week after paralysis onset. The cerebrospinal fluid white cell count can elevate into the hundreds, with a predominance of neutrophils early in the disease course. Although the poliovirus can be cultured from the cerebrospinal fluid early in the disease course, throat and rectal swabs provide a greater yield. When a particular viral serotype is identified, serial serum antibody titers can be used to verify the cultures.

The most important cause of paralysis on the differential diagnosis that must be considered and excluded is Guillain-Barré syndrome, which, unlike the acute polio infection, causes more symmetric muscle weakness. Acute paralysis can result from peripheral neuropathies caused by infectious mononucleosis, Lyme disease, or porphyria. Paralysis also can result from inflammatory myopathies, electrolyte abnormalities, toxins, or other viruses, such as coxsackieviruses, mumps, echoviruses, and nonpolio enteroviruses. Paralysis also can result from acute spinal cord compression, vascular lesions, and transverse myelitis, all of which should produce a sensory level and sphincter disturbances. In children, it is necessary to exclude spinal muscular atrophy, which can be undiagnosed until it is manifested by dramatic limb weakness caused by an acute febrile illness.

Postpolio Syndrome Patients with **postpolio syndrome** complain of muscle fatigue, joint pain, worsening of skeletal deformities, or weakness in muscles that were spared during the initial viral infection.[85] When muscle weakness is observed, atrophy, pain, and fasciculations may be noted both in previously unaffected muscle groups and in those previously involved. Patients may also develop new bulbar, respiratory, or sleep difficulties. For example, laryngeal muscle weakness can cause progressive dyspnea, dysphagia, and/or hoarseness. Some patients complain of abnormal movements in sleep that disturb normal sleep, requiring therapy with benzodiazepines or dopaminergic drugs.[86] These symptoms occur independently of any concurrent neurologic, orthopedic, psychiatric, or systemic medical illness.

To diagnose postpolio syndrome, the patient should have a history of acute paralytic poliomyelitis with stable recovery of motor function associated with residual muscle atrophy, weakness, and areflexia with normal sensation in at least one limb. Additionally, there should be new muscle symptoms or weakness not attributable to an acute injury, neuropathy, radiculopathy, or systemic, neurologic, or psychiatric illness.

Treatment of the new muscle weakness seen with postpolio patients is primarily symptomatic, with the use of analgesic and anti-inflammatory medications. Most patients with postpolio syndrome benefit from muscle training[87] and daily exercise.[88] An additional therapeutic option is lamotrigine (Lamictal). When used in conjunction with an exercise routine, lamotrigine may improve the quality of life in postpolio patients.[89]

Acknowledgments: The authors would like to thank Edward P. Sloan for his work on previous editions of this chapter.

REFERENCES

The complete reference list is available online at www.TintinalliEM.com.

CHAPTER 174

Central Nervous System and Spinal Infections

Mary E. Tanski
O. John Ma

BACTERIAL MENINGITIS

INTRODUCTION AND EPIDEMIOLOGY

Bacterial meningitis is a life-threatening emergency that affects 1.38 out of 100,000 people, with a case fatality rate of 14.3%.[1] Although the incidence of bacterial meningitis has declined significantly since the initiation of vaccination programs, the disease is still prevalent and associated with significant morbidity and mortality.[2-4] In the United States, the most common causes of bacterial meningitis are *Streptococcus pneumoniae* (58.0%), group B *Streptococcus* (18.1%), *Neisseria meningitidis* (13.9%), *Haemophilus influenzae* (6.7%), and *Listeria monocytogenes* (3.4%).[1] *Escherichia coli* in the neonatal population and *Mycobacterium tuberculosis* in immunocompromised hosts are also important considerations.[5]

PATHOPHYSIOLOGY

Organisms enter the cerebrospinal fluid either through hematogenous or direct contiguous spread. In hematogenous spread, bacteria colonize the upper airway and invade the bloodstream, gradually making their way to the subarachnoid space. The subcapsular components of *S. pneumoniae*, *H. influenzae* type b, and *N. meningitides* induce an inflammatory cascade, and leukocyte toxins cause cellular swelling and inflammation of the brain and meninges.[6] Blood–brain barrier permeability increases, allowing protein and water to enter and leading to vasogenic edema. Cerebrospinal fluid drainage is inhibited by reduced absorption of the arachnoid granules with resultant obstruction and hydrocephalus, and cerebrospinal fluid is forced into the periventricular parenchyma causing interstitial edema. Disruption of cell membrane homeostasis causes cytotoxic edema. As the brain and meninges rest in a fixed-volume skull, this leads to an elevation in intracranial pressure. Vasculitis decreases cerebral blood flow and can cause ischemia and thrombosis. Additionally, neurons are directly injured by free radicals from granulocytes and endothelial cells.[7]

In direct contiguous spread, organisms gain entry into the cerebrospinal fluid from adjacent infections such as sinusitis, brain abscess, or otitis media. Organisms can also enter directly with penetrating traumatic injury, through congenital defects, or during neurosurgical procedures. In these cases, the organisms and their pathophysiologic effects vary.

