DIAGNOSTIC NEURORADIOLOGY

MR vessel wall imaging in cerebral bacterial and fungal infections

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Abstract

Purpose Central nervous system (CNS) bacterial and fungal infections can cause secondary vasculitis which worsens the prognosis due to development of complications like infarctions or hemorrhages. In this prospective study, we aim to study intracranial vessel wall imaging findings in bacterial and fungal infections.

Methods We included 12 cases of nontubercular bacterial and fungal CNS infections each, in whom definitive microbiological diagnosis could be made. High-resolution vessel wall imaging (VWI) and time of flight MR angiography (TOF MRA) were incorporated in the routine imaging protocol. All cases were evaluated for the presence of vascular enhancement, pattern of enhancement, and stenosis on VWI. Statistical analysis was done to evaluate association between findings of vessel wall imaging and infarctions.

Results We found infarctions in 5 out of 12 cases (41.7%) of the bacterial group and 7 out of 12 cases (58.3%) of the fungal group. Vessel wall enhancement was seen in 5 cases (41.7%) of the bacterial group and 9 cases (75%) of the fungal group. There was a significant association between infarctions and vessel wall enhancement in the fungal group. However, pattern of enhancement or stenosis on VWI was not significantly associated with presence of infarction. VWI detected more cases of vascular involvement than TOF MRA.

Conclusion Secondary infectious vasculitis in bacterial and fungal infections can be detected by VWI, which can play an important role in better patient management as detection of vascular involvement can prompt early treatment to prevent complications like infarctions or hemorrhages.

Keywords Bacterial infection · Fungal infections · CNS vasculopathy · Vessel wall imaging

Abbreviations

ACA	Anterior cerebral artery
AICA	Anterior inferior cerebellar artery
BA	Basilar artery
CP	Cerebellopontine
COVID	Coronavirus disease
CSF	Cerebrospinal fluid
DSA	Digital subtraction angiography
FOV	Field of view
FS	Fat suppressed
GCS	Glasgow coma scale
ICA	Internal cerebral artery
ICAD	Intracranial atherosclerotic disease
MCA	Middle cerebral artery
MRA	Magnetic resonance angiography
PCA	Posterior cerebral artery
PCR	Polymerase chain reaction
PICA	Posterior inferior cerebellar artery
TOF	Time of flight
VA	Vertebral artery
VWI	Vessel wall imaging

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Introduction

Secondary vasculitis is a serious complication of CNS infections and is known to occur in tubercular, bacterial, viral, fungal, and parasitic infections etc. [1]. The morbid complications of infective vasculitis encompass ischemic or hemorrhagic stroke, venous thrombosis, and aneurysm formation [2]. Imaging evaluations should be directed to detect these complications in early stage for better disease prognostication. Mechanisms of vascular involvement include infiltration of vessels by basal exudates, extension of inflammation via meninges, hematogenous spread via vasa vasorum, immune-mediated, toxic effects of released endotoxin or exotoxin by inciting organisms, or infection-induced procoagulant state [1, 3, 4]. Inflammation of the vessel wall leads to circumferential mural thickening, stenosis, beading, or thrombosis. Necrotizing inflammation causing vascular destruction may cause aneurysm formation and hemorrhage. Inflammation of the venous walls may lead to venous thrombosis. In earlier times, the diagnosis of vasculitis was done by cortical and meningeal biopsies. However, with the advent of vessel wall imaging, diagnosis of these vascular complications has become easier.

CT angiography, MR angiography, and DSA can show luminal abnormality in the form of stenosis, dilatation, or irregularity with no information about the abnormalities of the vessel wall. There are many pathologies like intracranial atherosclerosis (ICAD) or vasculitis which may not cause any apparent change in lumen diameter but can cause changes in the vessel wall which may be missed in routine imaging [5]. Vessel wall imaging can directly image the vessel wall using high-resolution spin echo MR imaging technique. Luminal blood and surrounding CSF are suppressed by various techniques which enable visualization of intervening vessel wall and its morphology [6].

The cerebrovascular complications may produce focal neurological deficits, seizures, or altered sensorium. However, many times clinical diagnosis is difficult as symptoms are masked by the presence of other manifestations of CNS infections, like altered sensorium. In these cases, VWI plays an important role for the identification of vascular involvement. On the detection of vascular involvement, appropriate early management in the form of antiplatelets and anti-inflammatory drugs can be initiated to prevent complications. Enhancement on VWI is an indicator of activity of the disease, thus plays a role in deciding the duration of treatment [7]. VWI is also helpful in guiding sites of involvement for biopsies [7].

Common organisms responsible for infective vasculitis in bacterial infections are *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Neisseria meningitidis*, *Mycoplasma pneumoniae*, and *Haemophilus influenzae*. Vascular complications are also seen in fungal infections, especially in cases of angioinvasive hyphae forming larger fungi, e.g., *Aspergillus* and *Mucor*. Small fungi like *Candida* and *Cryptococcus* may also cause vascular involvement, through involvement of microcirculation. These vascular complications are common in advanced stage of disease and in immunocompromised individuals.

