Imaging Aspects of Pyogenic Infections of the Central Nervous System

Nelson Paes Diniz Fortes Ferreira, MD,* Gilberto Miyazaki Otta, MD,* Lázaro Luís Faria do Amaral, MD,* and Antônio José da Rocha, MD†

Abstract: Although pyogenic infections of the central nervous system are not a frequent group of diseases, their morbidity and mortality are very high. For this reason they require prompt diagnosis and treatment to avoid several complications that can lead to an undesired outcome. In this article, we review the imaging findings of these infections according to the anatomic site, their complications, and their differential diagnosis. Special attention is given to the different techniques of magnetic resonance imaging like perfusion, spectroscopy, and diffusion, for each specific situation such as meningitis, abscess, ventriculitis, purulent extra axial collections, and vascular complications.

Key Words: brain, meningitis, MRI, pyogenic abscess

Central nervous system (CNS) infections constitute a group of life-threatening diseases, which present themselves with various clinical and imaging manifestations, forming an interesting and challenging pattern for diagnosticians. The brain has some unique peculiarities like absence of lymphatics, lack of capillaries in the subarachnoid space, and presence of cerebral spinal fluid (CSF), which is an excellent culture medium for dissemination of infectious processes, in the subarachnoid space and into the ventricular system. Anatomically, pyogenic infections can be divided into four main categories as follows: 1. Diffuse: meningitis 2. Focal: cerebritis and abscess 3. Extra-axial: empyema and subdural effusions 4. Ventricular infections: ventriculitis.

Central nervous system infections are not frequent, accounting for 1% of primary hospital admissions and 2% of nosocomially acquired infections1,2 and when encountered, require prompt diagnosis and initiation of specific treatment.

Pyogenic infections are one of the few curable categories of diseases affecting the CNS, where the untreated cases rapidly progress to a fatal outcome and most of the deaths occur within the first 24 hours of hospitalization.1,3

Acute bacterial meningitis can be caused by a range of pathogens. Streplococcus pneumoniae is responsible for approximately 47% of the cases, Neisseria meningitidis for 25%, group B Streptococcus for 12%, and Listeria monocytogenes for 8%.4,5 The agents vary according to the age of the patient. In the Schuchat et al5 series, the main pathogen in the neonatal group was group B Streptococcus; in infants (1 to 23 months), S. pneumoniae caused 45% and N. meningitidis caused 31% of the cases; through the ages 2 to 18 years, N. meningitidis was the main causative agent. Pneumococcus was responsible for 62% of cases in persons older than 19 years old.4,5

Focal suppurrative process within the brain parenchyma is frequently secondary to parasanal sinuses infections with 25% of the cases occurring in pediatric patients, with peak age occurrence between 4 and 7 years. The most common causative agents isolated are S. aureus, Enterobacteriaceae, S. pneumoniae, H. influenzae, streptococci of intermedius group, and Bacterioides.4,6

Significant improvements in imaging modalities, like magnetic resonance imaging (MRI), making possible earlier diagnoses and advances in the treatment of bacterial infections, have resulted in a decline in the incidence of complications and of the mortality rates.5 More recently, the advanced MRI techniques, such as proton MR spectroscopy (H-MRS), diffusion-weighted imaging (DWI), and perfusion-weighted imaging (PWI), have improved even more the detection and characterization of infectious lesion in the CNS.

DIFFUSE PYOGENIC INFECTIONS (MENINGITIS)

Meningitis refers to an acute or chronic inflammatory process of the pia-arachnoid (leptomeninges) and CSF. Infectious meningitis is clinically classified into:

Acute pyogenic

Aseptic (usually viral), not discussed in this article

Chronic (fungus, parasites) also not discussed in this article.

