White matter (WM) consists of myelinated axons that arise from either the neuronal cell bodies in the cerebral cortex or the nuclei of deep gray matter structures. In the brain, most of these axons are located centrally, whereas in the spinal cord, they are positioned peripherally. Any WM injury regardless of mechanism is associated with inflammation and/or edema. The damaged axons lose their myelin and subsequent gliosis results in volume loss. The term “white matter disease” is an imaging reference to magnetic resonance imaging (MRI) or computed tomography (CT) findings. These imaging findings reflect a variety of pathologic processes that can be acute, subacute, or chronic in nature and have concomitantly affected the WM of the brain and/or spinal cord.

Significance of white matter disease

The appearance of white matter disease (WMD) on imaging studies is often nonspecific. However, the imaging appearance of WMD on cross-sectional imaging may aid in classification and diagnosis. Furthermore, the presence of WMD on an imaging study may initiate additional imaging and clinical investigation so that a working diagnosis can be established and appropriate medical treatment initiated. The clinical presentation in patients with WMD, in turn, is quite variable. Patients can be affected at any age from childhood to adulthood. Patients can present with significant acute neurologic deficits, gradual neurologic deterioration, or no symptoms at all. Disease entities may result in monophasic illness or may manifest in progressive or relapsing fashion. Nevertheless, it is some sort of neurologic symptom or sign that prompts imaging of the central nervous system with subsequent identification of a WM abnormality within the brain and/or spinal cord. These abnormalities are most elegantly depicted on MRI studies of these structures. Occasionally, however, in situations where the patient’s medical condition precludes MRI, WM lesions may indeed be seen, though with less sensitivity, on CT studies of the brain (Figure 1). On CT, multiple sclerosis (MS) lesions present as small foci of decreased attenuation, which may demonstrate enhancement following contrast administration.

Classification of white matter disease

The differential diagnosis of WMD is extensive (Table 1). WMD traditionally has been divided into demyelinating and dysmyelinating processes. In the former category, normally formed myelinated axons are adversely affected with resultant destruction and loss of myelin. Dysmyelinating processes reflect the sequelae of enzymatic deficiencies that lead to abnormally myelinated axons and subsequent breakdown of the abnormal myelin. An example of a few entities in this latter category include adrenoleukodystrophy, metachromatic leukodystrophy, Canavan’s disease, Alexander’s disease, Krabbe’s disease, and others.

Dr. Ortiz is the Chairman of the Department of Radiology and Dr. Baadh is a Resident, in the Department of Radiology, Winthrop-University Hospital, Mineola, NY; and Dr. Lustrin is a Diagnostic Radiologist at NRAD Medical Associates, Lake Success, NY.
White matter disease and sudanophilic leukodystrophy. In general, many of these metabolic disorders are most frequently encountered in children and young adults. This article will focus on demyelinating conditions that manifest as WMD on neuroimaging studies of the craniospinal axis, as these entities overall are more common and likely to be encountered in both inpatient and outpatient radiology practice settings. An emphasis will be placed on clinical and imaging findings that distinguish these entities, especially as they compare to multiple sclerosis.

Multiple sclerosis

Multiple sclerosis (MS) is an inflammatory demyelinating disease, in which there is autoimmune mediated injury to myelin sheaths surrounding axons in the brain and spinal cord.1 Recent studies have proposed chronic cerebrospinal venous insufficiency as a potential etiologic factor. These studies have used color Doppler ultrasound to demonstrate obstructive anomalies of extracranial veins, such as the internal jugular and azygous along with venographic evidence of significant stenoses in venous structures adjacent to the central nervous system.2 Additional studies from other centers are forthcoming to further assess this venous insufficiency model. MS is included as part of the working diagnosis in a large and diverse set of neurologic presentations, particularly in young adults in their 2nd through 4th decades of life. Twenty percent of patients are > 40-years-old and 10% of patients are < 20-years-old. An age of onset > 55-years-old is rare and in this situation the possibility of an alternative diagnosis should be considered.3 The estimated prevalence of MS is between 2 and 150 cases per 100,000 people, depending on racial/ethnic background and geography.4 MS is defined as an idiopathic inflammatory demyelinating disease of the central nervous system characterized by the presence of focal plaques of demyelination with reactive scarring in the cerebral and spinal cord WM (Figure 2).5 Cerebrospinal fluid abnormalities, such as the presence of oligoclonal bands, are not always present and are

