CHAPTER 3 IMAGING OF INTRACRANIAL INFECTIONS
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Intracranial infections are usually diagnosed by clinical assessment and laboratory investigations, particularly cerebrospinal fluid (CSF) analysis, combined with radiologic findings. Imaging plays an important role by providing or narrowing the differential diagnosis and occasionally identifying a particular entity that has a characteristic appearance, such as herpes simplex virus encephalitis, pyogenic abscess, or empyema. Imaging is also crucial for identifying complications of disease and assessing response to treatment. Finally, imaging contributes to the evaluation of opportunistic infections in immunocompromised patients and other patients at high risk for infection.

Here, we emphasize the overall strategy for imaging intracranial infections and highlight specific entities in which imaging findings contribute to diagnosis or management. We stress the major complications of intracranial infections and address special considerations for immunocompromised patients.

IMAGING STRATEGY

Patients suspected of harboring intracranial infection who present with altered mental status, seizures, or focal neurologic deficits should emergently undergo noncontrast computed tomography (NCCT) to exclude life-threatening conditions. In the acute setting, NCCT is the test of choice to assess for hydrocephalus, cerebral edema, mass lesions, or hemorrhage and is often performed prior to lumbar puncture (LP) to exclude impending brain herniation. NCCT is widely available, and the images are rapidly acquired, making the examination well tolerated even by critically ill patients.

Clinically stable patients in whom immediately life-threatening conditions have been excluded by NCCT often require further evaluation with contrast-enhanced magnetic resonance imaging (MRI), which has a greater sensitivity for leptomeningitis, ventriculitis, cerebral abscess, and empyema as well as downstream complications of infection such as infarctions. MRI lacks ionizing radiation, so it is relatively safe to perform, but specific contraindications include pacemakers and other implanted metallic devices or metallic foreign bodies. The risks and benefits of MRI should be weighed carefully in pregnant patients. Studies have not proven any negative effects of MRI to the fetus, but the American College of Radiology recommends deferring MRI in pregnancy due to the risk for nephrogenic systemic fibrosis (2). Administration of gadolinium-based contrast should be avoided in pregnancy due to the unknown effects of exposure to free gadolinium ions on the developing fetus (1).

According to the American College of Radiology Appropriateness Criteria for headache (3), both NCCT and contrast-enhanced MRI of the head are usually appropriate for patients presenting with new headache and suspected meningitis or encephalitis, with the choice of test depending on local preference and availability. When MRI is unavailable or contraindicated, contrast-enhanced CT may be a suitable alternative. Cerebrovascular complications of infection are relatively frequent, and therefore magnetic resonance angiography (MRA) and magnetic resonance venography (MRV), either with or without contrast, may also be appropriate tests. Computed tomography angiography (CTA) may be performed when there is strong suspicion for vascular disease or to further evaluate abnormalities detected by MRA. Other advanced imaging techniques such as computed tomography perfusion (CTP) or magnetic resonance perfusion (MRP), magnetic resonance spectroscopy (MRS), and nuclear medicine studies such as single-photon emission computed tomography (SPECT) and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) or PET/CT are usually only performed for problem solving after the standard imaging evaluation has been performed.

For evaluation of a new headache in an HIV-positive or immunocompromised individual, MRI with or without contrast is usually appropriate as the initial imaging test (ACR Appropriateness Criteria “Headache” [3]). For an indeterminate cerebral mass in an immunocompromised patient, additional problem-solving techniques such as FDG-PET/CT, SPECT, MRS, and MRP may be helpful to narrow the differential diagnosis.

In neonates in whom the anterior fontanelle is patent, cranial ultrasound may be used to evaluate for hydrocephalus, subdural and epidural collections, and parenchymal masses (4). Uncomplicated rhinosinusitis is usually managed clinically without the need for imaging, but for suspected intracranial or orbital complications of sinusonal disease, both NCCT and contrast-enhanced MRI of the head, orbits, and paranasal sinuses are usually appropriate, with CT and MRI serving as complementary examinations (ACR Appropriateness Criteria “Sinonasal Disease” [5]). Brain imaging is critical if there is a concern for intracranial extension and is best accomplished with contrast-enhanced MRI. If the patient is unable to tolerate gadolinium contrast, noncontrast MRI augmented with contrast-enhanced CT of the head and sinuses is recommended. Immunocompromised patients with acute or subacute rhinosinusitis are at high risk for developing intracranial or orbital complications, and therefore the threshold for obtaining imaging should be lower than for immunocompetent patients.