Important risk factors for bacterial meningitis are listed in **Table 174-1**.

CLINICAL FEATURES

The presentation of fever, headache, stiff neck, and altered mental status is commonly seen in patients with bacterial meningitis. Although most patients have at least two of four of these symptoms, their absence does not exclude meningitis. Headache is the most common symptom and is seen in more than 85% of patients. Fever is the second most common symptom.[7] Seizures and focal neurologic deficits are seen in 25% to 30% of patients.

History Assess historical data in order to elicit risk factors suggestive of certain pathogens. *N. meningitidis* is associated with close living

TABLE 174-1 Important Risk Factors for Bacterial Meningitis

Acute or chronic otitis media
Sinusitis
Immunosuppression/splenectomy
Alcoholism
Pneumonia
Diabetes mellitus
Cerebrospinal fluid leak
Pneumonia
Endocarditis
Neurosurgical procedure/head injury
Indwelling neurosurgical device/cochlear implant
Advanced age
Malignancies
Liver disease
Unvaccinated to *Haemophilus influenzae* type b, *Neisseria meningitidis*, or *Streptococcus pneumoniae*

quarters, such as in military barracks and college dormitories. Unvaccinated patients are at risk for *H. influenzae*. Consider *L. monocytogenes* in older adults and alcoholics.[8] Penetrating head trauma makes *S. pneumoniae* more likely. *Staphylococcus aureus*, coagulase-negative staphylococci, and streptococci are the most commonly implicated organisms after craniotomy, whereas coagulase-negative staphylococci are commonly seen after ventriculoperitoneal shunt and spinal surgery.[4] Immunocompromised patients, such as those with human immunodeficiency virus, on chronic steroids, or with a history of splenectomy, are susceptible to meningitis with encapsulated organisms.

Physical Examination Evaluate for focal neurologic dysfunction such as hemiparesis, facial asymmetry, visual field deficits, or disordered eye movements. Increased intracranial pressure can cause papilledema, decreased venous pulsations, or cranial nerve palsy especially involving cranial nerves 3, 4, 6, and 7. Assess for meningeal irritation with Brudzinski sign (flexion of hips and knees in response to passive neck flexion) and Kernig sign (contraction of the hamstrings in response to knee extension while the hip is flexed). Examine the skin for cutaneous stigmata such as petechiae, splinter hemorrhages, and pustules, and consider aspirating to send for culture.[9] Percuss the sinuses and examine the ears for signs of primary infection.

DIAGNOSIS

Lumbar Puncture The diagnosis of meningitis is based on cerebrospinal fluid results obtained by lumbar puncture (LP). Withhold LP if there is coagulopathy, as evidenced by thrombocytopenia or anticoagulant or antithrombotic use, until coagulopathy is corrected. As a general rule, a platelet count ≤20,000/μL (and some prefer ≤50,000/μL) or INR ≥1.5 is a contraindication to performing an LP on an emergent basis.[10] The risk of bleeding complications such as epidural hematoma resulting from LP in the presence of aspirin, antiplatelet agents, and nonsteroidal anti-inflammatory drugs is not known, and risks and benefits of LP must be considered in such circumstances.[11,12] Send cerebrospinal fluid for studies including Gram stain and culture, cell count with differential, glucose, and protein.[7] Typical cerebrospinal fluid findings for bacterial, viral, fungal, and neoplastic meningitides are listed in **Table 174-2**,[13-16] but there is considerable overlap in findings.