The role of VWI in the detection and characterization of vascular involvement in tubercular meningitis has been described [5, 7, 8]. However, vessel wall imaging findings in non-tubercular bacterial and fungal CNS vasculitis have not been described in literature yet. In this study, we attempt to characterize vascular complications of bacterial and fungal infections using vessel wall imaging. This will allow us to understand the pathophysiology of vascular involvement in these CNS infections which can contribute to modify management in order to avoid vascular complications like infarction or hemorrhage.

Materials and methods

We included vessel wall imaging in routine imaging protocol of consecutive cases of suspected bacterial and fungal CNS infections referred for MRI evaluation. The cases were followed up for definitive diagnosis of infective pathology. Only those cases in which definitive diagnosis could be made by CSF gram staining/CSF culture/biopsy/PCR were included in the study. We had a total of 12 cases of proven bacterial infection. Three were known cases of staphylococcal sepsis. Gram staining of CSF was positive for cocci in 2 patients. CSF culture in 4 patients revealed streptococci, staphylococci, and *Haemophilus influenzae*. Surgery was performed in 2 patients (one case of right temporal abscess and the other case of left CP angle abscess) and microbiological examination of post op specimen was positive for *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*. One case of scrub typhus had positive CSF PCR for *Orientia tsutsugamushi*.

We had a total of 12 cases of proven fungal infections. Seven cases had proven fungal sinusitis (*Aspergillus* and *Mucor* infections) and had cerebral extension. Two cases had cerebral fungal abscesses which were aspirated. One case of *Candida* infection was biopsy proven. Two cases of *Cryptococcus* infection had positive India ink and *Cryptococcus* antigen in CSF examination.

Vessel wall imaging MRI acquisition

All cases underwent MR scanning either in 1.5 T Siemens Magnetom Aera System, Erlangen, Germany or 3 T GE

Discovery MR 750w, Norwalk, Connecticut, USA or 3 T Philips Ingenia Koninklijke MRI System, Best, Netherlands. For vessel wall imaging, high-resolution pre- and post-contrast 3D T1 FS sequences (SPACE, CUBE, and VISTA in Siemens, GE, and Philips respectively) were acquired. MRI protocols on a 1.5-T Siemens scanner were as follows: TR = 600 ms, TE = 7.2 ms, flip angle = 90, FOV = 250, slice thickness = 1, matrix = 256, and number of slices = 192. The protocols on a 3-T GE scanner were as follows: TR = 650 ms, TE = 13 ms, flip angle = 90, FOV = 220, slice thickness = 0.7, matrix = 256, and number of slices = 176. Protocols on a 3-T Philips scanner were as follows: TR = 400 ms, TE = 19 ms, flip angle = 90, FOV = 202, slice thickness = 1, matrix = 240, and number of slices = 200. Other routine sequences and 3D TOF MRA were also acquired.

Image analysis

Supraclinoid ICA, A1 and A2 segments of ACA, M1 and M2 segments of MCA, P1 and P2 segments of PCA, and basilar artery were evaluated on VWI for the presence of enhancement. Categorization of enhancement pattern into smooth and nodular was done. If part of circumference of the vessel wall was showing enhancement or if part of enhancing wall was twice as thick as the rest of the wall, then it was termed as nodular enhancement. Stenosis of the arteries was measured and classified into grade I (< 50% stenosis), grade II (50–70% stenosis), and grade III (> 70% stenosis).

Results

Bacterial CNS infections (Table 1)

We found infarctions in 5 of 12 cases (41.7%) of bacterial infections. Three cases had single territory infarcts while 2 cases had multi-territory infarcts. Maximum number of infarcts were seen in MCA territory (n = 5, 41.7%) and watershed territories (n = 3, 25%), followed by PCA (n = 2, 16.7%) and ACA territories (n = 1, 8.3%). Vessel wall enhancement was seen in 5 cases, 3 of which had infarcts in the territory of involved vessel. Three out of 5 cases of infarcts showed enhancement in the responsible artery, while 2 cases of infarcts did not show any vascular involvement. Most common sites of vessel wall enhancement were ICA (n = 4; bilateral in 2 cases and unilateral in 2 cases) and MCA (n = 4, bilateral in 2 cases and unilateral in 2 cases) followed by ACA (n = 2), PCA (n = 2), and BA (n = 2). No significant association was found between infarctions and vessel wall enhancement (p = 0.1) (Table 3). Three cases showing vessel wall enhancement had shown stenosis of the artery. Enhancement pattern was smooth in 4 cases and nodular in 1 case. No significant association between infarction

and pattern of enhancement or stenosis on VWI was found (p > 0.05). TOF MRA showed abnormality in 3 cases in the form of stenosis but failed to detect vascular involvement in 2 cases which showed enhancement on VWI without significant stenosis.

