Imaging Spectrum of CNS Vasculitis

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Abbreviations: ANCA = antineutrophil cytoplasmic antibody, APLA = antiphospholipid antibody, CNS = central nervous system, CSF = cerebrospinal fluid, DSA = digital subtraction angiography, DW = diffusion-weighted, FLAIR = fluid-attenuated inversion recovery, HIV = human immunodeficiency virus, IgA = immunoglobulin A, PACNS = primary angiitis of the CNS, RCVS = reversible cerebral vasoconstriction syndromes, SLE = systemic lupus erythematosus, SW = susceptibility-weighted, VZV = varicella-zoster virus

RadioGraphics 2014; 34:873–894

Published online 10.1148/rg.344315028

Content Codes: MR, NR, VA

Introduction

Cerebral vasculitis is defined as the inflammation of blood vessel walls with or without necrosis, leading to obstruction of the lumen, increased coagulation due to the effects of proinflammatory cytokines, alteration of vascular tone, a loss of neurologic function, and a wide variety of neurologic manifestations. Central nervous system (CNS) vasculitis occurs as part of a systemic vasculitis defined as inflammatory damage to the walls of large, medium-sized, small, and variable-sized vessels; however, single-organ CNS vasculitis may also occur as an idiopathic disorder restricted to the CNS. In addition, vasculitis may be associated with systemic connective tissue disorders or may be secondary to infection, malignancy, drugs, or radiation therapy (1–4).

The pathogenesis of vasculitis remains poorly understood, and the role of the immune response in vascular injury varies with the disease. For almost all forms of vasculitis, the triggering element (eg, antigen) initiating and driving this inflammatory response is unknown (3–5).

Diagnosing vasculitis is challenging for physicians, especially in patients who present with nonspecific symptoms (eg, fever, fatigue, night sweats, and weight loss) or signs of systemic inflammation. Symptoms of cerebral vasculitis may be neurologic, psychiatric, or both, and cognitive deterioration may be a leading feature. When the cerebral symptoms are part of a systemic disorder, the diagnosis may be easier, unless the cerebral symptoms are the first or only manifestations (3–6). Important clinical factors that merit consideration...
In this article, we discuss various types of CNS vasculitis in terms of classification, imaging methods, and imaging appearances. Reversible cerebral vasoconstriction syndromes (RCVS) and moyamoya disease are also discussed, since they may simulate single-organ vasculitis.

### Classification

Vasculitis can be classified according to its cause or the location of the affected vessels. More commonly, however, vasculitis is classified according to the caliber of the affected vessels. The terminology from the 2012 revised International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides is the most widely used terminology for distinguishing among various forms of vasculitis (13).

The 2012 Chapel Hill Consensus Conference defined vasculitis in terms of (a) the size of the involved arteries and (b) associated pathologic lesions (Tables 1–3) (14).

### Table 1: Classification of Vasculitis according to the 2012 Revised International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides

<table>
<thead>
<tr>
<th>Type of Vasculitis</th>
<th>Disease Entities</th>
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<tbody>
<tr>
<td>Large-vessel vasculitis</td>
<td>Takayasu arteritis&lt;br&gt;Giant cell arteritis</td>
</tr>
<tr>
<td>Medium-sized vessel vasculitis</td>
<td>Polyarteritis nodosa&lt;br&gt;Kawasaki disease</td>
</tr>
<tr>
<td>Small-vessel vasculitis</td>
<td>IgA vasculitis&lt;br&gt;Microscopic polyangiitis&lt;br&gt;Granulomatosis with polyangiitis&lt;br&gt;Eosinophilic granulomatosis with polyangiitis</td>
</tr>
<tr>
<td>Variable-sized vessel vasculitis</td>
<td>Behçet disease&lt;br&gt;Cogan syndrome</td>
</tr>
<tr>
<td>Single-organ vasculitis</td>
<td>PACNS</td>
</tr>
<tr>
<td>Vasculitis associated with systemic disease</td>
<td>SLE&lt;br&gt;Sjögren syndrome&lt;br&gt;Rheumatoid arthritis&lt;br&gt;APLA syndrome&lt;br&gt;Scleroderma</td>
</tr>
<tr>
<td>Vasculitis associated with probable etiology</td>
<td>Infection-induced vasculitis&lt;br&gt;Acute septic meningitis&lt;br&gt;Mycobacterium tuberculosis&lt;br&gt;Neurosyphilis&lt;br&gt;Viral (HIV-related vasculitis, varicella-zoster vasculopathy)&lt;br&gt;Fungal (mucormycosis, aspergillosis)&lt;br&gt;Parasitic (cysticercosis)&lt;br&gt;Malignancy-induced vasculitis&lt;br&gt;Drug-induced vasculitis&lt;br&gt;Radiation-induced vasculitis</td>
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Note.—APLA = antiphospholipid antibody, HIV = human immunodeficiency virus, IgA = immunoglobulin A, PACNS = primary angiitis of the CNS, SLE = systemic lupus erythematosus.
ischemic white matter lesions, particularly lesions near the brain-CSF interface. Contrast-enhanced T1-weighted images may show leptomeningeal enhancement or associated intraparenchymal lesions. During the acute stage of infarction, DW MR imaging helps distinguish acute from chronic ischemic abnormalities. Within a few days, acute infarctions progress to a subacute stage with resultant angiogenesis and may enhance. In addition, wall thickening and intramural contrast material uptake are frequently seen in patients with active cerebral vasculitis affecting large brain arteries (9–12). SW MR imaging aids in the detection of microhemorrhages associated with vasculitis (15). Perfusion MR imaging plays a role in the assessment of blood flow in patients with vasculitis. At present, two different perfusion MR imaging methods are used: dynamic susceptibility contrast-enhanced MR imaging and arterial spin labeling. The former method involves the rapid acquisition of sequential images at a given location as a contrast material bolus moves through the brain (“first pass”). From the first pass curve,
several physiologic maps may be derived, including cerebral blood volume, cerebral blood flow, time to peak, and mean transit time. Arterial spin labeling, on the other hand, does not require a contrast agent and instead relies on the collection of “unlabeled” (subtracted from “labeled”) MR images (16). This labeling is usually performed with an inversion pulse at the neck in a continuous or interval fashion, and signal from this labeling is sampled in the head. Conventional MR angiography can help detect changes in the arteries but has limited resolution (17). Contrast-enhanced MR imaging at 3.0 T may depict thickening and enhancement in the wall of large arteries (18). MR angiography has a sensitivity and specificity of 100% for the diagnosis of Takayasu arteritis (11).

