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Cortical Restricted Diffusion From Arrest to Mad Cow: A Clinicoradiologic Approach

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After participating in this educational activity, the radiologist should be better able to identify cortical restricted diffusion, develop a differential diagnosis, and explain the clinical history and pertinent ancillary tests necessary to confirm the diagnosis.

Category: Neuroradiology
Modality: MRI, CT

Key Words: Brain Injury, Cerebral Infarction, CNS Infection, Cortical Restricted Diffusion, Diffusion-Weighted Imaging, Metabolic Disease, Venous Infarction

Diffusion-weighted imaging (DWI) is a powerful tool in MRI of the brain. DWI assesses the ability of water molecules to freely move within tissues through Brownian motion. Water that is extracellular has rapid diffusivity, whereas water within an intracellular compartment has decreased diffusivity. DWI assesses the ease with which these water molecules diffuse from the intracellular to extracellular compartments and out of the region of interest through phase and refocusing gradients, and imaging will demonstrate a hyperintense signal when the molecules are unable to freely diffuse.

DWI is acquired through use of different b-value acquisition in which sensitization gradients are either turned on (e.g., b1000) or off (b0). Using a mathematical algorithm, an apparent diffusion coefficient (ADC) map is generated, which shows a measurement of true restricted diffusion, as T2 "shine effects" can increase signal on DWI acquisitions. In the setting of true diffusion restriction, or the inability of water molecules to freely move from the area of interest, the ADC map will be hypointense corresponding to areas of DWI hyperintensity, whereas if an area is hyperintense on both sequences, this will correspond to inherently increased T2-weighted image (T2WI) or T2 fluid-attenuated inversion recovery (FLAIR) signal, or T2WI shine-through, typically seen in areas of high water content such as cerebrospinal fluid (CSF) and extracellular vasogenic edema.

DWI can be quickly acquired, adding minimal time to the total examination, and is paramount in MRI, as it limits the differential diagnosis, guides treatment, and in some instances, improves outcomes.[1] Its standard uses span from the establishment of a pyogenic brain abscess to the assessment of age of infarct to the determination of hypercellularity of a neoplasm.

Familiarization with the pattern of cortical restricted diffusion and accompanying integration of the patient's history, physical examination, and ancillary tests can narrow this differential to a unifying diagnosis and expedite management.

The pattern of restricted diffusion can also be important, offering a specific diagnosis or a short list of differential diagnoses. In the setting of cerebral infarction, the areas of restricted diffusion will classically correspond to vascular

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territories or watershed areas in arterial disease, but in the setting of venous infarction, they can be more complex due to different drainage pathways and can appear superficial, cortical, or geographic. Other patterns of restricted diffusion involve the white matter, deep gray matter, cortex, or a combination of these. In this article, we discuss the differential diagnosis for cortical restricted diffusion in adults, breaking it down into vascular, metabolic, and infectious categories, primarily seen in general practice. Familiarization with the pattern of cortical restricted diffusion and accompanying with integration of the patient's history, physical examination, and ancillary tests can narrow this differential to a unifying diagnosis and expedite management.

Vascular Causes

Vascular insults can occur in a variety of ways. The most common presentation will be cerebral ischemia secondary to arterial occlusion, resulting in cerebral infarction. An acute arterial ischemic insult (if large) will classically follow an arterial vascular distribution on DWI and is the most frequently encountered pattern of restricted diffusion. Arterial infarcts may present with focal cortical diffusion restriction, but when one arterial vessel is involved, the restricted diffusion should involve a single vascular territory. This will often have additional corresponding subcortical and deep white matter ischemic changes within this same territory. Venous infarcts may also be cortical or geographic, extending into the subcortical white matter. As single vessel arterial and venous infarcts are extensively described in the literature, this article focuses on global hypoxic-ischemic insults to the brain.

Anoxic Brain Injury

Anoxic brain injury, or global hypoxic-ischemic injury, is most commonly caused by cardiac arrest, but can also be seen in the setting of carbon monoxide poisoning, strangulation/hanging, drowning, or any other asphyxiating event that deprives the body of oxygen exchange. It is being more frequently encountered, as outside of hospital resuscitation is improving, and often brings with it a devastating prognosis, especially when not diagnosed and treated quickly.[2] Much like acute thrombotic/ischemic events, global anoxic injury incites cytotoxic processes, restricting the mobility of extracellular water molecules. In this setting, however, it is a diffuse process, not confined to a vascular territory, and preferentially impacts the high oxygen requiring gray matter.