Fungal CNS infections (Table 2)

Infarcts were seen in 7 out of 12 cases of fungal infections (58.3%) while 9 cases (75%) showed vessel wall enhancement. Causative fungi were *Aspergillus* in 6 cases, *Mucor* in 3 cases, *Cryptococcus* in 2 cases, and *Candida* in 1 case. Six had acute infarcts and 1 had chronic infarct. Multi-territorial infarcts were seen in 4 cases (33.3%) and single territory infarcts was seen in 3 cases (25%). Common locations of infarction were ACA territory (n = 2), MCA territory (n = 2), BA territory in the brainstem (n = 2), and watershed territories (n = 3). Seven of the 9 cases which showed vessel wall enhancement had infarction in the territory of involved vessel. Two cases showed vascular enhancement but no infarcts. All 7 cases with infarct showed enhancement of the responsible artery. Significant correlation was found between infarctions and vessel wall enhancement (p = 0.04) (Table 3). The most common site of vessel wall enhancement was ICA (n = 5; bilateral in 1 case and unilateral in 4 cases), followed by basilar artery (n = 4), MCA (n = 3), and ACA (n = 3). Seven cases showed stenosis on VWI. Enhancement pattern was smooth in 5 cases and nodular in 4 cases. No significant association between infarction and pattern of enhancement or stenosis on VWI was found (p > 0.05). TOF MRA showed abnormality in the form of stenosis in 7 cases, but failed to detect vascular involvement in two cases, in which VWI showed enhancement without significant stenosis.

Discussion

Bacterial CNS infections (Figs. 1 and 2)

High morbidity and mortality is seen in bacterial infections of the CNS. These infections spread to the CNS from primary focus elsewhere in the body through contiguous or hematogenous spread. Contiguous spread may be seen secondary to sinusitis or post-traumatic skull base fracture or through iatrogenic inoculation of infections.

Pneumococcal meningitis commonly develops due to contiguous spread of infection from primary infections of PNS, temporal bone, or skull base fracture or hematogenous spread from primary lung infection. Comorbidities like DM, hypertension, and immunocompromised status increase the risk of CNS involvement. Streptococcal meningitis is more common than Staphylococcal meningitis [9]. *Streptococcus*

Table 1 Details of cases of bacterial infections

Sr. no	Age (in years)	Sex	Imaging findings	Infarcts	TOF MRA	VWI-sites of enhancement	Grade of stenosis on VWI	Pattern of enhancement on VWI	Organism
1	0.5	M	Left Sylvian fissure abscess, meningitis (Fig. 1)	Left MCA territory acute infarct	Nonvisualization of left ICA and left MCA	Left ICA, left MCA	3	Nodular	*Streptococcus pneumoniae, Haemophilus influenzae*
2	11	M	Ventriculitis, meningitis	Focal acute infarct in left MCA territory	Normal	No enhancement	-	-	*Staphylococcus*
3	20	M	Hydrocephalus, meningitis	No infarct	Normal	No enhancement	-	-	Cocci in gram staining of CSF
4	57	M	Post-traumatic CSF rhinorrhea, meningitis, encephalomalacia in bilateral frontal and left occipital lobe	No infarct	Normal	No enhancement	-	-	*Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes*
5	27	F	Right temporal abscess	No infarct	Normal	No enhancement	-	-	*Staphylococcus, Streptococcus pyogenes, Streptococcus pneumoniae*
6	10	F	Meningitis, subdural empyema along the clivus (Fig. 2)	No infarct	Normal	BA	No stenosis	Smooth	*Staphylococcus*
7	60	M	Ventriculitis	Acute infarcts in right ACA, left PCA, right MCA, left ACA-MCA and B/L MCA-PCA watershed territory	Stenosis of right A2 ACA	B/L ICA, right M1 MCA, B/L A2 ACA, B/L P1 PCA	1	Smooth	*Streptococcus* b
8	73	M	Ventriculitis	Acute left MCA territory and B/L ACA-MCA watershed territory infarcts	Normal	Right ICA, B/L MCA	No stenosis	Smooth	Cocci in gram staining of CSF
9	35	F	Left CP angle abscess	No infarct	Normal	No enhancement	-	-	*Staphylococcus, Streptococcus pyogenes*
10	15	M	Meningitis	Multiple hemorrhagic acute infarcts in left MCA, B/L ACA-MCA watershed territory, and B/L PCA territories	Normal	No enhancement	-	-	*Staphylococcus*
11	14	F	Meningitis, ventriculitis, diffuse cerebral edema	No infarct	Stenosis of B/L ICA, B/L MCA, B/L PCA, BA	B/L ICA, B/L MCA, B/L PCA, BA	2	Smooth	*Staphylococcus, Streptococcus pneumoniae*
12	20	F	Scrub typhus-thalamic altered signal intensity	No infarct	Normal	No enhancement	-	-	*O. tsutsugamushi*