### Table 1. Classification of WMD

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demyelinating</td>
<td>1. Autoimmune/idiopathic</td>
</tr>
<tr>
<td></td>
<td>Multiple sclerosis (MS)</td>
</tr>
<tr>
<td></td>
<td>Acute disseminated encephalomyelitis (ADEM)</td>
</tr>
<tr>
<td></td>
<td>Neuromyelitis optica (NMO)</td>
</tr>
<tr>
<td></td>
<td>Acute transverse myelitis (ATM)</td>
</tr>
<tr>
<td></td>
<td>Subacute sclerosing panencephalitis (SSPE)</td>
</tr>
<tr>
<td></td>
<td>2. Infection</td>
</tr>
<tr>
<td></td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>HIV encephalitis</td>
</tr>
<tr>
<td></td>
<td>Progressive multifocal leukoencephalopathy (PML)</td>
</tr>
<tr>
<td></td>
<td>3. Vascular</td>
</tr>
<tr>
<td></td>
<td>Vasculitis</td>
</tr>
<tr>
<td></td>
<td>Primary central nervous system</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
</tr>
<tr>
<td></td>
<td>Cerebral autosomal dominant arteriopathy</td>
</tr>
<tr>
<td></td>
<td>Subcortical infarcts</td>
</tr>
<tr>
<td></td>
<td>Subcortical arteriosclerotic encephalopathy</td>
</tr>
<tr>
<td></td>
<td>Normal aging with gliosis and myelin pallor</td>
</tr>
<tr>
<td></td>
<td>Susac’s syndrome</td>
</tr>
<tr>
<td></td>
<td>Posterior reversible encephalopathy syndrome</td>
</tr>
<tr>
<td></td>
<td>PRES</td>
</tr>
<tr>
<td></td>
<td>Hypoxic encephalopathy</td>
</tr>
<tr>
<td></td>
<td>4. Toxic</td>
</tr>
<tr>
<td></td>
<td>Radiation necrosis</td>
</tr>
<tr>
<td></td>
<td>Disseminated necrotizing leukoencephalopathy</td>
</tr>
<tr>
<td></td>
<td>5. Metabolic</td>
</tr>
<tr>
<td></td>
<td>Osmotic demyelination syndrome</td>
</tr>
<tr>
<td></td>
<td>Machiafava-Bignami</td>
</tr>
<tr>
<td></td>
<td>Subacute combined degeneration</td>
</tr>
<tr>
<td></td>
<td>6. Traumatic</td>
</tr>
<tr>
<td></td>
<td>Diffuse axonal injury</td>
</tr>
</tbody>
</table>

---

FIGURE 1. **CT findings in 30-year-old woman with MS.** Contrast-enhanced axial CT image of the brain in a patient with MS shows ring enhancing (small arrow) and nodular enhancing (large arrow) lesions within the subcortical and periventricular WM. Nonenhancing low-attenuation foci are seen within the WM. Cerebral atrophy is also present in this patient, who initially presented to the emergency room with alteration in mental status.

FIGURE 2. **Low-power photomicrograph (Luxol fast blue with a PAS counter stain)** from biopsy of patient subsequently proven to have MS shows periventricular foci of demyelination (arrows).
not necessarily specific to the diagnosis. The clinical presentation and course in patients with MS is variable. To better characterize a clinical course that includes clinical exacerbations or relapses, periods of quiescence, and/or neurologic progression, a consensus statement groups the disease course into 4 major categories:

1. Relapsing/remitting MS,
2. Progressive relapsing MS,
3. Secondary progressive MS, and
4. Primary progressive MS.

This classification is significant in that, in the United States, medical treatments are presently approved by the Food and Drug Administration only for relapsing/remitting MS.