There are some routes of entry for infectious agents into the CNS like hematogenous spread (more frequent), direct inoculation (trauma, surgery), and local extension secondary to an infection in the parasanal sinuses or in the mastoids.7

Pathologically the infectious process results in congestion and inflammation of meningeal vessels and cerebral capillaries, increasing the permeability of the blood-brain barrier and in distension of the subarachnoid space (SAS) by
exudates containing polymorphonuclear neutrophils, making cerebrospinal fluid cloudy and sometimes purulent. The meningeal exudates, containing leukocytes and fibrins, can sometimes result in blockage of CSF absorption in arachnoids villi leading to hydrocephaly. The progression of meningeal inflammation can complicate with vasculitis and thrombosis of the superficial pial vessels leading to ischemia and infarction. Patients initially present with headache and fever, followed by meningismus and decreased level of consciousness. Seizures and focal neurologic deficits may also occur. The diagnosis is based in clinical and physical signs, and confirmed by lumbar puncture and CSF analyses.

ROLE OF IMAGING

The initial imaging study is cranial computed tomography (CT) scanning to exclude conditions that contraindicate lumbar puncture, to detect possible complications and to exclude other conditions. Most of the CT scanning studies in patients with uncomplicated meningitis are normal. CT and MRI scanning can demonstrate obliteration of SAS and basal cisterns, ventriculomegaly and meningeal enhancement.

Comparing CT and MRI, obviously the latter is more sensitive, but its sensibility varies with the performed sequences.

MAGNETIC RESONANCE IMAGING

T1 weight (T1WI) post-contrast images are more sensitive than CT to demonstrate meningeal enhancement and this finding is noted in approximately 55% to 70% of patients with clinically proven meningitis. The literature is controversial if T1WI post contrast is more effective than Fluid Attenuated Inversion Recovery (FLAIR) sequences with or without contrast material in the diagnoses of meningeal diseases. Some authors have reported that T1WI post contrast is superior to FLAIR and post-contrast FLAIR acquisitions.

On the sequence FLAIR without contrast, the high signal of CSF is effectively nullified by an inversion recovery pulse after an inversion time. Many authors have described that FLAIR sequences are very sensitive to detect leptomeningeal diseases. This is explained by the elevation of protein levels in SAS, causing a decrease in T1 relaxation time and resulting in hyperintensity (Fig. 1). Detection of nonhemorrhagic SAS conditions has increased to approximately 88% with FLAIR acquisitions. In spite of the high sensitivity of FLAIR images to detect hyperintensity within SAS, this finding is not specific for meningitis and might be encountered in several diseases and in normal conditions. For this reason one must keep in mind that several clinical conditions can occur with CSF hyperintensity on FLAIR images and some cautions should be taken, as follows:

After lumbar puncture the enhancement of the leptomeninges and the dura can persist over several weeks. For this reason, in cases of suspected meningitis, the MR study should be performed before the lumbar puncture.

The hyperintensity of the SAS on FLAIR images related to high levels of protein, is encountered in other pathologies like subarachnoid hemorrhage, leptomeningeal metastasis, and moyamoya disease.

It has been recently described that slow arterial flow (arterial hyperintensity sign) and retrograde collateral slow flow in engorged pial arteries, via leptomeningeal anastomosis (ivy sign), encountered in acute stroke and severe arterial occlusive disease, may also cause leptomeningeal hyperintensity on FLAIR images. Other conditions in which there is hyperintensity of the leptomeninges on FLAIR images, like leakage of gadolinium into SAS (eg, disruption of blood-brain barrier with previous contrast enhanced MR) (Fig. 2) and paramagnetic effects of supplemental O2 administration, have been described.

Another FLAIR finding, uncommonly encountered in ischemia, multiple sclerosis, and Sturge Weber disease, and has also been described in meningitis, encephalitis, and leptomeningeal metastasis, is subcortical low intensity on T2-weighted FLAIR images. This finding is probably due to deposition of free radicals, and is generally associated with leptomeningeal enhancement and cortical hyperintensity on FLAIR images.