Table 2 Details of cases of fungal infections

Sr. no	Age (in years)	Sex	Imaging findings	Infarcts	TOF MRA	VWI-sites of enhancement	Grade of stenosis on VWI	Pattern of enhancement on VWI	Organism
1	35	F	Altered signal intensity lesions in basal ganglia	No infarcts	Normal	No enhancement	-	-	*Cryptococcus*
2	10	M	Leptomeningitis with hemorrhages in left Sylvian fissure	Left MCA territory subacute infarct	Stenosis of left ICA and MCA	Left ICA, left M1 and M2 MCA, left A1 ACA, left P1 and P2 PCA	Grade 1 in left ICA and MCA	Smooth	*Candida*
3	21	F	Fungal sinusitis, enhancing masses in bilateral cavernous sinuses and along bilateral tentorium, meningitis	Acute infarcts in right ACA, left AICA, and left PICA	Severe stenosis of BA, right ACA	B/L ICA, right ACA, B/L MCA, BA	3 (BA and right ACA)	Nodular	*Aspergillus*
4	51	M	Right temporal fungal abscess, meningitis	No infarct	Normal	Right ICA	No stenosis	Smooth	*Aspergillus*
5	60	M	Peripherally enhancing bifrontal fungal masses with hemorrhages in left frontal lobe, meningitis	No infarct	Normal	No enhancement	-	-	*Aspergillus*
6	68	M	Fungal sinusitis, meningitis, IVH, hydrocephalus (Fig. 3)	B/L ACA, B/L ACA-MCA watershed hemorrhagic acute infarcts	Right A2 ACA severe stenosis, mild stenosis of left A2 ACA, mycotic aneurysm of right A2 ACA	B/L ACA, mycotic aneurysm of right A2 ACA	Grade 3 in right A2 ACA	Nodular	*Aspergillus*
7	17	M	Leptomeningitis	No infarct	Normal	No enhancement	-	-	*Cryptococcus*
8	42	M	Skull base osteomyelitis, pachymeningitis, B/L cavernous sinus involvement (Fig. 4)	Acute infarcts in left hemipons, left cerebellum, right ACA-MCA watershed territory	Normal	BA	No stenosis in 1st scan, occlusion of BA in follow-up scan	Nodular	*Mucor*
9	35	M	Rhino-orbito-cerebral mucormycosis, left frontal abscess, pachymeningitis, left cavernous sinus involvement	Left ACA-MCA watershed acute infarcts	Stenosis of left cavernous and supraclinoid ICA	Left supraclinoid ICA	2	Smooth	*Mucor*
10	27	M	Basal exudates, sphenoid sinusitis, clival involvement	Chronic infarct in left MCA territory	Stenosis of left MCA	Left M1 MCA and BA	2 (left M1 MCA)	Smooth	*Aspergillus*

Table 2 (continued)

Sr. no	Age (in years)	Sex	Imaging findings	Infarcts	TOF MRA	VWI-sites of enhancement	Grade of stenosis on VWI	Pattern of enhancement on VWI	Organism
11	54	F	Right frontal abscess, pachymeningitis, right cavernous sinus involvement, right trigeminal nerve enhancement	No infarct	Right ICA occlusion	Supraclinoid right ICA	Occlusion of cavernous ICA and grade 2 stenosis of supraclinoid ICA	Nodular	*Mucor*
12	35	M	Homogenously enhancing fungal mass in prepontine cistern with clival involvement, meningitis	Chronic infarct in right hemipons and right cerebellum	Basilar occlusion	BA, left V4 VA	Grade 3 in BA	Smooth	*Aspergillus*

Table 3 Association between enhancement on VWI and infarctions

		Infarct +	Infarct −	p value
Bacterial infections	VWI +	3	2	0.5
	VWI −	2	5	
Fungal infections	VWI +	7	2	0.04
	VWI −	0	3	

pneumoniae has poorer prognosis than meningococcal infection because of the more invasive nature of *S. pneumoniae* [10]. Meningococcal, Haemophilus, and pneumococcal meningitis commonly affects children and young adults; however, due to vaccinations in the current era, incidence in children is reducing and adults are predominantly affected [11].

The pathophysiology of infective vasculitis in bacterial infections involves release of inflammatory cytokines which disrupt the blood–brain barrier and cause involvement of the vascular structures [12]. The adventitia of the subarachnoid vessels is formed by the arachnoid. So, it is believed that vascular involvement may be present since the early stage of the disease itself. The neutrophils infiltrate the intima with proliferation of intimal cells and endothelium. These cells accumulate below the intima and elevate it. Histopathological examinations have revealed that media remain unaffected and the adventitia was found to be contiguous with exudates [13]. In late stages, proliferative angiitis may develop which can cause partial arterial stenosis, while complete occlusion is rare. Necrotizing inflammation of the arterial wall may cause thrombosis, SAH, or mycotic aneurysm formation [14]. Mycotic aneurysms have very high rupture rate. The bacteria may also clog the small vessels in cases of florid bacteremia leading to infarcts.

Out of all the cases in our study population, infarction was seen in 5 cases (41.7%). Various studies have reported incidence of infarctions in bacterial infections ranging from 10 to 31% [13, 15–17]. Smith and Landing studied 34 post-mortem cases of *H. influenzae* meningitis and reported vascular involvement (arterial in 6 and venous in 10) in 16 of them [18]. Lyons and Leeds did cerebral angiography in a 6-month-old infant suffering from *Haemophilus influenzae* meningitis and found stenosis, occlusion, vasospasm, irregular dilatations, and slow arteriovenous transit [19]. Stroke rate is reported to be higher with *Streptococcus pneumoniae* (36%) than with *Neisseria* meningitidis (9%) [20]. Infarction in bacterial infections develops in the acute phase of the disease, unlike in tuberculosis where infarcts may develop in the chronic stage of the disease. We found maximum number of infarcts in the MCA territory ($n = 5$, 41.7%) and watershed territories ($n = 3$, 25%). Previous studies have shown that infarcts are multiple and typically formed at deep gray nuclei, gray–white junction, and thalami [4]. We also found such multiple focal infarcts in 3 cases.