MRI with conventional and advanced imaging techniques is the gold standard for diagnosing and monitoring patients with suspected or clinically proven MS. MRI is used to identify other WMD processes that may clinically mimic MS. MRI findings are also used to provide prognostic information. MRI is used not only to monitor a patient’s response to medical therapy but also to assess for any complications that might be caused by a treatment. All major clinical research trials that are attempting to assess possible treatments for MS utilize MRI as a fundamental part of the research design to report, quantify, and monitor treatment outcomes.

MS lesions are often located in a perivenular distribution. They tend to have a predilection for areas of high perivenular density, such as the periventricular and subcortical WM, the optic nerves and chiasm, the cerebral and cerebellar peduncles, and the lateral columns of the spinal cord. MRI is sensitive for detecting WM lesions in the brain and spinal cord (Figure 3). Proton-density, T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences are ideal for detecting and characterizing MS plaques. On MRI, the typical MS lesion presents as an ovoid or flame-shaped, hyperintense lesion on the aforementioned sequences. Periventricular WM lesions often have a perpendicular orientation relative to the margins of the lateral ventricles (Figure 4). The lesions are of variable size and often > 3 mm in diameter. These lesions can manifest a dynamic imaging appearance with respect to signal intensity and morphology over time, regardless of treatment status (Figure 5). The MRI signal changes reflect the presence of inflammatory cells and foci of demyelin-
White matter disease can also manifest as foci of remyelination. Lesions may also show a thin, less-T2-hyperintense rim along their periphery (Figure 6). Rarely, as seen in patients with Balo’s concentric sclerosis, prominent alternating bands of hyperintensity and demyelinating component may undergo sufficient blood-brain barrier disruption as to show enhancement with gadolinium contrast agents (Figures 8-11). This contrast enhancement, however, like the underlying lesion, is dynamic in that it is transient. Reactivated MS lesions may also show contrast enhancement. The absence of contrast enhancement should not mistakenly be equated with lesion quiescence or absence of disease activity. In this case, the extent of inflammation, demyelination, and underlying tissue injury might be below a threshold that can be detected with current imaging approaches. Contrast enhancement occurs less frequently in the progressive forms of MS. A radiologically isolated syndrome has been described in patients who present with incidental imaging findings that are suggestive of possible MS. This condition is referred to as “pre-MS” because up to 33% of these patients convert to a clinically isolated syndrome, or so-called first attack, within 5 years. These patients may have abnormal visual evoked responses, spinal cord involvement, and contrast-enhancing cerebral white matter plaques. The McDonald diagnostic criteria for MS were recently revised in 2010 to allow for a more prompt diagnosis of MS in patients who have experienced a clinically isolated syndrome. For example, a clinical presentation of 2 or more episodes of an inflammatory neurologic insult or attack, combined with MRI evidence of 2 or more brain lesions, would suffice to make a clinical diagnosis of MS based on the modified McDonald criteria. In instances of either one prior attack or one brain lesion detected by MRI, then additional data, such as evidence of dissemination of lesions in space or time within the brain and/or spinal cord, are required to confirm a diagnosis of MS.

The application of advanced MRI techniques in evaluating MS is still under investigation. These techniques include magnetization transfer (MT), diffusion weighted and diffusion tensor imaging (DWI and DTI), susceptibility-weighted imaging, functional MRI (fMRI), and MR spectroscopy (MRS) (Figure 3). For example, some studies have shown the MT changes precede the subsequent development of enhancing MS lesions in what are initially areas of normal-appearing white matter. Cerebral atrophy is a significant imaging finding that occurs over time in patients with MS. Patients with MS show an average annual cerebral volume loss of 0.6% to 0.8% per year compared to healthy controls (0.3% per year) as shown on volumetric MR studies. Initial reports have shown increased levels of iron accumulation within the deep gray matter nuclei, such
White matter disease
as the basal ganglia, of patients with MS compared to normal control subjects (Figure 12). The other key structures that can be affected by demyelination include the optic nerves and spinal cord. Indeed, optic neuritis can be the initial presentation as a clinically isolated syndrome in patients who subsequently are diagnosed with MS (Figure 13). Patients present with monocular visual loss and focal areas of T2 signal change and optic nerve enlargement. Focal enhancement of the lesion after contrast agent administration is best demonstrated with fat-suppressed, T1-weighted imaging and, when combined with the clinical presentation, often distinguishes optic neuritis from optic nerve-sheath neoplasms. Spinal cord involvement in MS often occurs with brain involvement, but it can occur as an isolated finding. The MS spinal cord lesion is located within the periphery of the spinal cord and occupies less than half of the cross-sectional area of the spinal cord (Figure 14). The lesions are focal and usually do not extend for more than 1 or 2 vertebral body segments. MS spinal cord lesions are isointense to hypointense on T1-weighted images, hyperintense on T2, and show varying amounts and types of enhancement after contrast administration. Spinal cord atrophy may also be observed, especially in patients with chronic disease.