Computed Tomography
Computed tomography (CT) is less sensitive than MR imaging in the assessment of cerebral vasculitis, with the exception of hemorrhage (1–3). CT angiography can be used to evaluate both the vessel walls and the lumen, and thus may show vessel wall alterations when the lumen is still unaffected at conventional catheter angiography. However, CT angiography cannot depict relatively small vessels. Compared with ultrasonography (US), CT angiography has less resolution, although it can help clearly differentiate between vascular and perivascular structures. CT carries a small risk owing to iodinated contrast material administration and exposure to radiation. CT angiography is useful for imaging large-vessel involvement in Takayasu arteritis and can help make an early diagnosis of this disease entity, since it allows evaluation of wall thickness as well as luminal narrowing. CT angiography demonstrates stenosis, occlusion, aneurysm, and concentric arterial wall thickening (19). It has been shown to allow accurate assessment of stenotic lesions in the carotid and vertebral arteries in patients with Takayasu arteritis, with a sensitivity and specificity of 93% and 98%, respectively (11). With use of a series of dynamically acquired CT images, perfusion CT measures the temporal changes in tissue attenuation after the intravenous bolus injection of contrast material. Perfusion CT provides crucial information about the capillary level hemodynamics within the brain, particularly the identification of tissue that is ischemic and potentially at risk for infarction (20). Perfusion CT provides maps that are similar to those provided by perfusion MR imaging performed with gadolinium-based contrast material.

Table 3: Imaging Findings of Vasculitis associated with Systemic Disease or Probable Cause

<table>
<thead>
<tr>
<th>Cause</th>
<th>Imaging Findings</th>
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<tbody>
<tr>
<td>SLE</td>
<td>Subcortical and periventricular white matter hyperintensity (60% of cases)</td>
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<tr>
<td></td>
<td>Cerebral atrophy (30%), and intracranial hemorrhage (3%)</td>
</tr>
<tr>
<td>Sjögren syndrome</td>
<td>Extensive white and gray matter lesions and microbleeding, enlarged lacrimal and</td>
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<tr>
<td></td>
<td>Salivary glands</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Pachymeningitis with leptomeningeal enhancement, dural nodules, and, rarely,</td>
</tr>
<tr>
<td></td>
<td>Cerebral vasculitis</td>
</tr>
<tr>
<td>APLA syndrome</td>
<td>Arterial or venous thrombosis, thrombocytopenia, and frequent miscarriages</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Nonspecific infarctions, macro- and microhemorrhages, and extensive calcifications</td>
</tr>
<tr>
<td>Acute septic meningitis</td>
<td>Cerebral infarcts in 5%–15% of adults and up to 30% of neonates with bacterial</td>
</tr>
<tr>
<td></td>
<td>Meningitis</td>
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<tr>
<td>Tuberculous vasculopathy</td>
<td>Vasculitis of smaller cerebral arteries leading to small infarctions in the basal</td>
</tr>
<tr>
<td></td>
<td>Ganglia and enhanced basal cisterns</td>
</tr>
<tr>
<td>Neurophilis</td>
<td>Strokes in young adults (most often affecting the middle cerebral artery)</td>
</tr>
<tr>
<td>VZV</td>
<td>MR imaging: unilateral or bilateral basal ganglia infarction in children</td>
</tr>
<tr>
<td></td>
<td>DSA: beaded appearance of anterior and middle cerebral arteries</td>
</tr>
<tr>
<td>HIV</td>
<td>Aneurysms, vessel occlusion, embolic disease, and venous thrombosis in children</td>
</tr>
<tr>
<td>Fungus</td>
<td>Paranasal sinus lesion with narrowed cavernous sinus and infarction in immuno-</td>
</tr>
<tr>
<td></td>
<td>Compromised or diabetic patients</td>
</tr>
<tr>
<td>Cysticercosis</td>
<td>MR imaging: subarachnoid cysticercosis</td>
</tr>
<tr>
<td></td>
<td>DSA: beaded appearance or tapered area of vascular obstruction</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Associated lymphoma and hematologic malignancy</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Vasculitis, vasospasm, infarction, and moyamoya-like vasculitis</td>
</tr>
<tr>
<td>Heroin</td>
<td>Spongiform leukoencephalopathy</td>
</tr>
<tr>
<td>Radiation</td>
<td>Wall thickening and prominent wall enhancement in affected large cerebral arteries</td>
</tr>
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</table>
Positron Emission Tomography/CT
Large-vessel vasculitis must be confirmed at histopathologic analysis of the arterial wall. At the time of initial diagnosis, positron emission tomography (PET)/CT helps confirm the presence of vascular inflammatory disease when clinical findings and other imaging findings are nonspecific. In addition, PET/CT has been used for the follow-up and monitoring of patients to detect disease activity (4,5,21).