PYOGENIC INFECTIONS

Meningitis

Meningitis refers to inflammation of the pia and arachnoid membranes. LP with CSF analysis is the test of choice for diagnosis (6), and imaging plays an ancillary role.
Meningitis may be classified based on the pattern of involvement. Pyogenic and viral meningitis typically involve the cerebral cortices. Granulomatous or chronic meningitis typically involves the basal surfaces of the brain (basilar meningitis) and may be due to infectious or noninfectious causes. Pyogenic infections may also produce a basilar pattern of meningitis.

The primary goals of imaging are to evaluate for contraindications to LP and to exclude unexpected clinical mimics or complications. NCCT can satisfy these goals, but not all patients with suspected meningitis require CT. Reported risk factors for an abnormal CT in patients with suspected bacterial meningitis include age 60 years or older, immunocompromise, recent seizure, focal neurologic deficits, and impaired consciousness (7). In the absence of these clinical indicators, CT may not be necessary.

Five percent of patients with acute bacterial meningitis suffer brain herniation, and herniation accounts for 32% of deaths (8). A causal relationship between LP and brain herniation has not been proven, but generally accepted imaging contraindications to LP include midline shift, effacement of the basilar cisterns, and posterior fossa mass effect (8, 9). Clinical signs of increased intracranial pressure are also a contraindication to LP.

Imaging is usually normal in cases of bacterial meningitis (10). Imaging findings supporting the diagnosis include cerebral edema, inflammatory material in the subarachnoid spaces, and leptomeningeal enhancement. Cerebral edema manifests as narrowed or compressed sulci, ventricles, and basilar cisterns. Inflammatory material in the subarachnoid spaces manifests as hyperdense or enhancing material on CT (Fig. 3.1A) and abnormal fluid-attenuated inversion recovery (FLAIR) signal hyperintensity (Fig. 3.1B), enhancement, or restricted diffusion (11) on MRI. Leptomeningeal enhancement manifests as thin, linear enhancement extending along the sulci and basilar cisterns in a gyriform pattern (12). Leptomeningeal enhancement should not be confused with pachymeningeal enhancement, which refers to enhancement of the dura mater.

Imaging is also helpful to assess for complications of meningitis, including extensive cerebral edema resulting in brain herniation, infarcts, hydrocephalus, extraaxial pus collections, ventriculitis, cerebritis, and cerebral abscess. Sterile subdural effusions occur with meningitis but, unlike infected extraaxial collections, generally resolve spontaneously. Sterile subdural effusions may develop internal membranes or septations and occasionally become infected, resulting in subdural empyema (SDE) (13). Subdural effusions occur more often in children with bacterial meningitis and typically develop over the frontal and temporal lobes (13). Sterile effusions appear similar to CSF in density or signal intensity or may be mildly proteinaceous, resulting in slight signal hyperintensity on FLAIR compared to CSF. They may be mistaken for prominent subarachnoid spaces, a normal finding in infants. One distinguishing feature is the finding of bridging vessels crossing the collections, which are present in prominent subarachnoid spaces but not subdural effusions (14).

Hydrocephalus is a potentially life-threatening complication of meningitis resulting from impaired resorption of CSF by the arachnoid granulations or by diminished CSF outflow due to viscous material in the ventricles or basilar cisterns. Hydrocephalus may be the only imaging finding in patients with meningitis, particularly those with basilar meningitis (Fig. 3.2). In some cases, proteinaceous or enhancing material may also be evident in the basilar cisterns on CT (Fig. 3.2A) or MRI (Fig. 3.2B).

Cerebritis

Cerebritis refers to focal brain inflammation due to any cause, including pyogenic infection (15). Unlike meningitis, which is localized to the pia and arachnoid, cerebritis involves the brain parenchyma and may occur adjacent to infected subdural or epidural collections.
Cerebritis has a nonspecific imaging appearance. CT findings include focal low attenuation (16) without enhancement or with nodular or peripheral enhancement, which may resemble infarct or mass lesion. MRI findings include hyperintensity on T2 and FLAIR (Fig. 3.3B) with variable enhancement (Fig. 3.3C). There may be hemorrhage or restricted diffusion. MRI appearance may be similar to that seen in status epilepticus, ischemia, or neoplasm.