**Autoimmune/Idiopathic**

**Acute disseminated encephalomyelitis (ADEM)**

Acute disseminated encephalomyelitis (ADEM) is an autoimmune disorder that affects the white matter in the brain and spinal cord. This is often a monophasic WMD process that occurs within a few weeks of a prior viral or bacterial infection or vaccination. ADEM has an estimated incidence of 0.8/100,000 population per year. Cerebrospinal fluid analysis shows increased albumin and proteins with absent oligoclonal bands. Oligoclonal bands are rarely present in the cerebrospinal fluid and when observed, are transient. Gray matter structures, such as the basal ganglia or cortex, may also be affected. Children are most frequently affected, but ADEM may also be observed in adults. MRI shows either multiple small or large flocculent T2 or FLAIR hyperintense lesions within the subcortical WM (Figure 15). These lesions may show patchy or partial peripheral enhancement. Unlike MS, gray matter involvement is commonly seen with ADEM.
ADEM, however, tends to spare the corpus callosum and does not show the peri-venular distribution seen with MS. Spinal cord involvement in ADEM is often patchy, but it can be quite extensive. ADEM is a self-limited process in the majority of cases and follow-up imaging will show lesion stability or resolution in those patients who go on to recover. ADEM, however, may cause permanent neurologic deficits. Current treatments for ADEM include anti-inflammatory or immunosuppressive medications. ADEM should be suspected in a child that develops neurologic symptoms and WMD shortly after an infection or vaccination.

**Subacute sclerosing panencephalitis (SSPE)**

Subacute sclerosing panencephalitis (SSPE) is a rare, measles-mediated encephalitis associated with progressive neurologic deterioration and death.

This disease has a subacute course and is often seen in children with prior measles infection. SSPE is rare in adults. Cerebrospinal fluid analysis will show elevated antibody titers against measles and elevated gamma globulin. The MR imaging appearance is one of asymmetric, T2-hyperintense, nonenhancing lesions within the periventricular and subcortical WM of the cerebral hemispheres (Figure 16). Corpus callosum and deep gray matter involvement may be observed. Cerebral swelling may
White matter disease

be seen. Cerebral volume loss with reduced gray matter volume may be observed in the frontal and temporal cortex. MRS may show normal to increased choline and myoinositol and decreased n-acetyl aspartate.

Neuromyelitis optica

Neuromyelitis optica, or Devic’s disease, is a unique idiopathic WM inflammatory process in which there is an auto-antibody response against aquaporin 4. A highly specific serum marker, NMO-IgG, is identified in 60% of patients. Both optic nerve and spinal cord involvement are observed in patients with Devic’s disease (Figure 17). Both optic nerve and spinal cord lesions tend to enhance in the acute phase of the illness. The cerebral WM is spared or may show the presence of nonspecific WM lesions, a key differentiating feature from multiple sclerosis. The clinical presentation is monophasic and rapidly disabling, with a subsequent relapsing disease process that is associated with a poor prognosis. Rituximab therapy, a treatment employing a monoclonal antibody against CD20 B lymphocytes, has been shown to potentially decrease the frequency of relapses as well as the associated disability. Acute transverse myelitis (ATM) is an idiopathic inflammatory disorder that

Figure 13. 48-year-old woman with acute vision loss involving the left eye. (A) T2-weighted and (B) fat-suppressed contrast-enhanced T1-weighted coronal MR images show focal swelling and T2-signal change and enhancement within the left optic nerve (arrows). The MRI of the brain at the time of the orbit study was unremarkable. (C) Subsequent study of the brain 6 months later showed several WM lesions (arrows) as shown on FLAIR axial image.