Color Duplex US
Color Duplex US has been used for the assessment of vasculitis of large arteries, depicting the arterial walls and providing information about blood flow within the artery. At US, temporal arteries show hypoechoic edematous wall swelling (“halo sign”) in acute temporal arteritis, which in most patients disappears in 1–3 weeks with corticosteroid treatment (22). The reported sensitivity and specificity of US for the halo sign are 69% and 82%, respectively (11). In addition, US plays a role in selecting the appropriate site for biopsy of a superficially located abnormal artery (11).

Digital Subtraction Angiography
Digital subtraction angiography (DSA) accurately demonstrates stenosis, occlusion, a beaded appearance, and irregularities in medium-sized to large arteries. Additional changes have been reported in vasculitis, including aneurysms, collateral flow, isolated areas of vessel narrowing in multiple branches, circumferential or eccentric vessel irregularities, and multiple occlusions with sharp cutoffs. DSA has better resolution than CT angiography and MR angiography for the detection of changes in small arteries (1). However, it is invasive and is associated with minor morbidity, radiation exposure, and contrast agent toxicity. In addition, visualization is limited to the vessel lumen, so that direct evaluation of the vessel walls is not possible (1,7–10).

Biopsy
Despite the utility of noninvasive imaging techniques for the diagnosis of CNS vasculitis, biopsy of the vessel wall remains the standard of reference for definitive diagnosis. US and MR imaging can help detect areas of arterial wall thickening that are suitable for biopsy (1,7,22).

Interpretation
Parenchymal Changes
Involvement of small perforating arteries results in ischemic lesions localized in the deep or subcortical white and gray matter. When larger arteries are occluded, the resulting infarctions can be found in both cortex and white matter (1). Routine T2-weighted, FLAIR, and DW MR images all have a role in the detection of ischemic changes and infarction. Vasculitis may be associated with frank intracerebral hematoma, subarachnoid hemorrhage, and microbleeding. Advanced MR imaging techniques such as SW imaging improve detection of frank hemorrhage and microbleeding (2–4).

Vascular Changes
Vasculitis may be associated with a variable degree of stenosis and occlusion of the affected arteries as well as segmental dilatation of the vessels. Vascular wall thickening with enhancement of the temporal arteries is seen in patients with giant cell arteritis. Stenosis with thickened carotid artery walls is seen in patients with Takayasu disease. Intracranial or carotid artery aneurysm has been reported in patients with polyarteritis nodosa and HIV-related vasculitis (1–3). Occluded carotid arteries with collateral vessels are seen in patients with moyamoya disease, and reversal of arterial changes after 3 months is seen in patients with RCVS. Vasculitis affecting large vessels of the neck may extend into the aorta in pathologic conditions such as Takayasu vasculitis or into specific arteries (eg, the temporal artery) in giant cell arteritis, whereas in moyamoya disease, stenosis or occlusion occurs in the intracranial supraclinoid internal carotid artery (3–7).

Associated Findings
Other imaging findings may suggest certain types of vasculitis. Venous sinus thrombosis has been reported in patients with APLA syndrome and Behçet disease (1,2). Leptomeningeal enhancement is seen in patients with tuberculous meningitis, and pachymeningeal enhancement is seen in those with rheumatoid arthritis–related vasculitis. Granulomas in the paranasal sinuses and orbits are seen in patients who have granulomatosis with polyangiitis. Nasal infection with extension into the cavernous sinuses is seen in patients with fungal vasculitis, and enlarged lacrimal glands or salivary glands are seen in patients with Sjögren disease. Some types of vasculitis, such as Kawasaki disease and IgA vasculitis, have been reported in children (5–9).

Large-Vessel Vasculitis
Takayasu Arteritis
Takayasu arteritis is an idiopathic chronic inflammatory disease affecting the aorta and its major branches, including the carotid and vertebral arteries. Intracranial involvement is uncommon. The disease is most frequently seen in Asia, the...
Mediterranean basin, South Africa, and Latin America. Takayasu arteritis commonly occurs in the 2nd and 3rd decades of life. Its exact cause remains unknown (23). Takayasu arteritis leads to inflammation and fibrosis in the involved vessel walls, resulting in luminal stenosis, occlusion, dilatation, and aneurysm formation. Clinical manifestations of Takayasu arteritis are usually divided into early- and late-phase manifestations. Affected patients present with arm claudication and neurologic symptoms. Cerebrovascular manifestations of Takayasu arteritis include transient ischemic attack, stroke, and hypertensive encephalopathy (1,23).