COMPARING POST-CONTRAST T1WI AND FLAIR IMAGES

Although T1-weighted sequences are primarily used for gadolinium-enhanced brain MR imaging, attempts have been made to use the T1WI contrast of FLAIR imaging to evaluate this sequence after gadolinium intravenous contrast.

FIGURE 1. Patient with fulminate hepatic failure and meningitis presenting with seizures. A, Axial T1WI post contrast shows that there is not any important leptomeningeal enhancement. B, Axial FLAIR demonstrating hyperintensity of the CSF space (arrow). C, Axial DWI shows pus in the high convexity CSF spaces and restricted diffusion in the adjacent cortex, probably due to cerebritis (arrows).
Initial clinical evaluations of FLAIR post contrast were done for intraparenchymal lesions and, after that, some authors have described that post-contrast FLAIR imaging is more sensitive for detecting SAS diseases than T1WI post gadolinium. At the moment this point is controversial, with some authors affirming that post-contrast FLAIR is better than T1WI and vice versa.

The opinion of the authors is that both have advantages and disadvantages and both should be performed in individual patients (Figs. 4 and 5).

For those that defend the post-contrast FLAIR the main advantages are:
Postcontrast FLAIR images do not show contrast enhancement in vessels with slow-flowing blood. This finding is observed on T1-weighted post-contrast images and can be confused with meningeal enhancement.
FLAIR has a higher sensibility compared to T1 weight to detect low concentrations of gadolinium extravasations from pial vessels in the SAS.

As stated earlier, the imaging findings of meningeal infectious disease is unspecific and the interpretations must be made in association with clinical settings and physical signs.

**FOCAL PYOGENIC INFECTIONS (CEREBRITIS AND ABSCESS)**

Abscess is the most common focal infectious lesion of the brain and frequently arises secondary to hematogenous dissemination, by direct inoculation (trauma or surgery), by contiguous dissemination from an extracranial site or complicating a meningitis.

Pathologically the process begins with the arrival of bacteria to the gray or white matter and is followed by migration of inflammatory cells leading to vascular congestion, increased capillary permeability, perivascular exudates, petechial hemorrhage, and microthrombosis. Later on occur perifocal edema, necrosis, and mass effect (early cerebritis). In later cerebritis phase, the necrotic zone coalesces, and the lesion becomes circumscribed. Early abscess phase occurs with organization of the granulation tissue peripherally, leading to the formation of collagenous capsule, within approximately weeks, which results in reduction of circumjacent edema and liquefaction of the necrotic center. Finally, in the late abscess phase, the capsule thickens and sometimes calcifies. With effective treatment, the central cavity may involute, and the

**FIGURE 2.** Patient with clinical history of trauma and subdural hematoma. A, Axial FLAIR imaging without contrast demonstrating such lesion (arrow). B, Axial post-contrast T1WI shows no enhancement of this hematoma (arrow). C, Post-contrast axial flair showing enhancement of this space due to contrast leakage (arrow).

**FIGURE 3.** A, Axial FLAIR. Notice the marked subcortical hypointensity in the right frontal lobe, suggesting leptomeningeal/SAS abnormality (arrows), confirmed by the post-contrast T1WI axial image (arrow in B).
**FIGURE 4.** Patient with CSF analysis positive for meningitis. A, Axial FLAIR imaging without contrast shows no abnormality. B, Axial post-contrast T1WI without leptomeningeal enhancement. C, Axial post-contrast FLAIR imaging. Note in this example how this sequence shows significative leptomeningeal enhancement (arrows) comparing to the T1WI.

**FIGURE 5.** Another example comparing post-contrast T1WI (A) and post-contrast FLAIR (B). Notice that in the latter, the leptomeningeal enhancement is much better identified.