Laboratory Testing Bacterial meningitis is associated with an elevated opening pressure >170 mm H_2O, and WBCs are elevated greater than 1000/mm^3 with a neutrophilic predominance. Gram stain is positive in 60% to 80% of patients before antibiotics are initiated, with a significant decline once antibiotics have been started. Cerebrospinal fluid protein is often elevated above 200 milligrams/dL, and glucose is often decreased below 40 milligrams/dL or the glucose serum–to–cerebrospinal fluid ratio is <0.4.[13-15] Although it is not specific for bacterial meningitis, cerebrospinal fluid lactate is a promising indicator to assist with differentiation between aseptic and bacterial meningitis.[16]

Sterilization of the cerebrospinal fluid is possible within 2 hours of initiating parenteral antibiotics in meningococcal and 6 hours in pneumococcal meningitis, highlighting the importance of timely LP.[17] Without antibiotics, Gram stain is positive in 60% to 80% of cases, but in patients treated with antibiotics, the Gram stain is positive in 7% to 41%.[15] Cerebrospinal fluid culture is positive in 80% to 90% of cases if cerebrospinal fluid analysis is preformed before antibiotics are initiated, although results are not available during the course of the ED stay. **However, when bacterial meningitis is considered, never withhold empiric antibiotic therapy in order to collect the cerebrospinal fluid sample.**[18]

Rapid latex agglutination tests can be used to detect bacterial antigens and improve bacterial identification. These tests are available for *S. pneumoniae, group* B streptococci, *H. influenzae, E. coli*, and *N. meningitides*, but are associated with false-positive and false-negative results and limited sensitivity and specificity. Polymerase chain reaction testing is highly sensitive for organisms such as *S. pneumoniae, N. meningitides*, group B streptococci, *H. influenzae, L. monocytogenes*, and *M. tuberculosis* but does not provide information on antimicrobial susceptibility.[7] Serum procalcitonin, C-reactive protein, and cerebrospinal fluid lactate concentrations have been studied as adjuncts to diagnosis of bacterial meningitis with negative cerebrospinal fluid examinations, but are not a substitute for decision making in the treatment of an individual patient.[19] If suspicion is great despite negative initial cerebrospinal fluid results, admit for empiric antibiotic treatment and consider repeat LP.[13]

CT Scan before Lumbar Puncture Perform the LP as soon as possible to secure the diagnosis of meningitis. Concern about the complication of cerebral herniation from LP has led to controversy regarding whether patients require a CT scan of the brain prior to the procedure.[15]

Risk factors for brain herniation are listed in **Table 174-3**. Order a head CT prior to LP in patients exhibiting any of these high-risk criteria. Although a CT scan can help identify contraindications for an LP, a normal CT scan does imply that there is no risk of herniation with LP if a patient exhibits clinical predictors of impending herniation such as deteriorating mental status, posturing, irregular respirations and pupillary changes, or seizures.[20]

TREATMENT

After addressing airway, breathing, and circulation status, immediately initiate empiric antibiotic therapy if bacterial meningitis is clinically suspected. **Never delay administration of empiric antibiotic therapy for neuroimaging or to perform LP, because antibiotic treatment takes precedence over definitive diagnosis.**[6] Obtain blood cultures to assist in identification of the organism and to help guide inpatient therapy if it will not delay time to antibiotics. Base antibiotic selection on the clinical scenario including age, immunization status, living conditions, and past medical history.

Empiric Treatment for Presumptive Bacterial Meningitis The empiric antibiotic regimen for adults between 18 and 49 years of age is a third-generation cephalosporin, such as ceftriaxone, 2 grams IV, plus vancomycin, 15 milligrams/kg IV, to cover the common pathogens *S. pneumoniae* and *N. meningitides*. For adults over the age of 50 years who

TABLE 174-2 Cerebrospinal Fluid (CSF) Diagnostic Evaluation

	Opening Pressure (<170 mm H_2O)*	Color (clear)	Gram Stain (negative)	Cell Count (<5 WBC, 0 PMN)	Glucose (>40 mg/dL)	Protein (<50 mg/dL)	Cytology (negative)
Bacterial	Elevated	Cloudy, turbid	Positive (60%–80% before antibiotic, 7%–41% after antibiotic)	>1000–2000/mm^3 WBC, neutrophilic predominance, >80% PMN	<40 mg/dL, CSF/blood glucose ratio <0.3–0.4	>200 mg/dL	Negative
Viral	Normal	Clear or bloody	Negative	<300/mm^3 WBC, lymphocytic predominance, <20% PMN	Normal	<200 mg/dL	Negative
Fungal	Normal to elevated	Clear or cloudy	Negative	<500/mm^3	Normal to slightly low	>200 mg/dL	Negative
Neoplastic	Normal	Clear or cloudy	Negative	<300/mm^3	Normal to slightly low	>200 mg/dL	Positive

*Normal values and findings are in parentheses.

Abbreviation: PMN, polymorphonuclear lymphocyte.