Although symmetric imaging findings may be a reassuring pattern to the learner, this mantra applies neither to hypoxic-ischemic brain injury nor to many other patterns of cortical restricted diffusion. In the setting of global anoxia in adults, there is classically diffuse, symmetric cortical hyperintensity on DWI, with corresponding hypointensity on ADC consistent with restricted diffusion (Figure 1). To further confound, deep gray structures of the basal ganglia and thalamus also can be symmetrically involved, as can the cerebellum in severe cases. Understanding the normal appearance of the cortex and deep gray matter on high b-value DWI sequences and on ADC is important to distinguish symmetric restricted diffusion from normal brain. Corresponding hyperintense T2WI/FLAIR signal can also be seen in the cortex, basal ganglia, thalamus, and cerebellum, with associated cortical gyral swelling. Hyperintense DWI signal can be seen within 1 hour of insult but can pseudonormalize by the end of the first week, fading to near-normal intensity.[3,4] Cortical enhancement can occur in the subacute phase, followed by cortical laminar necrosis. Although rare, delayed global anoxic injury will have a different imaging appearance altogether, with diffuse

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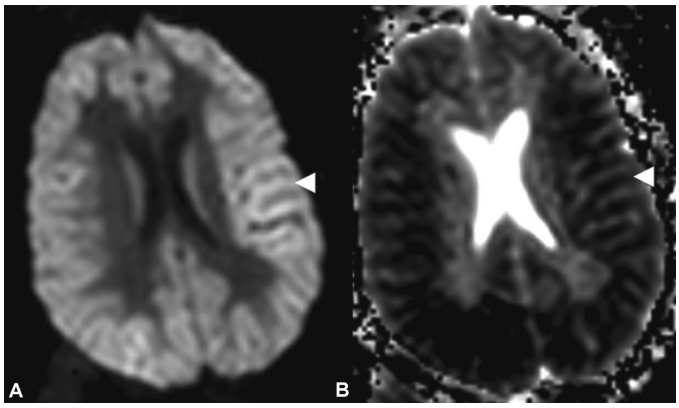

Figure 1. Global anoxic brain injury from asphyxiation. *A*: This b1000 DWI sequence shows diffuse, symmetric cortical hyperintense signal (*arrowhead*). *B*: ADC shows corresponding hypointense signal (*arrowhead*).

cerebral white matter restricted diffusion from postanoxic leukoencephalopathy.[5]

Additional imaging findings helpful in making the diagnosis is cerebral edema on CT, and in some cases a reversal of the normal gray-white attenuation pattern. MR spectroscopy (MRS) may show elevated lactate and glutamine-glutamate (1.3 ppm and 2.2–2.4 ppm, respectively, and field strength independent[6]), markers of ischemia and cytotoxicity. A good clinical history is extremely important. These patients are often intubated, especially in the more severe cases, and early on will demonstrate hypoxemia and hypercapnia on arterial blood gas samples.

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Posterior Reversible Encephalopathy Syndrome

Posterior reversible encephalopathy syndrome (PRES) is a disease process with multiple causes, with the common underlying component of endothelial or autoregulatory dysfunction and vasoconstriction.[7] Examples of these entities include preeclampsia/eclampsia, drug toxicity, severe infection, acute glomerulonephritis leading to uremic encephalopathy, and others. These acute episodes result in a breakdown of the vascular endothelium and blood-brain barrier, leading to vasogenic edema most prominently in the occipital and posterior parietal lobes in 94% to 98% of cases.[8,9] This posterior parietooccipital predominant vasogenic edema presents as cortical/subcortical T2WI/FLAIR hyperintense lesions on MR with corresponding T1-weighted image (T1WI) hypointensity and patchy gadolinium enhancement. Typical PRES does not demonstrate restricted diffusion; however, atypical PRES can present with cortical restricted diffusion from progression to cytotoxic edema in 17% of cases[9] (Figure 2), which can lead to infarction in the adjacent parenchyma in some of these cases and represent as a poor prognostic factor.[10] Additional differences in atypical PRES is involvement of the frontal lobes, cerebellum, basal ganglia, or brainstem.