In the early stages of the disease, high-resolution US depicts increased intimal-medial thickness, which is a reliable marker for active disease (1). Similarly, unenhanced CT may show high-attenuation arterial walls of variable thickness in the aorta and its branches, along with calcifications. Contrast-enhanced CT may show vessel wall enhancement (24). T2-weighted MR imaging can show subtle wall thickening and bright signal in and around an inflamed vessel. During the acute phase, contrast enhancement of the vessel wall and periadventitious soft tissues can be observed. During the late phase, there is segmental dilatation with stenotic regions of the common carotid and subclavian arteries associated with dilatation of the ascending aorta (Fig 1) (25,26). In advanced-stage disease, CT angiography and MR angiography may reveal complete occlusion of supraaortic arteries at their origin, with multiple bypass collateral vessels (Fig 2). At DSA, involvement of the aorta or of at least two medium-sized branches is considered essential for diagnosis (23).

Giant Cell Arteritis
Giant cell arteritis is a chronic, granulomatous vasculitis of large arteries. It predominantly involves the superficial temporal artery but may involve the occipital artery and usually occurs in patients over 55 years of age. There are two common constellations of findings in giant cell arteritis: temporal arteritis and polymyalgia rheumatica. Symptoms of giant cell arteritis include unilateral headache, facial pain, jaw claudication, and loss of vision. Giant cell arteritis is confirmed at temporal artery biopsy (1–4). A diffusely thickened hypoechoic arterial wall (halo sign) is a characteristic gray-scale US feature of giant cell arteritis involvement of the temporal artery. Color and Doppler US may depict turbulent flow and stenosis of the affected vessel (22). CT angiography shows an attenuated superficial temporal artery (Fig 3). Contrast-enhanced high-resolution MR imaging may depict mural thickening and enhancement (27). Vessel wall edema may be detected on T2-weighted images, and the degree of activity can be determined by assessing the intensity of contrast enhancement (28).

Vasculitis of Medium-sized Vessels
Polyarteritis Nodosa
Polyarteritis nodosa is a focal, panmural necrotizing vasculitis affecting medium-sized arteries and can involve any organ. The kidneys are
involved in 70%–80% of patients and the CNS in 10% (29). Characteristic pathologic findings include multiple aneurysms of small and medium-sized arteries. In chronic polyarteritis nodosa, wall thickening produces areas of stenosis or occlusion, which may lead to ischemia or infarction (Fig 4). At DSA, polyarteritis nodosa manifests with aneurysms and stenosis or occlusion (29,30).

**Kawasaki Disease**
Kawasaki disease is a necrotizing vasculitis of medium-sized arteries. It usually affects children under 5 years of age and is associated with abrupt onset of high fever, bilateral conjunctival congestion, inflammation of oral mucous membranes, exanthema, and cervical lymph node swelling. Coronary artery vasculitis is the most serious complication of Kawasaki disease. Mild coronary artery dilatation occurs in up to 50% of patients, and 20% of coronary artery lesions progress to aneurysms (31). Up to 30% of patients with Kawasaki disease exhibit involvement of the CNS, which may include subdural effusions, cerebral infarctions, atrophy, a lesion with reversible T2 hyperintensity in the splenium of the corpus callosum, subcortical lesions, and posterior reversible encephalopathy syndrome (31,32).

Figure 4. Polyarteritis nodosa in a 27-year-old woman. (a) DSA image (lateral view) obtained after internal carotid artery injection shows multiple arterial narrowings but no aneurysms. (b) Axial FLAIR image shows high-signal-intensity sulci in the left medial parietal region (arrow). Axial postcontrast T1-weighted imaging showed leptomeningeal enhancement posteriorly in both parietal regions.
Small-Vessel Vasculitis

**IgA Vasculitis**

IgA vasculitis (Henoch-Schönlein purpura syndrome) is an IgA immunocomplex disease characterized by the involvement of multiple organs, including the gastrointestinal tract, skin, synovial membranes, and kidneys. It is the most common vasculitis in children between 4 and 7 years of age. Characteristic clinical features include palpable purpura concentrated in dependent areas, arthralgia or arthritis, abdominal pain, and glomerulonephritis (33). CNS manifestations are rarely encountered and are related to hypertensive or uremic encephalopathy, although focal ischemic or hemorrhagic lesions have been described (Fig 5) (34).

**Microscopic Polyangiitis**

Microscopic polyangiitis is a necrotizing vasculitis associated with the presence of ANCA and leads to glomerulonephritis, skin manifestations, and mononeuritis multiplex. CNS involvement is common in microscopic polyangiitis (37%-72% of patients). Peripheral neuropathy occurs more frequently than brain involvement (35). CNS manifestations vary widely and include cerebral hemorrhage, pachymeningitis, nonhemorrhagic cerebral infarction, and variable degrees of small-vessel disease with involvement of both white and gray matter (Fig 6) (36,37).