TABLE 174-3 Criteria for Obtaining Head CT before Lumbar Puncture[6,15,20]

Altered mental status or deteriorating level of consciousness
Focal neurologic deficit
New-onset seizure
Papilledema
Immunocompromised state
Malignancy
History of focal CNS disease (stroke, focal infection, tumor)
Concern for mass CNS lesion
Age >60 y

are immunocompromised, add ampicillin, 2 grams IV, to cover *L. monocytogenes*.[6] If patients have a severe allergy to penicillin, options include replacing ceftriaxone with chloramphenicol and substituting ampicillin with trimethoprim-sulfamethoxazole. Consider adding acyclovir if herpes simplex virus (HSV) encephalitis is suspected.[13] Use a fourth-generation cephalosporin, such as cefepime, plus vancomycin for patients who have recently undergone neurosurgery.[14] Initiate antibiotics as soon as possible in order to increase survival and reduce morbidity.[3,7]

The second priority is administration of steroids to patients with presumptive pneumococcal meningitis. Administration of dexamethasone before or with the first dose of antibiotics has been shown to reduce cerebrospinal fluid inflammation, reduce the risk of morbidity and mortality in adults, and reduce hearing loss and other neurologic sequelae in children, especially with *S. pneumoniae* infection.[8,21] The recommended dosage of dexamethasone is 10 milligrams IV for adults.[21]

Current guidelines provide no recommendation for the most common ED situation, in which the first dose of empiric antibiotics is given before LP is performed or before results of LP are received. Common sense suggests that dexamethasone could be administered just before, or concurrently with, empiric antibiotics to patients with strong suspicion for bacterial meningitis or to patients in whom grossly purulent cerebrospinal fluid is obtained at the time of LP. Infectious Disease Society of America guidelines state that dexamethasone should not be given to adults who have already received antibiotics.

SPECIAL SITUATIONS

Bacterial Meningitis Resulting from Sinusitis or Otitis The prevalent use of antibiotics has decreased the frequency of suppurative intracranial complications from sinusitis and otitis, but bacterial meningitis resulting from these diseases still occurs. The virulence of the affecting organism and host factors, such as immunocompromised state, influence spread to the CNS. In the ear, bacteria can spread through endolymphatic channels, bony erosions, or osteothrombophlebitis of small vessels. Thrombophlebitis of veins is a common mechanism by which bacteria disseminate from the sinuses; this may result in cavernous sinus thrombosis or empyema.[22] CT imaging is very sensitive for sinusitis and permits earlier diagnosis with demonstration of air-fluid levels in the involved sinuses. CT is nonspecific, however, and should be interpreted with the clinical background in mind (**Figure 174-1**). Infections are often polymicrobial. Initiate empiric antibiotic therapy with fluoroquinolones, such as levofloxacin or moxifloxacin, or with a third-generation cephalosporin, such as ceftriaxone, plus metronidazole.[23] Invasive infections and those with intracranial spread require emergency consultation for surgical drainage.

Additional Adjunctive Treatment for Bacterial Meningitis Monitor patients with meningitis closely for complications or signs of clinical deterioration, especially evaluating their respiratory and neurologic status.[8] Treat hyperpyrexia and manage seizures with anticonvulsants. Avoid hypotonic fluids, and monitor serum sodium level serially to detect syndrome of inappropriate antidiuretic hormone or cerebral salt wasting.[7,21] Closely evaluate for signs of increased intracranial pressure and vasculopathy that may lead to brain ischemia. If signs of elevated intracranial pressure are detected, elevate the bed to 30 degrees, use 25% mannitol or hypertonic 3% saline for diuresis, and consider a trial of mild hyperventilation.[7] Measurement of intracranial and systemic arterial pressure may be useful in severe cases to monitor cerebral perfusion pressure. Consider admission to the intensive care unit to ensure proper level of care.[8]