Figure 14. 42-year-old woman s/p MVA with neck pain and paresthesias. (A) T2-weighted sagittal and (B) axial image show an ovoid-shaped hyperintense intramedullary lesion that involves the posterior columns (arrows).

Figure 15. 12-year-old male with ADEM. T2-weighted axial MR image shows diffuse periventricular WM abnormality (arrows).

Figure 16. 9-year-old girl with declining academic performance. T2-weighted axial MR image shows focal signal abnormality within the peri-atrial WM (arrows).
White matter disease affects the spinal cord in adolescents and young adults.23 Patients may have experienced a prior infectious event prior to presenting with ATM. Furthermore, MS is eventually diagnosed in a small percentage of patients with ATM. Patients typically present with motor deficits, autonomic dysfunction, and a sensory disturbance. MR imaging shows involvement of > 2/3 of the cross-sectional area of the spinal cord that extends for 3 or more vertebral segments. An extensive T2-hyperintense lesion, which may be associated with a cord expansion that shows peripheral contrast enhancement, is the most common imaging finding (Figure 18). Advanced imaging techniques with DTI show decreased fractional anisotropy values in both the affected spinal cord segment and in the adjacent distal normal-appearing spinal cord in patients with ATM.24 With respect to spinal-cord imaging findings, there is overlap between ATM and NMO, and MS isolated to the spinal cord.

Infection
Lyme neuroborreliosis
Lyme neuroborreliosis is a multisystem infectious disease that affects the cerebral WM, cranial nerves, the cauda equina, eye, joints, heart, and skin. The causative agent is a spirochete, *Borrelia burgdorferi* in the United States and *Borrelia garinii* and *afzelii* in Europe that is transmitted by a tick bite. There is usually a seasonal pattern to exposure to these tick bites during the spring and summer in endemic areas. An erythema migrans rash with a target-like appearance, arthritis, and carditis are common clinical presentations. MRI abnormalities in patients with Lyme disease are rare.25 When present, MRI shows small nonspecific, T2-hyperintense periventricular WM lesions that variably enhance (Figure 19). Unlike MS, cranial nerve, cauda equina, or meningeal
White matter disease enhancement may be observed in Lyme disease. Early diagnosis is important as prompt treatment may reduce or prevent disease progression.

Progressive multifocal leukoencephalopathy (PML)

Progressive multifocal leukoencephalopathy (PML) is a demyelinating process that results from infection with the John Cunningham (JC) virus of the myelin-producing oligodendrocytes in patients that are immunsuppressed. Immuno-compromised patients that are affected include patients with acquired immunodeficiency syndrome, organ transplant patients on immunosuppression therapy, patients receiving chemotherapy, steroid therapy, or treatment for multiple sclerosis. Patients with PML present with progressive neurologic deterioration. The MRI findings include one or more variable sized confluent, yet asymmetric, WM T2-signal abnormalities that involve the subcortical WM, including the U-fibers, and extend to the periventricular WM (Figure 20). Corpus callosum involvement may be observed. PML usually shows no contrast enhancement (Figure 21). When large confluent areas of WM involvement are seen, the absence of mass effect is notable. In patients who are infected with the human immunodeficiency virus (HIV), the clinical and imaging appearance of PML may simulate that of HIV encephalitis. In HIV encephalopathy, the white matter T2-signal abnormality may show a less discrete or a fuzzy appearance with a diffuse periventricular predisposition and relative sparing of the subcortical U fibers. Cerebral atrophy is common in both PML and HIV encephalitis. Advanced imaging techniques, such as MT, show a decreased MT relaxation in PML compared to HIV encephalitis. As with PML, mass effect and contrast enhancement are often lacking. Contrast enhancement in HIV-positive patients receiving antiretroviral therapy may be due to the immune reconstitution inflammatory syndrome, which is attributed to an aberrant immune response and is associated with worsening of a pre-existing disease.
White matter disease