Fig. 1 A case of bacterial meningitis in a 5-month-old male child with abscess in left Sylvian fissure showing central restriction of diffusion (thick arrows in **a** and **b**). Restricted diffusion is also seen in left MCA territory suggesting acute infarction (**c**). Coronal MIP TOF MRA image (**d**) showing nonvisualization of left ICA and MCA. Post-contrast axial and oblique coronal vessel wall imaging showing peripherally enhancing lesion in left Sylvian fissure (thick arrow in e and f) with nodular enhancement (inset in **e**) and severe stenosis of left M1 and M2 MCA (thin arrows in **e** and **f**)

Vessel wall enhancement was seen in a total of 5 cases (41.7%). There was no significant association between infarctions and vessel wall enhancement. Three cases showed stenosis on VWI and the findings corroborated on TOF MRA as well. In two cases, enhancement was present on VWI, but TOF MRA failed to detect vascular abnormality. In the study by Jan et al., TOF MRA was done in 5 of 13 cases of bacterial meningitis and vasculitic features were found in 3 of them [15]. We also had one case of scrub typhus which is caused by *Orientia tsutsugamushi*. Bilateral thalamic T2 and FLAIR hyperintensity was seen; however, no vascular complication or vessel wall enhancement was seen. Scrub typhus is known to be associated with cerebrovascular complications, as it causes widespread endothelial injury [21].

Fungal CNS infections (Figs. 3 and 4)

Vascular complications can be seen in fungal infections by both smaller yeasts as well as hyphae forming larger fungi. Yeast infections of the CNS (*Cryptococcus*, *Candida*, histoplasma, coccidioidomycosis etc.) occlude the smaller sized vessels leading to microabscesses, micro/focal infarcts, and microhemorrhages. These smaller sized fungi can easily travel to the microcirculation and invade the leptomeninges, leading to leptomeningitis.

Hyphae-forming fungi (e.g., *Aspergillus*, *Mucor*) on the other hand cause infarcts of variable sizes, ranging from punctate to lobar. Clinical course of the patients is generally indolent with recurrent and progressive ischemic symptoms. These larger fungi are angioinvasive and produce elastase, which destroys the elastin present in the arterial walls [22]. They affect medium- and large-sized vessels leading to thrombosis. The bland infarcts may also evolve into secondary abscesses. The infarcts are commonly seen in anterior circulation [23]. However, we found infarcts in all territories. Anterior circulation site predilection may be explained by the primary site of involvement, i.e., sinonasal fungal disease, from where fungus may invade anterior skull base and involve anterior parts of cerebral hemispheres. Intracranial spread from sinonasal infection is the most common mode of spread in India [24]. Cavernous sinus may get thrombosed with further involvement of cavernous ICA [3]. Such pattern of disease

Fig. 2 A 10-year-old female child, a known case of staphylococcal sepsis, presented with headache and fever. Axial DWI (**a**) shows restriction of diffusion along the ventral aspect of the brainstem (arrow), suggestive of subdural empyema. Sagittal FLAIR image (**b**) shows FLAIR hyperintense contents (arrow) along the clivus extending inferiorly up to the cervicomedullary junction. Post-contrast axial (**c**) and sagittal (**d**) vessel wall imaging shows smooth enhancement in the basilar artery (thick arrows in c and d, inset in **c**) and leptomeningitis along the cerebellar folia (thin arrows in **c** and **d**)
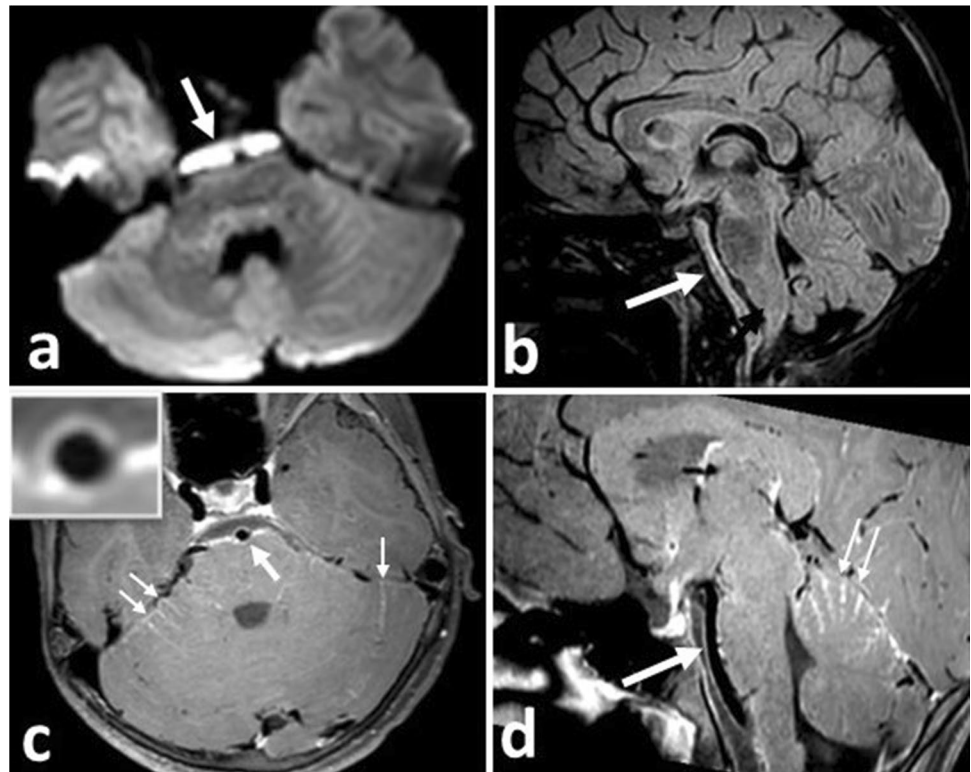
spread is seen in 10 to 20% of cases. We found anterior circulation involvement in 5 cases (41.7%). We also had 4 cases (33.3%) where basilar artery was involved secondary to extension of the pathology from sphenoid sinus to prepontine cistern. Apart from contiguous spread, hematogenous spread may also occur which causes angioinvasion by initial intimal necrosis in medium- and large-sized vessels. Perforating arteries are commonly involved with resultant infarction in the basal ganglia [1]. This predilection may be explained by invasion of vessel wall with involvement of origins of lenticulostriate and thalamoperforators. Fungal elements can also infiltrate the vessel wall with extension of hyphae in the lumen with subsequent embolization causing infarction [25].