**FIGURE 6.** Early cerebritis phase in post-contrast CT (A), T2WI (B), and post-contrast T1WI (C).
residual collapsed fibrotic capsule may remain indefinitely. Without treatment, the cavity may grow and the most serious complication, including compartmental herniation and intraventricular rupture, may occur.\(^3,22\)

Otitis media and mastoiditis are the most common origin of cerebellar abscesses that constitute 2\% to 14\% of all brain abscesses. Chronic infections of the face and scalp, particularly frontal sinusitis, may cause cerebritis or abscess in the frontal lobe, which is the most common place of occurrence of focal infection. Due to these reasons, on encountering an abscess on imaging study it is important to search for a local cause, such as mastoiditis, otitis, sinusitis, or ectodermal defects.\(^7\)

Patients may present with headache, nausea, ataxia, and papilledema owing to increased intracranial pressure. Concomitant fever, mental states changes, or focal neurologic deficits are present in half of individuals. Seizures, visual, and speech disturbances are less common manifestations.\(^3\)

**ROLE OF IMAGING**

Imaging diagnosis plays an important role in focal pyogenic brain involvement. The advent of CT and MR imaging has allowed timely diagnosis and decreasing of the mortality rate.\(^23\) The imaging findings vary according to the phase of the lesion and can be arbitrarily divided, for the benefit of comprehension, into four phases.

**Early Cerebritis Phase**

This phase is rarely imaged, and occurs between the third to fifth days.\(^24\) CT demonstrates low attenuation, ill-defined area with subtle mass effect (Fig. 6). MR images offer higher sensitivity for detection of the lesions than CT and show a hyperintense T2 weight and FLAIR lesion indistinguishable of edema and have isointense or hypointense T1-weighted signal.\(^25\) In cerebritis there is no purulent fluid and the key diagnostic sequence is the DWI. In this sequence there is marked diffusion restriction, depicted by high signal (that turns to low signal in apparent diffusion coefficients maps), which might be attributed to hypercellularity from abundant infiltration of inflammatory cells, brain ischemia, or cytotoxic edema (Fig. 7).\(^26\) Contrast enhancement is minimal or absent.\(^3\)

**Late Cerebritis Phase**

This phase develops during the second week.\(^24\) The CT is able to show that the central area becomes more hypodense,
due to necrosis, and continues to progress. The same aspects are observed on T1WI, but the periphery may demonstrate an isointense or slight hyperintense rim. On T2WI the rim is isointense or hypointense and the central area is hyperintense; peripherally to the rim is noted hyperintense vasogenic area of edema, (target lesion). The central area of necrosis has restricted water diffusion. After contrast administration, the enhancement is diffuse or nodular, progressing to thick, irregular-enhancing rim, according to the evolution of the central necrosis.\(^3\)

**Early Abscess Phase**

Close to the second week,\(^2^4\) the capsule formation is complete. CT demonstrates more demarcated isodense capsule or slight hyperdense margin, interposed between the hypodense central area of necrosis and hypodense circumjacent edema. In relation to later cerebritis phase, MR demonstrates more defined margins that are marked hypointense on T2WI, probably due to collagen or paramagnetic free radicals within macrophages and less probably due to hemorrhage, that will have hyperintensity on T1 weight image and hypointensity on Gradient-Echo images due to susceptibility effects of oxyhemoglobin and ferritin/haemosiderin.\(^2^7\) The capsule of abscess in this phase may be less developed on its ventricular side than on its cortical side, probably related to perfusion differences between these areas (Fig. 8). The circumjacent edema reduces in relation to the cerebritis phase and the restriction to water diffusion persists. The postcontrast images reveal intense and well-defined enhancement of the capsule. Daughter abscess (Fig. 9) becomes apparent in this phase.\(^8\) With the progression of the abscess, the capsule becomes smoothest and thinnest with edema reduction.