**Granulomatosis with Polyangiitis**

Granulomatosis with polyangiitis (Wegener granulomatosis) is an ANCA-positive systemic vasculitis that affects small arteries. The CNS is involved late in the disease course in up to 35% of patients (38). Granulomatosis with polyangiitis may lead to cerebral lesions due to invasion by granulomas located in the nasal cavities and paranasal sinuses and extending intracranially, or it may manifest as a necrotizing cerebral vasculitis, which nearly always occurs in the presence of active sinusitis, otitis, or lung disease. Leptomeningeal enhancement has been described in granulomatosis with polyangiitis. Nonspecific isolated intracranial or spinal lesions may be seen and may enhance (2,39). MR imaging and CT of the paranasal sinuses and mastoids are important in the evaluation of cerebral involvement to rule out continuous extension. A nasal granuloma is seen as a soft-tissue mass at CT and is hypointense with both T2- and T1-weighted MR sequences, with variable degrees of enhancement at contrast-enhanced CT and MR imaging. In the chronic phase, the walls of the residual paranasal sinuses demonstrate marked thickening, whereas the sinus volume is gradually reduced and the residual lumen may be filled with material having a “ground-glass” appearance. The nasal septum can be partially or completely eroded, and the turbinates appear truncated and shortened (Fig 7). Destruction of the hard palate with sinonasal-oral fistulas may also be seen (40,41).
Figure 7. Granulomatosis with polyangiitis in a 38-year-old woman with renal insufficiency. (a) DSA image (lateral view) obtained after internal carotid artery injection shows multiple arterial narrowings. (b) Coronal postcontrast fat-suppressed T1-weighted image shows complete erosion of nasal structures and enhancing soft tissue in the medial orbits and nasal vault extending to the cribiform fossae, where there is adjacent dural thickening and enhancement. Renal biopsy showed necrotizing glomerulonephritis.

**Eosinophilic Granulomatosis with Polyangiitis**

Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) is characterized by the triad of asthma, hypereosinophilia, and necrotizing vasculitis. It is characterized by a prodromal stage of asthma–allergic rhinitis, a second phase of eosinophilia, and a third stage of vasculitis proper with involvement predominantly of the lung, skin, and peripheral nerves (42). The CNS is commonly involved, and peripheral neuropathy is commonly seen in this disorder (43). CNS involvement includes confusion, seizures, and, in severe cases, coma. Cranial nerve palsies are frequently seen, with the most common manifestation being ischemic optic neuropathy. Cerebral ischemic or hemorrhagic changes may also be seen. MR imaging findings are variable, and the cerebral lesions are similar to those seen in many other vasculitides and consist of macro- or microinfarctions and micro- or macrohemorrhages (Fig 8) (43,44).

**Vasculitis of Variable-sized Vessels**

**Behçet Disease**

Behçet disease is a disorder characterized by the triad of recurrent orogenital ulcers, ocular inflammatory disease, and cutaneous manifestations. Neurologic involvement has been reported in 5%–30% of patients. The disease mainly affects young adults, is more frequently seen in men, and has a high prevalence in Turkey (45). Neuro-Behçet disease can be divided into two groups: the parenchymal group (80%), which includes brainstem lesions, hemispheric manifestations, meningoencephalitis, and lesions of the spinal cord and cranial nerve; and the nonparenchymal type (20%), which includes dural sinus thrombosis and arterial occlusion or aneurysm (46,47). On T2-weighted images, parenchymal lesions appear as isolated or confluent hyperintense lesions that predominantly affect the brainstem, but they may also affect the basal ganglia or centrum semiovale, and, somewhat less frequently, the periventricular regions (Fig 9), spinal cord, and cranial nerves. These lesions are more frequently seen and are larger and more extensive than those of multiple sclerosis. Leptomeningeal enhancement is present in patients with cranial nerve palsies or meningoencephalitis. Spinal cord lesions are visible on T2-weighted images and enhance after contrast material injection. Small and, occasionally, large infarctions may occur. Cerebral venous or sinus thrombosis may manifest with raised intracranial pressure (45,47).

**Cogan Syndrome**

Cogan syndrome is a rare multisystem disease characterized by nonsyphilitic interstitial keratitis and audiovestibular dysfunction. Neurologic symptoms of Cogan syndrome are seen in approximately 29% of patients and include headache, psychosis, coma, convulsion, neuropathy, and stroke. Vasculitis is seen in 12%–15% of patients with Cogan syndrome (48). Imaging shows areas of ischemic change or infarction, meningoencephalitis, cerebral venous sinus thrombosis, and cranial neuropathy. MR imaging and CT
may show obliteration or narrowing of the vestibular labyrinth. Contrast-enhanced T1-weighted imaging may show enhancement of the membranous labyrinth (49).

**Single-Organ Vasculitis**

**Primary Angiitis of the CNS**

PACNS is an idiopathic inflammatory disease of medium-sized to small arteries affecting the CNS or peripheral nervous system, with no evidence of generalized inflammation (50). It is most often observed in the 5th and 6th decades of life, and patients present with nonspecific symptoms such as acute or subacute confusion, headache, paresis, cranial neuropathy, hallucinations, or loss of consciousness (1,51). Laboratory findings include elevated inflammatory markers (particularly erythrocyte sedimentation rate), and CSF analysis may reveal an elevated opening pressure and a high protein level (12). Leptomeningeal and brain parenchymal biopsies remain the standard of reference for the diagnosis of PACNS, but a negative biopsy result does not rule out the condition. PACNS is managed with high-dose steroids and cytotoxic agents (50–52).