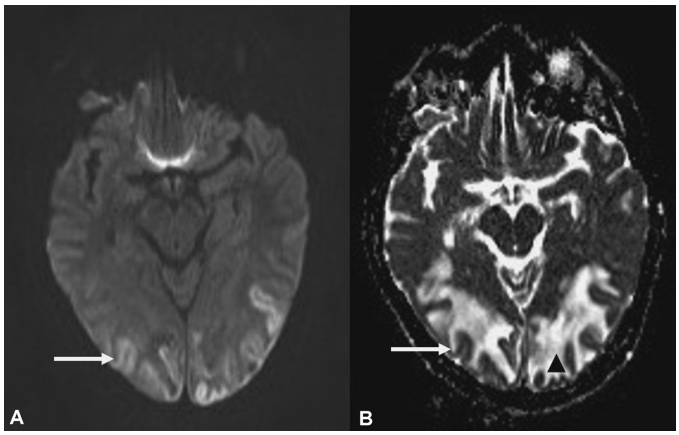


Figure 2. Atypical PRES. *A*: This b1000 DWI sequence shows posterior parietal and occipital cortical ribbon hyperintense signal (*arrow*). *B*: Corresponding ADC hypointensity (*arrow*). Additional confluent subcortical white matter hyperintense signal (*black arrowhead,* left occiptal lobe) from T2 shine secondary to vasogenic edema.

Often a noncontrast CT examination will be normal, although CT may occasionally demonstrate subtle confluent cortical/subcortical parietooccipital hypodensity corresponding to the vasogenic edema.

Clinically, these patients can present with headaches, disturbed vision, seizures, and/or altered mental status. Patients of any age can be affected, with a slight predilection for younger patients, with women more commonly affected than men. Typical clinical presentations are: (1) a pregnant, hypertensive woman past 20 weeks' gestation with headache; (2) a renal transplant patient with altered mental status; or (3) a cancer/transplant patient undergoing chemotherapy or immunosuppressive therapy with headaches and visual disturbances. Treating the underlying cause generally resolves or reverses this entity, even in cases of cytotoxic conversion and restricted diffusion,[11] although subsequent infarction in the affected area can develop if it is longstanding and unrecognized. Another consideration in younger patients presenting with headache and visual disturbances is migraine headache, although oftentimes migraine will present with more focal, typically unilateral transient signal abnormality that often spans more than one vascular territory. The clinical history of visual aura preceding the headache, and the typically unilateral imaging findings, will help elucidate this from PRES, and not conforming to a single vascular territory helps differentiate it from infarction.

Metabolic Causes

The brain, more specifically the gray matter, is very metabolically active, and as such, is extremely susceptible to toxic and metabolic derangements. Extensive testing may be required to elucidate the source of derangement but may not always be successful or timely. In some instances, the imaging patterns may help narrow the list or even imply certain offending agents.

Hypoglycemia

Low blood glucose can either be caused by poor intake or additionally combined with subsequent overdose of insulin in diabetic patients, oral hypoglycemic medication ingestion or overdose, or in the setting of an insulin-secreting neoplasm.[4,12] Symptoms vary with severity of serum glucose levels, with most pronounced presentations below 50 mg/dL, seen as a coma that may be preceded by seizure. On MRI,

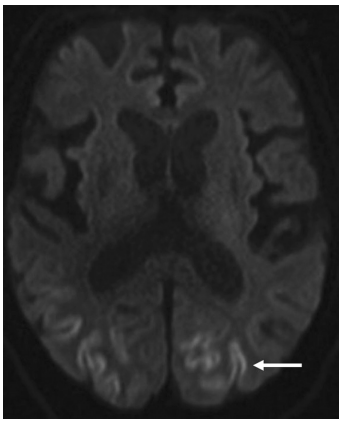


Figure 3. Hypoglycemic encephalopathy. On this b1000 DWI sequence, thin cortical hyperintense restricted diffusion is seen within the occipital lobes (*arrow*), extending into the posterior parietal lobes. (Corresponding ADC hypointensity indicated true restricted diffusion; not shown.)

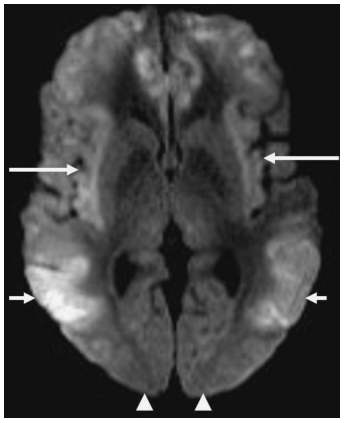
patients can present with gyral thickening and T2WI/FLAIR hyperintensity in the cortical gray matter (commonly in a parietooccipital distribution and the insular region), the hippocampi, splenium of corpus callosum, and basal ganglia.[13] Subsequent vasogenic edema can be present in a similar distribution to PRES. Cortical restricted diffusion is present (Figure 3), much more commonly than in atypical PRES. The chronic phase of the disease can also demonstrate cortical laminar necrosis, resulting in gyral T1WI hyperintensity. The thalami, brainstem, cerebellum, and deep white matter, except the splenium, is typically spared in hypoglycemic encephalopathy. MRS will demonstrate increased lactate and decreased *N*-acetylaspartate (NAA) in the areas demonstrating signal abnormality and edema. Cortical/subcortically based parietooccipital hypoattenuation/cerebral edema may be the only finding on CT.