In immunocompromised or diabetic individuals, mycotic aneurysms may be formed due to elastase-induced vessel wall destruction [26]. Infiltration and necrosis of vessel wall may cause SAH or ICH. The most common causative organism of mycotic ICA aneurysms is *Aspergillus* [27]. In one of our cases of sinonasal aspergillosis, there was formation of fusiform mycotic aneurysm in right A2 ACA which showed enhancement and had ruptured, leading to IVH (Fig. 3). Fungal mycotic aneurysms are generally fusiform in shape and proximal in location, as long segments of proximal larger vessels are involved, while bacterial mycotic aneurysms are round in shape and smaller in size and commonly involve distal vessels [1, 28, 29]. Cavernous and supraclinoid ICA are common sites of fungal mycotic aneurysms which are

in close proximity to the affected sinuses [30, 31]. Fungal mycotic aneurysms have poor prognosis and carry high morbidity and mortality after rupture. These are managed by endovascular methods with concurrent antifungals. Unruptured mycotic aneurysms are primarily managed by antibiotics/antifungals and if they respond to medical treatment with reduction in size in follow-up imaging, then endovascular management is not required. However, increase in size or appearance of new aneurysms mandates interventional treatment [4].

Mucormycosis is a lethal opportunistic infection, seen in immunocompromised status, DM, etc. It causes necrotizing vasculitis with severe infiltration of intracranial structures, soft tissues of face, and adjacent neck spaces. *Mucor* has special predilection for internal elastic lamina of the arteries with fast hematogenous spread. The intracranial vessels show extensive damage to the endothelium, leading to its thrombosis. We also found vascular occlusion in 2 of 3 cases of *Mucor* infection. Posterior circulation involvement is seen in the advanced stage of the disease [32]. Watershed infarcts are seen when the artery is partially occluded [33]. We found such infarcts in 2 cases. In the current pandemic era of COVID-19, mucormycosis cases are on the rise which is likely related to treatment-induced immunosuppression, hyperglycemia, acidosis, or high ferritin levels [34, 35].