Imaging findings of PACNS are highly variable and nonspecific. CT may reveal areas of low attenuation suggestive of ischemic events. MR imaging is sensitive but not specific, showing dis-
crete or diffuse supra- and infratentorial lesions involving the deep and superficial white matter. In addition, areas of infarct and hemorrhage may be seen (Fig 10). The lesions enhance in 90% of cases (2,50). MR angiography is not informative but occasionally may show vessel irregularities. DSA may show focal or multifocal segmental narrowing or occlusion or irregularities of both small and medium-sized parenchymal and leptomeningeal blood vessels, collateral vessel formation, and prolonged circulation time. DSA supports the diagnosis of PACNS when biopsy is not undertaken or yields negative results despite other clinical and laboratory evidence. Microaneurysms are rarely seen. Vasculitic lesions usually affect both hemispheres (52,53).

Several subsets of PACNS that differ in prognosis and management have been identified. In the hemorrhagic form (11%–12% of cases), intracerebral hemorrhage is the most common finding, followed by subarachnoid hemorrhage, and may be related to hemorrhagic transformation of a recent infarction or caused by focal necrosis of an intracerebral blood vessel (52,53). In the pseudotumoral form (15% of cases), MR imaging reveals nonspecific mass lesions, which are
commonly misinterpreted as malignant neoplasms of the brainstem or brain because they may be characterized by central necrosis, surrounding edema, infiltration of adjacent structures, mass effect, and variable contrast enhancement. Rapidly progressive primary vasculitis of the CNS represents the most ominous subset of PACNS and often has a fatal outcome. Typically, numerous bilateral lesions of the large cerebral vessels are seen at DSA, along with several bilateral cerebral infarctions. The response to conventional immunosuppressive treatment is poor (53,54). Spinal cord abnormalities are found in about 5% of patients but are rarely the only manifestation; when they do occur, however, the thoracic cord is predominantly affected. Angiography-negative, biopsy-positive PACNS is a subset in which only very small arteries or arterioles are affected. Affected patients often demonstrate cognitive dysfunction, markedly elevated concentrations of CSF protein, meningeal or parenchymal enhancing lesions at MR imaging, favorable response to treatment, and a good outcome (Fig 11) (50,51). Childhood PACNS differs from adult PACNS in that the abnormalities are more commonly unilateral, proximal, multifocal, and supratentorial. There is similar involvement of gray and white matter overall, but there is a strong tendency toward central lesions involving the basal ganglia or lateral lenticulostriate vasculature territory. The most common MR angiographic finding is involvement of the terminal segment of the carotid artery and of the proximal segments of the anterior and middle cerebral arteries (55).

Reversible Cerebral Vasoconstriction Syndromes

The term reversible cerebral vasoconstriction syndrome refers to various disorders that are characterized by brain vasoconstriction (ie, Call-Fleming syndrome, postpartum angiopathy, migrainous vasospasm, and benign angiopathy of the CNS) (56,57). RCVS may be spontaneous or secondary to postpartum angiopathy or various vasoactive substances (cannabis, selective serotonin recapture inhibitors, and nasal decongestants). The pathologic mechanism may be related to a transient disturbance in cerebral autoregulation. RCVS is characterized by recurrent thunderclap headaches, variable focal neurologic deficits, and multifocal segmental arterial narrowings (Fig 12), all of which resolve within 3 months. Major complications of RCVS include brain edema (38% of cases), localized convexity subarachnoid hemorrhage (22%), posterior reversible encephalopathy syndrome (9%–14%), and, less frequently, ischemic or hemorrhagic stroke (57,58).

Moyamoya Disease

Moyamoya (Japanese, “puff of smoke”) disease is characterized by progressive occlusion of the terminal segments of the intracranial internal carotid arteries and compensatory development of tortuous, dilated collateral networks with im-
Pairment of the cerebrovascular reserve capacity. The term *moyamoya syndrome* is used when there is an underlying cause (sickle cell anemia, Down syndrome, Marfan syndrome, or coarctation of the aorta) (1,59). This condition is usually bilateral but may be asymmetric and, occasionally, unilateral. Most cases are found in East Asian countries. The disease has a bimodal age distribution (1st and 4th decades of life) (60,61). MR imaging reveals stenosis or occlusion of the distal internal carotid arteries and the presence of moyamoya vessels with signal voids within the basal ganglia and thalami, as well as ischemia and infarction. SW imaging may depict microbleeding in 15%–44% of patients. On FLAIR images, diffuse leptomeningeal collateral vessels may appear as sulcal hyperintensity (“ivy sign”) (61). Contrast-enhanced T1-weighted images show marked leptomeningeal enhancement along the cortical sulci as well as enhancement of moyamoya vessels. DSA shows stenosis or occlusion of the terminal internal carotid artery and the presence of collateral vessels (Fig 13). Perfusion CT and MR imaging reveal decreased cerebrovascular reserve with decreased and regional cerebral perfusion (1,62).