If inadequately treated, cerebritis may develop into a cerebral abscess, following a well-described progression through the stages of early cerebritis, late cerebritis, early abscess formation, and late abscess formation (16,17) (Fig. 3.3C and D). Features suggesting the formation of an abscess within an area of cerebritis include development of a ring-enhancing mass with restricted diffusion of the central cystic or necrotic core. This is in contrast to the restricted diffusion that may be seen with cerebritis, which affects the brain parenchyma itself.

Abscess

Cerebral abscess refers to a focal pus collection within brain parenchyma with a surrounding capsule (15). Abscesses may result from direct extension of local infection or from hematogenous spread. Local infections associated with cerebral abscesses include otomastoiditis, sinusitis, and odontogenic infections (18). Bloodborne infections may be associated with intravenous drug use, bacterial endocarditis, pulmonary infections, pulmonary arteriovenous malformations, congenital heart disease, and other causes (18–21). Cerebral abscesses may also occur after trauma or neurosurgical intervention.

Abscesses from bloodborne infections tend to be multiple and located at the gray–white junction, most commonly in the frontal lobes (18–21). Abscesses arising from local spread are often spatially related to the primary infection. For example, a frontal abscess may develop adjacent to frontal sinusitis. In these cases, the primary infection is usually visible on imaging.

Regardless of etiology, abscesses share common imaging features. On NCCT, abscesses appear as hypodense masses with surrounding vasogenic edema, sometimes with a hyperdense rim corresponding to the abscess capsule (16) (Fig. 3.4A). MRI also shows a localized mass with a T2-hyperintense necrotic core and a markedly T2-hypointense rim surrounding the collection that corresponds to the capsule (22) (Fig. 3.4B). The central core demonstrates markedly restricted diffusion (hyperintense on diffusion-weighted image [DWI] sequence [Fig. 3.4C] and dark on apparent diffusion coefficient [ADC] maps). Quantitative ADC values of the necrotic core are significantly lower for abscesses than necrotic neoplasms (23).

On both CT and MRI, cerebral abscesses demonstrate thick smooth rim enhancement, sometimes with thinning of the medial wall. Focal wall rupture results in formation of a daughter abscess (22) (Fig. 3.4D). In immunocompromised patients, ring enhancement may be absent and vasogenic edema may be mild (15), requiring a high index of suspicion for diagnosis.

Complications of cerebral abscess include mass effect and brain herniation. It is important to evaluate for intraventricular rupture of the abscess with resulting ventriculitis because this is a marker of poor prognosis that requires aggressive treatment (21). Imaging findings indicating ventricular rupture include layering debris in the lateral ventricles and enhancement of the ependymal lining.

The differential diagnosis of a ring-enhancing mass includes high-grade glial neoplasm, metastasis, and less commonly, tumefactive demyelination or subacute infarction. Usually, the clinical scenario helps distinguish these entities, but in difficult cases, MRP and MRS may be helpful.

MRP allows comparison of the cerebral blood volume of the lesion with that of contralateral normal white matter, resulting in a measure of relative cerebral blood volume (rCBV). The enhancing component of high-grade tumors demonstrates elevated rCBV (increased perfusion) compared to normal white matter, whereas pyogenic abscesses demonstrate significantly reduced rCBV, which is less than that of contralateral normal white matter (23,24). It is important to evaluate the
FIGURE 3.3 Cerebritis progressing to abscess. NCCT (A) and MRI (B, C) on presentation shows focal parenchymal abnormality with decreased density on CT and increased FLAIR signal involving gray and white matter (white arrows), with ill-defined central enhancement (C) (white arrowhead). Despite treatment, contrast-enhanced MRI 2 weeks later demonstrated rim-enhancing abscess (D) (black arrowhead). Notice also development of leptomeningeal enhancement (black arrow).
Part I: Approach to the Patient and Diagnostic Evaluation

FIGURE 3.4 Pyogenic (*Streptococcus milleri*) abscess. NCCT (A) shows right frontal mass with slightly hyperdense rim (*white arrow*) and surrounding vasogenic edema. MRI T2 sequence (B) shows hypointense rim corresponding to abscess capsule (*black arrow*) and extensive surrounding edema. C: Central necrotic core demonstrates restricted diffusion (DWI). Postcontrast T1 sequence (D) shows thick rim enhancement with daughter abscess (*white arrowhead*).