We also had two cases of *Cryptococcus* infection, one with gelatinous pseudocysts in the basal ganglia and the other with leptomeningitis. There was no vascular
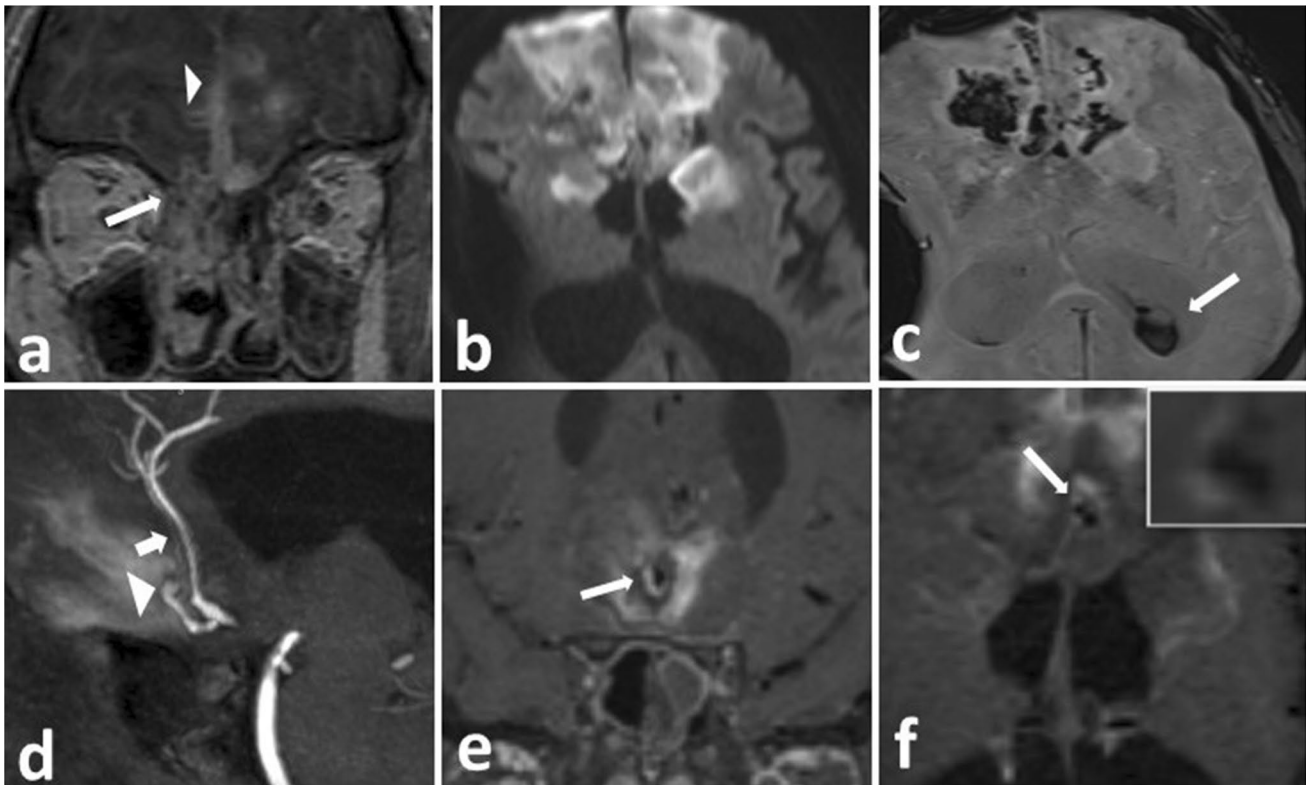
Fig. 3 A 68-year-old male patient, a known case of fungal sinusitis, presented with altered sensorium and bilateral paraparesis. Post-contrast coronal 3D-T1-weighted image (**a**) showing enhancing contents in right ethmoid air cells with erosion of right fovea ethmoidalis (arrow in **a**) and leptomeningeal enhancement in bilateral frontal lobes (arrowhead in a). Acute infarcts are seen in bilateral ACA territories (**b**) with hemorrhagic transformation as seen in SWI image (**c**). Susceptibility changes are seen in lateral ventricles (arrow in **c**) suggestive of intraventricular hemorrhage. MIP oblique sagittal image of TOF MRA (**d**) showing fusiform mycotic aneurysm arising from right A2 ACA (arrowhead in **d**) with severe attenuation of distal right A2 ACA (thick arrow in **d**). Post-contrast coronal (**e**) and axial (**f**) vessel wall imaging showing enhancement along the walls of aneurysm (arrow in e) and nodular enhancement (inset in **f**) with moderate stenosis of right distal A2 ACA (arrow in **f**)

involvement on vessel wall imaging or infarction. *Cryptococcus* meningitis has been reported to cause infarcts in 26% of cases [36].

Smooth or nodular enhancement pattern is determined by histopathological basis of vascular involvement. Intramural granuloma formation or chronic proliferative angiitis may produce nodular pattern of enhancement, which has been described in tubercular meningitis [8, 37]. Nontubercular bacterial infection produces vascular involvement predominantly by contiguous extension of inflammation through adventitia [13]. So, it can be hypothesized that they may predominantly produce circumferential smooth enhancement in acute stages, while long-standing cases with development of proliferative angiitis may show nodular or eccentric enhancement. We also found 4 cases of bacterial infections with smooth enhancement and only 1 case with nodular enhancement. On the other hand, fungal infections produce granulomatous inflammation and thus can show nodular enhancement. However, we found smooth enhancement in 5 cases and nodular enhancement in 4 cases. Our results are only speculative and further studies are needed to correlate radiological findings of vessel wall enhancement with histopathological evidence and to prove these hypotheses.