A presentation of a mentally altered or comatose adult with a history of diabetes or currently low blood glucose levels with the above imaging findings should raise high clinical suspicion for hypoglycemic encephalopathy. In a nondiabetic patient, an additional history of oral hypoglycemic medication ingestion, whether accidental or intentional, is also helpful. In the absence of any history of diabetes or medication ingestion, further investigation is warranted, to include evaluation of the abdomen for a possible insulinoma or other hypermetabolic lesion that is severely altering glucose utilization with arterial phase CT or Ga68-dotatate PET.

Hyperammonemia

Hyperammonemia results in hepatic encephalopathy as a sequela of acute or chronic liver disease. Most commonly seen in cirrhotic patients with portal hypertension and a portosystemic shunt, it can also be seen in cases of acute fulminant viral hepatitis. Cortical restricted diffusion may show a predilection for the insular cortex and cingulate gyrus, with additional diffusion restriction of the basal ganglia (Figure 4).[12] A similar pattern of hyperintensity in the insula, cingulum, and basal ganglia is seen on T2WI/FLAIR sequences. The basal ganglia also commonly demonstrate T1WI hyperintensity, although this is secondary to manganese deposition in chronic liver disease, not acute hyperammonemia. Sparing of the occipital lobe and perirolandic cortex is common. There is typically no contrast enhancement in this process. MRS may show increased glutamine-glutamate with decreased myoinositol and choline (3.5 and 3.2 ppm, respectively). If severe enough, CT may only be positive for diffuse cerebral edema. Ammonia PET can be helpful, as the increased

Figure 4. This b1000 DWI sequence shows diffuse, relatively symmetric frontal lobe cortical hyperintensity extending into the insula (*long arrow*) and parietal operculum (*short arrow*) but sparing the occipital lobes (*arrowhead*) (corresponding ADC not shown), consistent with restricted diffusion. This patient had an elevated serum ammonia level (146 μmol/L) and hyperammonemic encephalopathy of uncertain cause, thought to be multifactorial from infection, chemotherapy, and subsequent hepatic dysfunction.



ammonia content and cerebral deposition will demonstrate increased avidity on nuclear medicine imaging.

Clinically, these patients will present with altered mental status, psychiatric disorders, and sometimes seizures. The majority will have a known history of hepatic dysfunction. There is no age or sex predilection. Laboratory testing of hepatic enzymes; serum ammonia level (often >100 μmol/L in severe cases, normal 15–45 μmol/L); and other hepatic markers can help narrow the diagnosis, especially in those patients without a history of liver disease, as this can have a similar appearance to herpes or other infectious encephalitides.

MELAS

Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) is a genetic metabolic disorder inherited through maternal mitochondrial DNA (mtDNA). Commonly characterized by multiple stroke-like episodes, it can demonstrate cortical restricted diffusion on MRI. Areas of restricted diffusion commonly cross vascular territories and typically have a posterior predominance. Because many of the lesions are caused more by vasogenic edema rather than cytotoxic edema in a true ischemic stroke, hyperintense signal on DWI may not have the correlating strong hypointensity on ADC seen with typical restricted diffusion (Figure 5). Associated gyral edema/thickening can be seen in these cortical lesions, with additional imaging changes depending on chronicity. In the acute setting, there can be corresponding T2WI/FLAIR hyperintense signal and gadolinium enhancement, with areas of cortical laminar necrosis, as it progresses to the subacute stage. Chronic cases can present with calcifications, T2WI hyperintense lesions, and atrophy of the basal ganglia. Foci of hemorrhage are uncommon. Further evaluation with MRS can show an elevated lactate doublet (at 1.3 ppm) in two-thirds of cases in what otherwise appears as normal brain.[14] This lactate doublet is also commonly pronounced within the CSF.[15] Lactate can be near normal in one-third of cases in the brain parenchyma, so an additional ventricular voxel sample should be obtained for these reasons.[14]

Other ancillary tests that can be helpful are electromyography (EMG), which can show myopathic changes, and electroencephalography (EEG), which can demonstrate periodic electrical discharges. Identification of the most common mtDNA mutation in the *MT-TL1* gene (m.3243A>G) in approximately 80% of these patients can be performed without a biopsy by simply obtaining a urine or peripheral blood