Vascular

Central nervous system vasculitis

Central nervous system vasculitis may present with subcortical WM ischemic lesions in children and adults (Figure 22). The additional involvement of deep gray matter structures such as the basal ganglia or cortical gray matter may help to distinguish vasculitis from other WMD processes. Furthermore, acute lesions will show restricted diffusion on DWI sequences. Central nervous system vasculitis may require catheter angiography to show areas of
vascular contour irregularities or biopsy to confirm the diagnosis. Vasculitis may also be associated with other systemic vasculitides such as systemic lupus erythematosus and polyarteritis nodosa (Figure 23).

**CADASIL**

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a progressive, hereditary, small vessel angiopathy that affects young adults. The autosomal dominant NOTCH3 gene is located on chromosome 19. Patients present with recurrent symptoms due to transient ischemic attacks or subcortical stroke. As with vasculitis, the WMD involvement is that of T2 hyperintensity with restricted diffusion in acute ischemic lesions. Foci of microscopic hemorrhage manifest as areas of hypointensity on gradient echo and susceptibility-weighted images. The WMD in CADASIL may be present prior to symptom onset. The anterior temporal lobe WM and corpus callosum may also be affected, a finding that distinguishes CADASIL from subcortical arteriosclerotic encephalopathy (Figure 24). The latter condition is associated with hypertension. Unlike other vasculitides, gray matter involvement is rare and catheter angiography does not show vascular contour abnormalities. Perfusion imaging will show decreased cerebral blood flow and volume in the areas of signal abnormality. In elderly patients with extensive chronic ischemic WMD and lacunes, it may be difficult to distinguish from inflammatory conditions that affect the WM. Clinical parameters, such as patient age and a history of hypertension, help to identify these patients. Additionally, the absence of corpus callosum involvement, perivenular inflammatory change and contrast enhancement, and the presence of deep gray matter lacunar infarcts are more consistent with a diagnosis of chronic white matter ischemic change in the elderly.

**Susac’s syndrome**

Susac’s syndrome is another microangiopathy that can present with WMD in adults in their 3rd to 5th decades of life. In this condition, T2-hyperintense WM lesions are characteristically present within the body of the corpus callosum in addition to the subcortical WM, brainstem, and deep gray matter structures. Patients with Susac’s syndrome present with a clinical triad of encephalopathy, bilateral hearing loss and retinal artery branch occlusions. Other vascular etiologies that may also involve the cerebral WM include hypoxic encephalopathy and posterior reversible encephalopathy syndrome (PRES). The clinical presentations in these patients and the imaging findings,
White matter disease which may involve the gray matter structures in hypoxic encephalopathy and the parieto-occipital lobes in PRES, readily distinguishing these entities from more typical WMD pathologic conditions (Figures 25, 26). Hemorrhagic foci ranging from petechial hemorrhages to sulcal hemorrhages to hematoma may be seen in up to 15% of patients with PRES, particularly those who have received bone marrow transplants or are undergoing systemic anticoagulation.31

Acquired conditions
Radiation necrosis
Radiation therapy may be associated with WMD, as oligodendrocytes are very sensitive to radiation. WM injury may be seen at any point in time following radiation treatment to the brain for primary or metastatic tumors.32 The extent of WM damage may vary from edema to necrosis. Radiation necrosis may be focal or diffuse (Figure 27). The subcortical U fibers are spared while the periventricular WM is diffusely affected. In diffuse necrotizing leukoencephalopathy extensive areas of WM injury are present (Figure 28). This may also be seen in patients receiving chemotherapy. Increased T2-signal abnormality is present in areas of WM edema and/or necrosis. T1-hypointense signal is seen in areas of radiation necrosis. Peripheral, irregular or ring like contrast enhancement may be indistinguishable from underlying neoplasm. Advanced imaging techniques such as MRS show decreased NAA and increased lactate and lipid peaks or decreased cerebral blood volume with perfusion imaging. Radiation necrosis is hypometabolic on positron emission tomography. Radiation necrosis should be considered in the differential diagnosis of a new enhancing WM lesion remote to the original treated lesion or if there is interval development of lesion enhancement in what was initially a non-enhancing tumor, or if there is corpus callosal or periventricular WM enhancement that caps the ventricles.