**Vasculitis associated with Systemic Disease**

**Systemic Lupus Erythematosus**

SLE is an autoimmune disorder that results in a noninflammatory vasculitis of small arterioles and capillaries. Females are affected nine times more often than males, with a peak age at onset in the 2nd to 4th decades of life. Neuropsychiatric SLE occurs in 14%–75% of patients with SLE and is associated with morbidity and mortality rates of 7%–40% (63). Neurologic manifestations of neuropsychiatric SLE include psychosis, stroke, epilepsy, headache, and neurocognitive defects. Cerebral white matter lesions are the most common findings in neuropsychiatric SLE (60%–86% of patients). Small focal areas of hyperintensity are seen in the subcortical and periventricular white
Figure 14. SLE in a 14-year-old girl with facial rash in a typical “butterfly” pattern. (a) MR angiogram (base view) does not depict the left middle cerebral artery. All intracranial arteries show reduced diameters, and flow in the right internal carotid artery is diminished. (b) Axial DW image shows acute infarction in the head of the left caudate nucleus.

matter at FLAIR and T2-weighted imaging. Cerebral atrophy is seen in about 43% of patients. Intracranial hemorrhage may manifest as parenchymal or subarachnoid hemorrhage, subdural hematoma, petechial hemorrhage, or hemorrhagic infarcts. DSA and MR angiography show reduced diameter or occlusion of the intracranial carotid arteries (Fig 14). In the spine, myelopathy has a prevalence of 1%-3% and coexists with optic neuritis in 21%-48% of patients. MR imaging shows long-segment central T2 hyperintensity with variable contrast enhancement (63,64).

Sjögren Syndrome
CNS involvement is reported in 25%-30% of patients with Sjögren syndrome. Presenting symptoms include trigeminal neuropathy, recurrent aseptic meningoencephalitis, and unifocal or multifocal cerebral parenchymatous lesions (65). At MR imaging, extensive white and gray matter lesions have been reported, including infarctions. Microbleeding can be seen at SW imaging. DSA shows multiple arterial narrowings (Fig 15). Lesions in the posterior fossa and the spinal cord are rare (66). Involvement of salivary and lacrimal glands (the “sicca” manifestations) is usually evident before CNS symptoms are seen (65,66). The apparent diffusion coefficients of the lacrimal glands in Sjögren syndrome are significantly lower than those of normal glands (67).

Rheumatoid Arthritis
Rheumatoid arthritis is a chronic systemic inflammatory disorder in which the joints are a primary...
Figure 15. Sjögren syndrome in a 50-year-old woman with dry eyes and mouth. (a) DSA image (lateral view) obtained after internal carotid artery injection shows multiple arterial narrowings. (b) Axial DW image shows bilateral asymmetric areas of acute infarction in the cerebral hemisphere. Biopsy of a minor salivary gland helped confirm the diagnosis.

target. CNS involvement includes pachymeningitis, dural nodules, and, rarely, cerebral vasculitis (68). At MR imaging, rheumatoid pachymeningitis shows increased T2 signal in the hemispheric subarachnoid space and leptomeningeal contrast enhancement due to involvement of the blood vessels in that location. Intracranial hypotension can also be encountered in patients with rheumatoid dural or vertebral involvement, resulting in CSF leaks. CNS vasculitis is rare and occurs in patients with long-standing active rheumatoid arthritis (69).

APLA Syndrome
APLAs act against phospholipids and are found in a variety of clinical disorders. Pure APLA syndrome occurs in patients without predisposing conditions. Secondary APLA syndrome is found in up to 30%–50% of patients with SLE and in up to 30% of patients with HIV infection. The major clinical manifestations of APLA syndrome are arterial or venous thrombosis, thrombocytopenia, and frequent miscarriages (1–3). MR imaging shows white matter abnormalities suggesting small-vessel disease, and the gray matter may also be affected. DW imaging shows acute infarctions, whereas gradient-echo and SW sequences show microhemorrhages (70).

Scleroderma
Scleroderma (progressive systemic sclerosis) is a progressive disease that leads to hardening of the skin and connective tissues. MR imaging findings are nonspecific, and manifestations include infarctions in medium-sized artery territories. In addition, macro- and microhemorrhages and extensive calcifications may be present (71).

Vasculitis Associated with Probable Cause

Acute Septic Meningitis
Acute septic meningitis attributable to several strains of bacteria may cause vasculitis and cerebral infarcts in 5%–15% of adults and up to 30% of neonates with bacterial meningitis (72).

Tuberculous Vasculitis
*M.

Neurosyphilis Vasculitis
In the meningovascular form of neurosyphilis, vasculitis is believed to result from direct spirochete invasion of vascular endothelial cells. The
Most common manifestation is stroke in young adults, with the middle cerebral artery being most often affected, followed by the basilar artery (1,47).

**Varicella-Zoster Virus Vasculitis**

Varicella-zoster virus (VZV) vasculitis can complicate zoster (secondary VZV infection) or varicella (primary VZV infection). The spectrum of VZV vasculitis includes ischemic infarction of the brain and spinal cord, aneurysm formation, subarachnoid and cerebral hemorrhage, and focal middle or anterior cerebral artery dissection. DSA and MR angiography reveal segmental narrowing, thrombosis, and beading along proximal branches of the anterior and middle cerebral arteries (Fig 17) (74,75). If a child presents with unilateral basal ganglia infarction, VZV must be included in the differential diagnosis. Rarely, the disease may result in bilateral basal ganglia infarctions (Fig 17).

**HIV-related Vasculitis**

HIV-infected children have an increased prevalence of cerebrovascular disease that is associated with severe immune suppression due to acquired HIV infection or exposure to the virus in the neonatal period. Both medium-sized arteries and veins are involved, with the development of aneurysms, vessel occlusion, embolic disease, and venous thrombosis. Aneurysms tend to be fusiform and involve the major arteries of the circle of Willis as well as second- and third-order branches, which helps differentiate them from the typical berry...
anomalies. Vasculitis can be identified at both MR angiography and DSA as caliber variations and irregularities of vessels (Fig 18) (76,77).