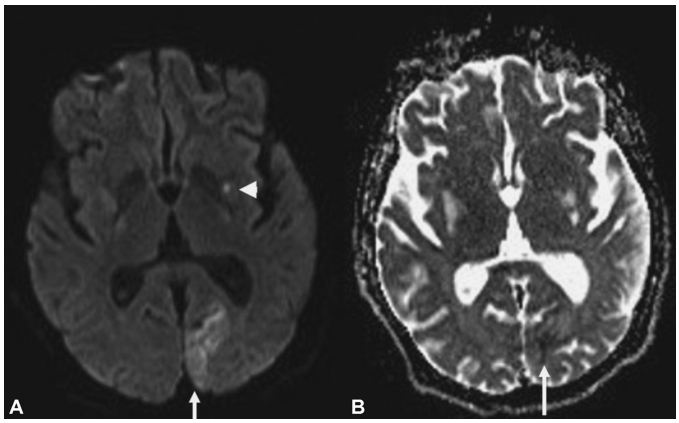


Figure 5. MELAS. *A*: This b1000 DWI sequence shows cortical hyperintense signal (*arrow*) extending from the left occipital pole anteriorly along the cuneus, calcarine fissure, and terminating at the lingual gyrus, with an additional hyperintense focus in the left external capsule (*arrowhead*). *B*: Corresponding ADC; mildly hypointense signal is seen within the occipital lobe (*arrow*) in this young woman.

sample.[16-19] Due to the heteroplasmy of mitochondrial DNA, this can lead to a false-negative result, and a skeletal muscle biopsy may still be needed to evaluate for ragged red fibers in these individuals and those who do not have this mutation. Elevated serum lactate and acidosis on arterial blood gas can be seen on laboratory evaluation.

Clinically, these are typically younger patients, often older children/young adults (mean age 15 years), although patients range in age from 4 to 40 years, without a significant sex predilection. As the name depicts, these patients classically present with multiple stroke-like episodes, seizures, and lactic acidosis. Additionally, they can demonstrate altered mental status, muscle weakness/myopathy, episodic vomiting, migraines, and sensorineural hearing loss.

Seizure

Seizures, whether related to epilepsy or secondary to other etiologies of encephalitis, can be devastating clinically. Often, they are focal and transient, but some individuals can experience prolonged episodes and status epilepticus, which results in brain hypermetabolism and corresponding hyperperfusion that is insufficient to maintain the underlying glucose demand.[20,21] This results in decreased energy production with cytotoxic effects and vasogenic edema, and in some cases, breakdown of the blood-brain barrier.

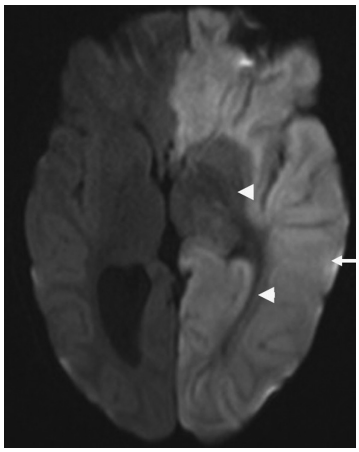


Figure 6. Prolonged seizure and status epilepticus. This b1000 DWI sequence shows left hemispheric cortical thickening and hyperintensity (*arrow*), sparing the white matter and deep gray nuclei (*arrowhead*) in this 3-year-old patient. Note the multiple vascular territories involved, making infarct less likely.

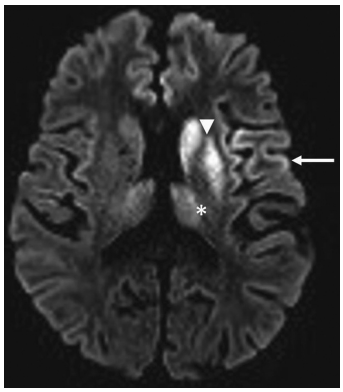


Figure 7. CJD. This b1000 DWI sequence shows diffuse, bilateral thin cortical ribbon of hyperintense signal (*arrow*), more prominent on the left, with additional hyperintense signal of the basal ganglia (*arrowhead*) and thalamus (*) in this male patient (corresponding ADC not shown).

