented with left weakness after a motor vehicle accident: (a) a three dimensional time-of-flight MR angiography demonstrating severe bilateral M1 and A1 stenosis with proliferation of lenticulostriate perforators, most marked on the left. (b) Axial proton density high-resolution vessel wall imaging showing marked negative remodeling of the entire M1 segment of the right middle cerebral artery (MCA) with a focal area of mild smooth circumferential tram track-like enhancement (Grade 1) (arrow). There was occlusion and essentially complete obliteration of the M1 segment of the left MCA without enhancement. The overall findings are most consistent with a moyamoya pattern.

Figure 6. A 55-year-old male with recent infarcts of deep grey structures and multiple areas of intracranial arterial stenosis on conventional angiography that were new since 1 year prior (not shown). Clinical evaluation found no evidence of infection, autoimmune disorder or systemic inflammation. (a, b) Axial proton density (PD) high-resolution vessel wall imaging (HR-VWI) with gadolinium demonstrating multiple areas of eccentric vessel wall enhancement (Grade 2) in the right (a) and left (b) middle cerebral artery branches. The patient was placed on steroid and cyclophosphamide treatment with a diagnosis of central nervous system vasculitis. (c, d) A follow-up axial PD HR-VWI with gadolinium at similar levels 5 months later demonstrating resolution of the previously seen enhancement. There were no new interval infarcts.

On HR-VWI, VZV can affect the large cerebral arteries, small cerebral arteries or both. The distal ICA and proximal M1 segments are most commonly involved.⁸ HR-VWI demonstrates smooth and

concentric vessel wall enhancement, similar to that seen in autoimmune vasculitis (Figure 8). Enhancement has been shown to decrease in response to antiviral treatment, although the time course

Figure 7. A 79-year-old male with a several-month history of fatigue, weight loss and neurologic symptoms including worsening memory and visual hallucinations: erythrocyte sedimentation rate (ESR) and C-reactive protein were elevated; anti-neutrophil cytoplasmic antibody and antinuclear antibody assays were normal. Biopsy revealed temporal arteritis. Despite several months of oral prednisone treatment and ESR reduction, he developed bilateral cerebral infarcts. (a) Axial PD HR-VWI demonstrates enhancement of the wall of the left superficial temporal artery. (b) Three-dimensional time-of-flight MR angiography demonstrating high-grade supraclinoid internal carotid artery (ICA) stenosis. Proton density high-resolution vessel wall imaging (HR-VWI) demonstrating concentric enhancement of the left superficial temporal artery (arrow). (c) There is also marked smooth thin circumferential enhancement (Grade 2) of the supraclinoid left ICA. An eccentric area of wall enhancement is extending posteriorly, extending beyond the area of luminal stenosis; areas of such eccentric enhancement are possible with vasculitis. The eccentric enhancement differs from typical atherosclerosis in that it is not associated with a plaque or positive remodeling and is contiguous with a region of smooth concentric enhancement. Similar HR-VWI findings on the right were present in the right ICA (not shown).

Figure 8. A 62-year-old female with left V1 varicella zoster 3 years prior, at which time a course of acyclovir was completed. However, some inflammation remained identifiable on ophthalmologic examination. The patient presents with new left middle cerebral artery infarcts. (a) Three-dimensional time-of-flight MR angiography demonstrating narrowing of the left supraclinoid internal carotid artery, M1 and A1 branches (not shown), unchanged from 2 years prior. She had no clinical evidence of vasculitis. (b) Coronal proton density high-resolution vessel wall imaging demonstrating areas of circumferential enhancement (Grade 1) (arrow), consistent with varicella zoster vasculopathy.

of response is variable and may be prolonged.⁸ Correlation with clinical presentation is important, since HR-VWI can look similar to other vasculitides such as giant-cell arteritis or PACNS.

REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

Reversible cerebral vasoconstriction syndrome typically presents with a sudden “thunderclap” headache and is most

commonly seen in young or middle-aged females with numerous described risk factors. Although the prototypical demographics and classic presentation differ from CNS vasculitis, diagnostic uncertainty may remain after conventional luminal imaging in some cases. Differentiating between the two diagnoses is important because reversible cerebral vasoconstriction syndrome does not require anti-inflammatory or immunosuppressive therapy.

Figure 9. A 50-year-old female with a recent thunderclap headache: (a) three-dimensional (3D) time-of-flight (TOF) MR angiography (MRA) revealing multiple segments of arterial narrowing in multiple territories (arrowheads). There was no subarachnoid haemorrhage on CT or MRI (not shown). The initial clinical evaluation by rheumatology and neurology rendered a differential diagnosis of reversible cerebral vasoconstriction syndrome (RCVS) vs vasculitis. Axial proton density high-resolution vessel wall imaging (HR-VWI) without (b) and with (c) these short areas demonstrating circumferential wall thickening/signal with no enhancement on VWI (Grade 0) (arrowheads). This was interpreted as most consistent with RCVS rather than vasculitis. Calcium channel blocker medication was instituted. The areas of arterial narrowing and circumferential wall thickening all markedly diminished or resolved on a 2-month follow-up (d) 3D TOF MRA and (e) HR-VWI consistent with the diagnosis of RCVS (arrowheads).

Figure 10. Identification of culprit aneurysm in the setting of subarachnoid haemorrhage. The initial CT angiogram at the time of presentation demonstrated an apparent infundibulum of the left supraclinoid internal carotid artery. (a) On CT angiography, this was seen as a small contour abnormality with a nearby coursing vessel that was thought to arise from the apex; this was interpreted as an infundibulum. (b, c) Coronal high-resolution vessel wall imaging without (b) and with (c) gadolinium demonstrated focal enhancement near the apex of this contour abnormality, suggesting a ruptured aneurysm (arrow). This abnormality was subsequently found to represent an aneurysm during surgery and was treated with a surgical clip.

HR-VWI demonstrates multiple areas of concentric vessel wall thickening with minimal to no enhancement corresponding to the areas of luminal stenosis (Figure 9).⁵ Such areas can be subtle, particularly in smaller vessels, and each arterial branch needs to be meticulously interrogated in its entirety. Both wall thickening and luminal stenosis should markedly improve on follow-up imaging.

CEREBRAL ANEURYSM

In general, the clinical and angiographic risk factors for aneurysm growth and rupture have been well established and include smoking, hypertension, size, irregular morphology and location. However, HR-VWI is emerging as an additional useful tool in risk stratification of intracranial aneurysms. Current studies indicate that >90% of saccular aneurysms without circumferential enhancement are unruptured, non-growing and asymptomatic.⁹ Therefore, lack of wall enhancement seems to strongly

predict aneurysm stability. Preliminary data suggest that most morphologically changing or unstable aneurysms demonstrate wall enhancement, whereas most stable aneurysms do not.⁹

In the setting of subarachnoid haemorrhage and multiple aneurysms, the culprit aneurysm typically demonstrates either circumferential enhancement or focal enhancement at the rupture site.¹⁰ Focal enhancement also has potential to identify small aneurysms that would have otherwise been unrecognized or misclassified (Figure 10).

SUMMARY

HR-VWI complements traditional luminal angiographic techniques in the characterization of intracranial stenosis and aneurysms. This technique can increase the specificity of diagnosis and for some conditions seems to serve as a biomarker for disease activity.

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