**Later Abscess Phase**

This phase develops after the second week and may persist for months.\(^2^4\) The central necrotic cavity decreases in size and the capsule looses the hypointensity on T2-weighted images, unless calcification is present. Enhancement may persist and progressively decreases. Hypointense remnants of the capsule may persist for years after resolution of the infection.\(^3\)

**DIFFERENTIAL DIAGNOSIS WITH OTHER RING ENHANCING LESIONS**

Frequently, with conventional techniques, the imaging characteristics alone may not clearly distinguish a cerebral abscess from other ring enhancing lesions, as for instance cystic/necrotic primary or secondary tumor, a resolving hematoma or postoperative change. For this purpose we can use new techniques, such as proton brain spectroscopy, DWI, and PWI in a tentative attempt to establish the correct diagnoses non-invasively.\(^1^2\)

**DIFFUSION WEIGHTED IMAGING**

Diffusion weighted imaging (DWI) plays an important role to differentiate pyogenic abscess from other ring enhancing lesions. It is important to know that the pyogenic abscess has restricted diffusion as a main characteristic and it is the easiest way to diagnose this pathology. The reason for this restriction, however, is poorly understood. For some authors, it might reflect high viscosity of inflammatory cells, but it is...
known that these conditions are not confined to abscess and might be present in various other brain diseases 28–31 like hemorrhagic primary (Fig. 10) or secondary tumors and resolving hematomas.

**PROTON MAGNETIC RESONANCE SPECTROSCOPY**

The brain metabolites in pyogenic abscesses are different from those found in normal brain and can help differentiate pyogenic brain abscesses from necrotic neoplasms. The predominant resonance peaks (N-acetylaspartate, choline, and creatine/phosphocreatine) that are usually observed in the parenchyma of the normal brain are hardly detectable in either tumoral or abscess necrosis. Increases in lactate (1.3 ppm), acetate (1.92 ppm), and succinate (2.4 ppm) presumably originate from the enhanced glycolysis and fermentation of the organism. Amino acids, including valine and leucine (0.9 ppm), are known to be the end products of proteolysis by enzymes released by neutrophils in pus (Fig. 11). Detection of resonance peaks from acetate, succinate, and such amino acids as valine and leucine has not been reported in proton MR spectra of brain tumors. Discrimination between amino acids (ie, valine or leucine at 0.9 ppm) and lipid (at 0.8 to 1.2 ppm) is important, because lipid signals may exist in both brain tumors and abscesses, whereas amino acids are not seen in proton MR spectra of brain tumors, suggesting that amino acids may be markers for brain abscesses. Therefore, if there are resonance peaks at around 0.9 to 1.5 ppm on proton MR spectra obtained with an echo time of 270, an additional spectrum obtained at an echo time of 135 would be necessary to discriminate lactate or amino acids signals from lipid signal. It is known that with an echo time of 135, phase inversion occurs as a result of J-coupling in lactate and amino acids, but not in lipid. 12,32–34 It has been reported that these spectral changes in brain abscess disappear with effective antibiotic treatment, so the spectral pattern may be important to evaluate the treatment responses, and the specificity of spectral is only valid for untreated infections. 34

**PERFUSION WEIGHTED IMAGING (PWI)**

More recently, some authors have reported the additional information given by MRI perfusion with relative cerebral blood volume (rCBV) maps to distinguish abscess from other ring enhancement lesions. The utilization of perfusion to...
distinguish low-grade from high-grade tumors has been previously related with success. As low-grade tumors, abscess rim seems to have lower rCBV values than high-grade tumors rim. In high-grade tumors the high rCBV values are probably due to high capillary density of the neovascularity formation. The abscess collagen capsule theoretically is associated with low capillary density and consecutively, low rCBV values. In our anecdotal experience with perfusion in abscess, we have noted that, in latter stages the abscess capsule might have high rCBV values, making the differential diagnoses (in individual patients) with tumor impossible with this technique (Fig. 12). However further studies are requires to establish the perfusion role in abscess.

EXTRA AXIAL FLUID AND PUS COLLECTIONS

Extra axial fluid collections may occur in the subdural and epidural spaces after meningitis. These collections can be sterile fluids (effusions) or infected purulent fluids (empyema). Empyemas are uncommon collections frequently related to sinusitis, mastoiditis, infection secondary to previous craniotomy, or post traumatic infection. Purulent meningitis in infants is often related to both empyemas and subdural effusions.