These patients have a more characteristic imaging appearance than others, with T2WI/FLAIR hyperintense, swollen gyri, cortical restricted diffusion, and variable enhancement, typically gyriform.[22] Lesions, generally transient, can be focal involving the temporal lobe, limbic system, or other location featuring an epileptogenic focus, or they can be diffuse and involve an entire hemisphere (Figure 6). Additional findings on MRI include crossed cerebellar diaschisis, hippocampal and thalamic diffusion restriction, and relative sparing of the subcortical and deep white matter. CT is often unhelpful but may show gyral swelling and sulcal effacement. Lesions are generally in a nonvascular distribution, which helps differentiate it from acute ischemia. Affected areas can demonstrate hyper- or hypoperfusion on CT/MR perfusion imaging, depending on the ictal or postictal state of the patient. EEG can also help identify epileptiform foci in these patients, although this may overlap with MELAS. Thus, seizure and MELAS need to be differentiated from each other, given these similar epileptiform foci and nonvascular lesion distribution. To help differentiate these, MRS can be performed. In seizure patients, CSF and uninvolved parenchyma should demonstrate a normal lactate on spectroscopy, whereas MELAS patients will demonstrate an elevated lactate in these areas.

Infectious Causes

Central nervous system infections can have differing imaging findings and clinical presentations, depending on the site

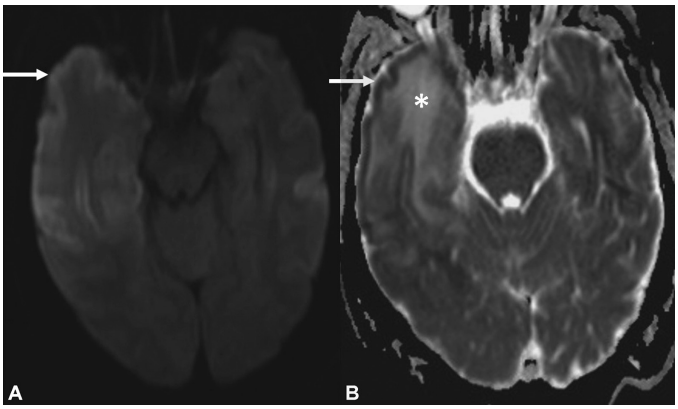


Figure 8. Acute HSV encephalitis. *A*: This b1000 DWI sequence shows unilateral, asymmetric thin cortical restricted diffusion with hyperintense signal. *B*: Corresponding ADC hypointensity within the right temporal lobe (*arrows*). There was extension into the right insula and inferomedial right frontal lobe (not shown). White matter edema can be seen on the ADC image as hyperintense signal in the anterior right temporal lobe (*).

and source of the infection. Oftentimes, the infectious cause is or remains unknown, but some specific pathogens can be suspected by their imaging appearance.

Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is a prion-related encephalopathy with multiple variants, including sporadic (sCJD, most common constituting about 85% of cases[3]), familial (fCJD), iatrogenic, and variant (vCJD) forms. Sporadic and familial forms are due to somatic mutation of the prion protein in sCJD, or genetic mutation in the *PRNP* gene in fCJD. The iatrogenic form is typically caused by infected surgical instruments, graft material, or transplants. vCJD is the more commonly known form due to its exposure in the media from bovine spongiform encephalopathy and transfer of the disease through infected meat. This form transferred from cattle is more common in the UK, although a similar process involving white-tailed deer has also been seen in the United States.

Gyriform, cortical restricted diffusion described as a cortical ribbon sign predominates in these cases (Figure 7).[23] In addition, diffusion restriction in the deep gray structures (basal ganglia, thalamus) is also common. T2WI/FLAIR hyperintensity within the basal ganglia (more pronounced in the caudate and putamen) and thalamus can be seen. In approximately 90% of the cases of the variant form, and to some extent the sporadic form, T2WI/FLAIR hyperintensity is seen within the pulvinar nuclei of the thalamus (pulvinar sign) and the dorsomedial nuclei (hockey stick sign, when combined with the pulvinar nuclei).[24,25] In the sporadic form, additional cortical and periaqueductal gray matter hyperintensity can be seen. Other signs to look for are cerebral atrophy, T1WI hyperintense globus palladi (in the sporadic form), and relative decreased glucose uptake/avidity on FDG-PET within the affected areas.

Clinically, these patients will demonstrate rapidly progressing dementia, often coupled with akinetic mutism and myoclonus/myoclonic jerky movements. Additional clinical signs and symptoms are cerebellar dysfunction and various pyramidal and extrapyramidal signs. There is no specific sex or ethnic predilection, although vCJD tends to affect younger patients, and sCJD typically older patients (sixth to seventh decades). Definitive diagnosis is from brain biopsy or autopsy, with positive tests for the prion protein. CSF studies to evaluate for 14-3-3 protein in conjunction with typical EEG findings of periodic sharp wave complexes, progressive dementia, and at least 2 or more clinical symptoms can lead to a probable CJD diagnosis. Unfortunately for patients with CJD, median survival after onset of symptoms (rapidly progressive dementia, myoclonus, etc) is 4 to 5 months.