Osmotic demyelination syndrome
Osmotic demyelination syndrome is a metabolic disorder that results from abrupt correction of serum sodium osmolality.33 This rare condition is observed in chronic alcoholic patients, but may also be seen in patients with liver failure, liver transplant patients being treated with cyclosporine, burn victims and patients with prolonged heavy use of diuretics. Rapid correction of hyponatremia in increments > 12 mmol/L/d results in destruction of the myelin sheath. Affected patients present with encephalopathy, spastic quadriplegia and/or pseudobulbar palsy. WMD in this condition is characterized by nonenhancing T2-signal hyperintensity within the central pons (Figure 29). Extrapontine sites of potential involvement within the brain include the basal ganglia, capsular region, hippocampi, lateral geniculate bodies and peripheral cortex. Lesions may be either isointense or hypointense on T1-weighted sequences. Anecdotal reports have shown restricted diffusion on DWI images in areas of acute demyelination. Patients are treated with supportive care with a variable prognosis, but few patients avoid permanent neurologic damage.

Marchiafava-Bignami
Marchiafava-Bignami is another rare toxic metabolic disorder also seen in chronic alcoholics and which primarily results in demyelination of the corpus callosum (Figure 30). A vitamin B complex deficiency is thought to be the cause of progressive laminar necrosis in the corpus callosum.34 WMD may also occur in the anterior and posterior commissures, the periventricular WM and the cerebellar peduncles. There is relative sparing of the subcortical U fibers. Patients present with alteration of mental status, seizures or cognitive deficits. T1-weighted images show foci of decreased signal intensity within the affected WM. These areas are hyperintense on T2-weighted and FLAIR images. The treatment for this disease is limited and includes supportive therapy with vitamin B complex replacement therapy.

Subacute combined degeneration (SCD)
Another condition that is associated with a vitamin B deficiency, in this case B12, is subacute combined degeneration (SCD). Numerous etiologies may result in B12 deficiency including malnutrition, prior surgeries of the gastrointestinal tract such as ileal resection, deficiency of intrinsic factor, malabsorption syndromes, Crohn’s disease, nitrous oxide abuse, and HIV infection. In contradistinction

**FIGURE 31.** 35-year-old man with history of nitrous oxide abuse presents with paresthesias. (A) T2-weighted sagittal image shows abnormal increased signal within the dorsal aspect of the spinal cord (arrows). (B) T2-weighted axial image shows location of signal abnormality within the posterior columns (arrows).
to Marchiafava-Bignami disease, SCD affects the posterior columns of the spinal cord. The imaging findings consist of an inverted “V” shaped focus of T2 hyperintensity on axial images within the dorsal aspect of the spinal cord with lateral greater than medial dorsal column involvement (Figure 31). A long continuous band of T2 signal abnormality is seen within the cervical and thoracic portions of the spinal cord on sagittal images. The lesion may be associated with spinal cord enlargement and mild enhancement may be observed. Patients with SCD present with the insidious onset of sensory disturbances, including paresthesias and abnormal proprioception with ataxia. The clinical presentation and the lack of cerebral WMD distinguish this entity from MS, NMO, ATM and ADEM.

**Diffuse axonal injury**

Diffuse axonal injury is another condition that may manifest with focal WM lesions on imaging. These lesions reflect the sequelae of shearing injury and are often found within the subcortical WM, the corpus callosum and the brainstem. A clinical history of significant head trauma along with the identification of hemorrhagic foci on gradient-echo or susceptibility-weighted images helps to confirm this diagnosis.

**Conclusion**

WMD comprises a variety of disorders that demonstrate overlap in MRI findings. MS is a common WMD process that affects young adults. MS is a dynamic disease process with respect to both clinical and imaging features. A better understanding of demyelinating WMD entities with respect to their more common clinical and imaging manifestations can assist in narrowing the differential diagnosis and potentially suggesting the diagnosis in certain clinical scenarios.

**References**