Subdural effusion is a collection secondary to irritation of the dura mater by infectious agents and its products or secondary to subdural veins inflammation.

ROLE OF IMAGING

Differentiating these situations (effusions and empyema) is very important. In the former, CT and MR imaging demonstrate the same density and signal intensity of cerebrospinal fluid, and these collections generally do not require specific

FIGURE 14. Neonatal male with left parietal brain abscess with ventricular drainage. Axial post-contrast T1WI demonstrates the diffuse ependymal enhancement (arrow) due to ependymitis and the communication between the parenchymal abscess and the ventricular system (arrowhead). B, DWI shows pus in the brain abscess (arrow) and within the ventricles (arrow head).

FIGURE 15. A, Axial post-contrast T1WI shows mastoiditis and meningeal enhancement (arrow). B, Axial DWI demonstrating pus in the left cerebellopontine cistern (arrow). C, Intracranial 3D TOF magnetic resonance angiography (MRA) demonstrates bilateral severe stenosis in the supra clinoid internal carotid arteries (arrows) due to arteritis, and the absence of the anterior cerebral arteries (ACA). D, Axial DWI shows acute bilateral infarction in the ACA territories (arrow).
treatment and resolve spontaneously after treatment of the meningitis.

Subdural empyema is usually secondary to retrograde thrombophlebitis via the calvarial emissary veins from an adjacent infection. Subdural empyema requires urgent neurosurgical treatment and the antibiotic therapy alone is not sufficient. Earlier diagnoses are necessary because the subdural empyemas may cause complications such as thrombophlebitis and cerebritis. CT demonstrates a lentiform collection slightly denser than cerebrospinal fluid. MRI is the modality of choice to differentiate subdural empyema from subdural effusion. Subdural empyemas present higher concentrations of proteins and demonstrate higher signal than cerebrospinal fluid in T1-weighted and FLAIR images. After intravenous contrast administration, the membranes of empyemas enhance. More recently this differentiation has been easily done with DWI, where, like in abscess, the empyema shows higher signal and low ADC values, and the effusion has facilitated diffusion (Fig. 13).

In epidural empyemas, the purulent collection is localized outside the dura mater, protecting brain parenchyma from complications. Thus, patients with epidural abscess have more insidious and benign course. This prolonged course explains the low or mixed signal intensity that may be encountered in diffusion weighted images because the pus becomes less viscous. The signal in T1- and T2-weighted images and the density in CT are the same of subdural empyemas, and the contrast administration shows a thicker dura mater enhancement.

VENTRICULITIS

Ventriculitis is an uncommon but serious complication of meningitis or rupture of brain abscess into the ventricular system. CT shows ventricular enhancement after intravenous contrast administration. MRI also shows this enhancement and demonstrates, especially on FLAIR and DWI, increased signal of pus into the ventricular system. Ventriculomegaly is often present (Fig. 14). The most common finding in MRI is the presence of "debris", and the best sequence and place to look for small amount of pus are respectively diffusion and the occipital horn of the lateral ventricles.

VASCULAR COMPLICATIONS

Central nervous system infarction associated with meningitis occurs due to inflammatory induced arterial spasms or because of direct inflammation of the walls of arteries/arterioles ending with an infectious arteritis. Most of these infarctions are ischemic in origin and occur in the basal ganglia. However, large arterial branch occlusion can occur resulting in cortical infarctions (Fig. 15). Another vascular complication is the mycotic aneurism. Recently this term has been used to describe all types of infective aneurysms, but the original description (Osler 1885) used this term to describe an infective aneurysm formation complicating bacterial endocarditis (Fig. 16).

ACKNOWLEDGMENT

The authors thank Sergio Santos Lima, MD, for his incentive and assistance.

REFERENCES