Herpes Encephalopathy

Adult herpes simplex virus (HSV) encephalitis is a viral encephalitis nearly always caused by the HSV1 strain of the disease. Classically, it affects the anteromedial temporal lobes, insula, and orbitofrontal regions, with more extensive involvement of the limbic system possible (e.g., cingulum). Cortical restricted diffusion is a common feature and T2WI/FLAIR hyperintensity, gyral swelling, and occasional contrast enhancement are seen on MRI. Commonly unilateral (Figure 8), these findings can often be seen bilaterally, but typically are asymmetric when bilateral. Sparing of the white matter and deep gray matter is typical.[3] Subtle anterior temporal lobe hypoattenuation on CT can be present in severe cases, but CT is generally normal early on. The imaging appearance can be indistinguishable from limbic encephalitis, a paraneoplastic process, except for diffusion restriction in limbic encephalitis is rare. Additionally, in older patients, HSV1 encephalitis can present with acute or subacute hemorrhage, slightly confounding the diagnosis.

Clinically, these patients present with a viral prodrome followed by headache, altered mental status, and seizures. HSV1 encephalitis can affect patients of any age with no sex predilection, with the majority occurring in patients older than 50 years.[26] If not diagnosed and treated early, it can rapidly progress to coma and death, with some reporting a more than 70% mortality rate.[3] With the appropriate history and corresponding temporal lobe/limbic system involvement, prompt treatment with an antiviral agent such as acyclovir should be initiated to improve overall outcome.

Conclusion

DWI is an essential adjunct within MRI for evaluation of the brain, with different patterns of restricted diffusion generating their respective differential diagnoses. A cortical pattern of diffusion restriction can narrow this differential diagnosis to a hypoxic/ischemic, metabolic, or infectious cause. Understanding this differential diagnosis and the different imaging findings can help narrow this list even further. With additional information such as clinical history, physical examination findings, and ancillary laboratory test results, the interpreting radiologist can determine the diagnosis and aid the ordering provider in appropriate next steps in care to help improve prognosis. (See Supplemental Digital Content 1, published online, http://links.lww.com/CDR/A2.)

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1. A 16-year-old adolescent boy presents with reports of seizure of possibly long, but unknown, duration. A CT scan is obtained and is normal. Subsequent MRI demonstrates T2WI/FLAIR hyperintense gyral thickening in the right parietooccipital lobe with cortical restricted diffusion. No hemorrhage or significant enhancement is seen. Which one of the following additional tests can be performed to differentiate MELAS from generalized seizure?

A. EEG
B. MRS with voxel over uninvolved brain parenchyma
C. MRS with voxel over involved brain parenchyma
D. Multivoxel MRS including brain parenchyma and ventricle
E. Peripheral blood sample for genetic testing

2. A 54-year-old man undergoes routine outpatient MRI for rapidly progressing dementia. MI images reveal gyral restricted diffusion and thalamic FLAIR hyperintensity within the pulvinar and dorsomedial nuclei. The radiologist suspects CJD. Which one of the following additional test will make the diagnosis definitive?

A. EEG
B. CSF evaluation for 14-3-3 protein
C. Brain biopsy for prion protein
D. None; CJD is a clinical diagnosis
E. None; MRI and clinical history are sufficient to diagnose CJD

3. Insula and cingulate gyrus cortical restricted diffusion are seen on the MR image of a 63-year-old alcoholic man. Which one of the following laboratory findings can aid in the diagnosis?
   - **A.** Serum fasting glucose 65 mg/dL (normal 70–99 mg/dL)
   - **B.** Serum aspartate aminotransferase (AST) 31 U/L (normal 5–40 U/L)
   - **C.** Serum lactate 1 mmol/L (normal 0.5–1 mmol/L)
   - **D.** Serum ammonia 150 µmol/L (normal 15–45 µmol/L)
   - **E.** Serum random glucose 225 mg/dL (normal <140 mg/dL)

4. A 22-year-old woman with diabetes presents with altered mental status, seizure, and hypertension. MRI demonstrates bilateral parietooccipital distribution, cortical restricted diffusion, and white matter edema. If her blood glucose level is normal, which one of the following would be the *most* likely differential diagnosis?
   - **A.** Posterior circulation infarct
   - **B.** PRES
   - **C.** Hepatic encephalopathy
   - **D.** HSV encephalopathy
   - **E.** Seizure