Thus, vessel wall imaging can detect vascular involvement in bacterial and fungal infections and can help to identify territory at risk. By incorporating vessel wall imaging in routine imaging, we can improve our ability of disease prognostication in terms of detection of vascular complications. On identification of vascular involvement, early treatment can be initiated in the form of antiplatelets, corticosteroids, and anti-inflammatory drugs to preclude development of vascular complication, which can have great positive impact on patient management [3, 20]. Vessel wall imaging can perform better than TOF MRA for the detection of vascular involvement, as in both groups, TOF MRA failed to detect vascular involvement in 2 cases each, which were detected by VWI.
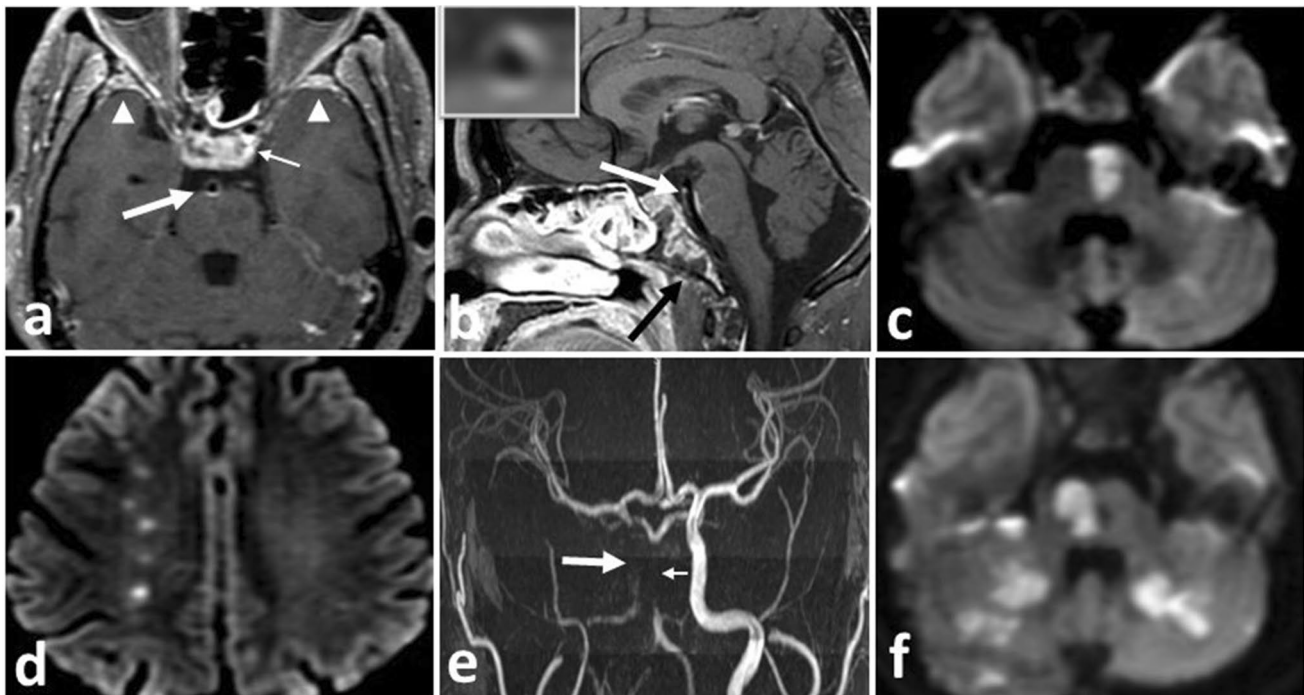
Fig. 4 A 42-year-old male patient, a known case of rhinocerebral mucormycosis, presented with altered sensorium. Axial (**a**) and sagittal (**b**) post-contrast vessel wall imaging shows heterogenous enhancement in the clivus (thin arrow in a and black arrow in **b**). Thick pachymeningeal enhancement was seen along the bilateral anterior temporal region (arrowheads in **a**). The basilar artery showed nodular enhancement pattern (thick white arrows in **a** and **b**, inset in **b**). Acute infarcts were seen in left hemipons (**c**) and right ACA-MCA watershed territory (**d**). The patient did not respond to the treatment and deteriorated. Repeat imaging done 1 month later revealed occlusion of the right ICA in distal petrous and cavernous segment (thick arrow in **e**) and basilar trunk (small thin arrow in **e**). New infarcts developed in bilateral cerebellum and right hemipons (**f**)

Other non-infective causes of vasculopathy in which vessel wall imaging plays an important diagnostic role include ICAD, primary CNS angiitis, RCVS, and Moyamoya disease [38]. ICAD can be differentiated from infective vasculitis on imaging by the presence of eccentric enhancing thickening which, on high-resolution T2WI, may also show presence of fibrofatty plaque [39]. Presence of positive remodeling is highly suggestive of ICAD as other stated etiologies cause stenosis of the involved arteries. Clinical profile and other distinctive parenchymal abnormalities in CNS infections are other pointers to differentiate the two. It is difficult to differentiate primary CNS angiitis from infective vasculitis in the absence of serological or CSF studies as both show circumferential enhancement on VWI [38]. Parenchymal imaging features are also similar in the form of infarcts, hemorrhages, and leptomeningeal enhancement. RCVS presents with thunderclap headache which resolves by 3 months, and is characterized by constriction of tunica media. The Moyamoya disease presents with recurrent strokes and is characterized histopathologically by fibrocellular intimal hyperplasia. Both RCVS and Moyamoya disease can be differentiated from infective vasculitis as both of them have characteristic clinical profile and show none to mild vascular enhancement on VWI [40, 41].

Limitation

Our study had few limitations. The sample size was small. Although all cases were proven CNS infections, we did not have any histopathological correlation of vascular findings. Cases were acquired in both 1.5-T and 3-T MRI scanners, which may have affected the results, as detection of vascular involvement is more accurate on 3 T. Also, it was difficult to assess distal vessels beyond second-order branches on VWI, which may have caused overlooking of some findings.

Conclusion

Cerebrovascular complications in CNS bacterial and fungal infections are poor prognostic markers. Vessel wall imaging can play a very significant role in identifying vascular involvement. VWI's detection rate of vascular involvement is better than TOF MRA. Detection of vessel wall enhancement may prompt early treatment with antiplatelets, steroids, and anti-inflammatory drugs to prevent development of vascular complications. Thus, incorporation of vessel wall imaging

in routine MRI should be considered for better management of these infections.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional FJ and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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