**Fungal Vasculitis**

Four fungal agents—*Aspergillus*, *Candida*, *Coccidioides*, and *Mucorales* species—are important CNS pathogens, particularly in the setting of leukopenia, sepsis, and immunosuppression. All four agents have the capacity to invade arteries of the CNS. Vasculitis may be acute, subacute, or a late complication of CNS infection. Cerebral infarctions result from direct vascular injuries, leading to aneurysm, thrombosis, and cerebral hemorrhage, or from microabscesses or extension along contiguous sites of infection. Mucormycosis and aspergillosis may be particularly aggressive in poorly controlled diabetes. There may be associated spread from the paranasal sinuses to the cavernous sinus and internal carotid artery, leading to focal thrombosis and cerebral infarctions (Fig 19) (1,78).

**Cysticercosis**

Vasculitis must be suspected in patients with cysticercosis when segmental narrowing, a beaded appearance, or an abrupt or tapered area of vascular obstruction is noted at DSA or MR angiography. Vasculitis is seen in up to 53% of patients with subarachnoid cysticercosis, including asymptomatic patients, with the middle and posterior cerebral arteries being most commonly affected. Multivessel involvement is noted in 50% of patients, with infarctions being seen in 2%–12% of these patients (Fig 20) (79).

**Malignancy-induced Vasculitis**

Lymphoma, particularly Hodgkin disease and, rarely, the non-Hodgkin type, has been associated
with CNS vasculitis (80). In addition, hematologic malignancies such as multiple myeloma, T-cell leukemia, and hairy cell leukemia may cause vasculitis (14).

**Drug-induced Vasculitis**
Antibiotics, chemotherapy, and illegal addictive drugs (cocaïne, heroin) can cause a vasculitis that affects medium-sized arteries and results in infarctions. MR imaging patterns in drug-induced vasculitis are inconsistent and depend on the vessels involved. Cocaine may lead to vasculitis, vasospasm, and increased platelet aggregation, resulting in infarction, leukoencephalopathy, and hemorrhage. Chronic cocaine dependency has been linked to a moyamoya-like vasculitis with obstructed vessels and extensive collateral circulation. DSA and MR angiography may show vasculitis and vasospasm in cocaine users (Fig 21) (81). Stroke and hemorrhage are seen less frequently in heroin users than in cocaine users. Spongiform leukoencephalopathy is far more common in heroin users (Fig 22) but has occasionally been described in cocaine users (82).

**Radiation-induced Vasculitis**
Radiation-induced injuries to large cerebral arteries result in stenotic or occlusive vasculitis. These injuries usually evolve slowly to produce ischemia years or even decades after irradiation. MR images show thickening and prominent enhancement of the walls of affected large cerebral arteries, which may be helpful in distinguishing radiation-induced vasculitis from other types of vasculitis (83).

**Conclusion**
CNS vasculitis is a heterogeneous group of disorders with diverse clinical manifestations. Cerebral...
vasculitis may affect large, medium-sized, small, and variable-sized blood vessels and single or multiple organs. In addition, cerebral vasculitis may be due to systemic connective tissue disorders, infection, malignancy, drug use, or radiation therapy. Different MR pulse sequences play an important role in the diagnosis of vasculitis, and CT may provide additional useful information. A variety of imaging findings—from small ischemic changes to frank infarction, hemorrhage, and white matter edema—may show contrast enhancement. Cerebral arteries may demonstrate a beaded appearance and wall enhancement at noninvasive imaging. Radiology plays an important role in narrowing the differential diagnosis. Correlation of imaging findings with clinical manifestations and laboratory test results helps establish the diagnosis of CNS vasculitis (Fig 23). It is possible that, in the near future, vessel wall imaging may shed further light on these diseases in terms of cause and diagnosis.

References
Figure 23. Flow chart illustrates an algorithm used to help establish the diagnosis of CNS vasculitis. MRA = MR angiography, MRI = MR imaging.


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Important clinical factors that merit consideration when vasculitis is being considered as part of the differential diagnosis include patient age, gender, and ethnic origin; presence of skin lesions (ulcers, palpable purpura); size of the involved vessel; involvement of other organs (especially the kidneys, lungs, and paranasal sinuses); use of medications; presence of drug abuse; and neurologic signs, including cognitive deterioration, focal deficits, transient ischemic attacks, stroke, and “thunderclap” headaches.

Imaging signs of cerebral vasculitis may be direct (e.g., vessel wall thickening and contrast material enhancement) or indirect (e.g., cerebral perfusion deficits, ischemic brain lesions, intracerebral or subarachnoid hemorrhage, and vascular stenosis).

The 2012 Chapel Hill Consensus Conference defined vasculitis in terms of (a) the size of the involved arteries and (b) associated pathologic lesions.

PACNS is an idiopathic inflammatory disease of medium-sized to small arteries affecting the CNS or peripheral nervous system, with no evidence of generalized inflammation.

M tuberculosis is the most common cause of chronic meningitis and typically follows rupture of a tubercle with the release of mycobacteria into the subarachnoid space. The thick, gelatinous, inflammatory exudate settles at the base of the brain along cisterns, particularly in the sylvian fissure, where vasculitis can form along traversing blood vessels. Resultant ischemic infarctions occur in up to 41% of patients.