5. A patient's MR image shows diffuse cortical restricted diffusion, with what appears to be additional thalamic and basal ganglia involvement. Follow-up DWI 1 week later shows near-normal signal with patchy, linear cortical enhancement. Which one of the following histories is *most* likely to apply to this imaging scenario?
   - **A.** 18-year-old drowning victim with prolonged, in-the-field resuscitative efforts
   - **B.** 61-year-old with rapidly progressing dementia
   - **C.** 23-year-old pregnant woman with preeclampsia
   - **D.** 16-year-old with minimally elevated liver function tests and ammonia
   - **E.** 42-year-old with vesicular perineal rash and altered mental status

6. A 56-year-old man has altered mental status. MRI demonstrates restricted diffusion within the temporal pole, insular cortex, and cingulate gyri, sparing the basal ganglia. Which one of the following is the *most* important next step to improve this patient's prognosis?
   - **A.** Check serum ammonia
   - **B.** Correct serum glucose
   - **C.** Administer thrombolytics
   - **D.** Administer antiviral medication
   - **E.** Perform genetic testing

7. An otherwise healthy 32-year-old woman with no medical history presents to the emergency department with altered mental status and lethargy. Initial head CT is normal. MRI demonstrates parietooccipital cortical restricted diffusion bilaterally. The patient responds well clinically to a dextrose infusion. Further questioning of friends and family notes no medication use, either prescription or recreational. Given the rapid response to IV dextrose and lack of history to support diabetes mellitus, which one of the following examinations would be *most* likely to elucidate the underlying condition that is causing this patient's change in mental status?
   - **A.** CT angiogram of the head and neck
   - **B.** CT chest without contrast
   - **C.** CT abdomen and pelvis with contrast
   - **D.** CT chest angiogram
   - **E.** CT abdomen and pelvis, multiphasic

8. Clinical history that would support imaging findings suspicious for PRES includes
   - **A.** renal transplantation and cyclosporine
   - **B.** 24-week pregnant woman with proteinuria
   - **C.** acute lymphoblastic leukemia and chemotherapy
   - **D.** all the above

9. Figure 9 shows DWI in a 22-year-old woman with a history of seizures, hearing loss, and muscle weakness. Her serum lactate level is elevated. Which one of the following additional imaging features would be expected in this patient?
   - **A.** Confluent subcortical white matter FLAIR hyperintensity in the occipital lobe
   - **B.** Scattered foci of hemorrhage on susceptibility-weighted images
   - **C.** Scattered basal ganglia calcifications
   - **D.** Periventricular lesions with incomplete ring enhancement
   - **E.** Arterial stenosis or filling defects

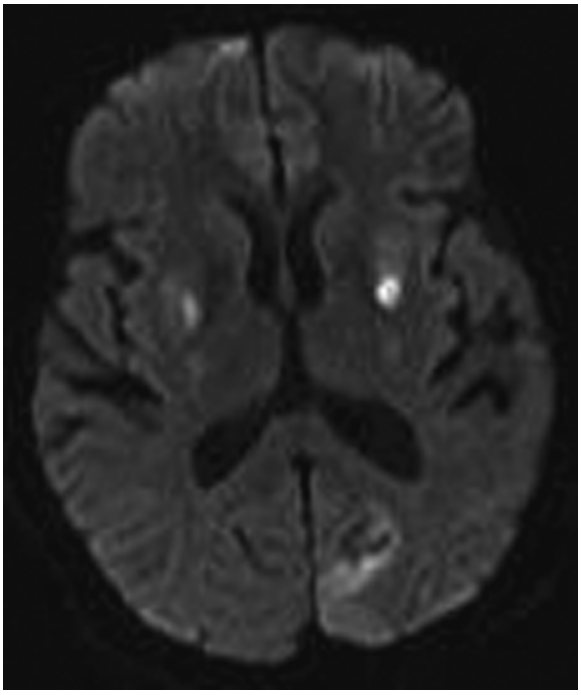

Figure 9.

10. An MR image demonstrates diffuse cortical restricted diffusion with relative sparing of the occipital lobes and perirolandic cortex. The ordering provider was too busy to supply pertinent history or clinical information other than "altered mental status." Which one of the following additional imaging examinations would be the *best* choice to support a diagnosis of hyperammonemia and hepatic encephalopathy?
   - **A.** CT chest without contrast
   - **B.** CT neck angiogram
   - **C.** MRI cardiac function
   - **D.** CT abdomen and pelvis, multiphasic
   - **E.** MRA of the head