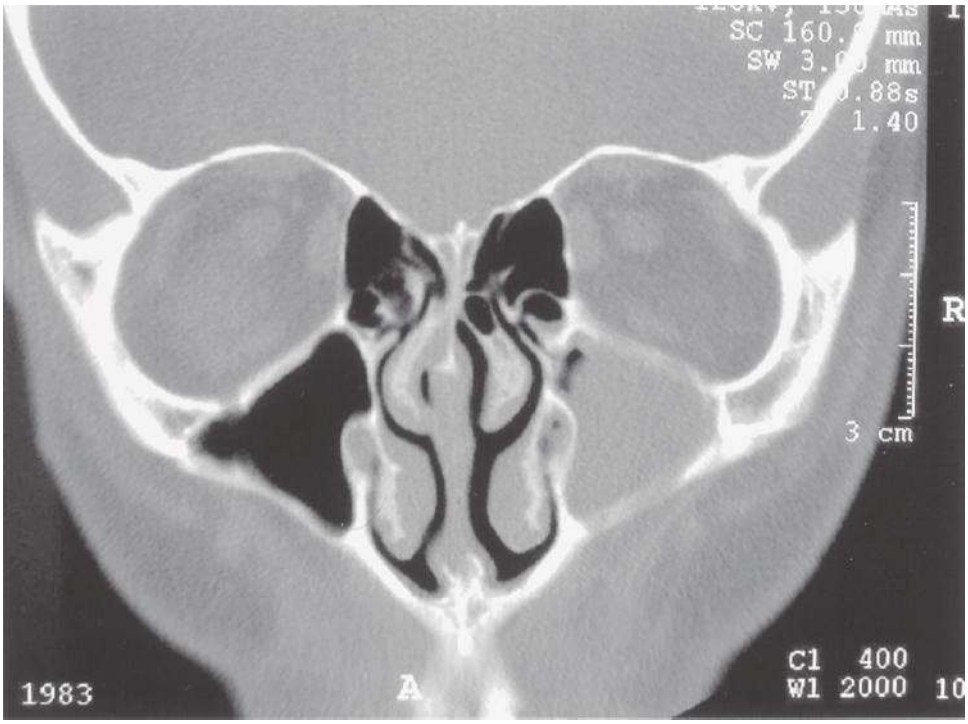

FIGURE 174-1. Acute sinusitis with opacification of the maxillary sinus. [Reproduced with permission from Brunicardi FC, Andersen D, Billiar T, et al: *Schwartz's Principles of Surgery*, 8th ed. New York, McGraw-Hill.]

Chemoprophylaxis for Those Exposed to Bacterial Meningitis

Bacterial meningitis is spread by droplets, and risk for developing bacterial meningitis after exposure is estimated to be 500 to 800 times higher than the general population.[14] Chemoprophylaxis has been shown to decrease transmission of *N. meningitidis* by 89% in close contacts. Chemoprophylaxis is recommended for individuals who have been exposed to patients diagnosed with *N. meningitidis* and *H. influenzae*.[9] It is not recommended for patients diagnosed with pneumococcal meningitis.[14] Close contacts include housemates, individuals exposed to secretions (shared utensils or toothbrushes, kissing, mouth-to-mouth resuscitation), and individuals who intubated the patient without a facemask. To be most effective, initiate chemoprophylaxis within 24 hours of contact. Risk of infection after a period of 2 weeks from exposure is considered rare, and prophylaxis is not recommended after this time period. Treatment options for high-risk contacts include rifampin 10 milligrams/kg to a maximum of 600 milligrams per dose every 12 hours for four doses, ciprofloxacin 500 milligrams orally once, or ceftriaxone 250 milligrams IM once.[9] Instruct all patients who receive chemoprophylaxis to seek medical attention immediately if they develop any symptoms of illness or meningitis.

DISPOSITION AND FOLLOW-UP

Admit all patients diagnosed with bacterial meningitis and those highly suspected of having meningitis to the hospital on droplet isolation.

VIRAL MENINGITIS

INTRODUCTION

Viral meningitis typically presents with subacute headache and fever and findings of meningeal irritation, such as nuchal rigidity. Several viruses can cause viral meningitis, including nonpolio enteroviruses, HSV, varicella-zoster virus, cytomegalovirus, adenovirus, and human immunodeficiency virus. Specific diagnosis depends on isolation of the virus or positive results on immunoassay of the cerebrospinal fluid. Nonpolio enteroviruses (echovirus, coxsackievirus, and enterovirus) typically are seen in summer through fall and account for more than 90% of all cases of viral meningitis.[4]

LABORATORY TESTING

Viral meningitis is associated with normal opening pressures and a negative Gram stain. WBCs are <300/mm^3 with a lymphocytic predominance, and usually less than 20% polymorphonuclear lymphocytes.[20] Protein is often slightly elevated, but not typically above 200 milligrams/dL, and cerebrospinal fluid glucose is normal. The percentage of polymorphonuclear cells may be higher in early viral meningitis, and in some cases, glucose levels may be decreased.[13] Consider partially treated bacterial meningitis if a patient with symptoms consistent with meningitis had previously been treated with antibiotics and the LP suggests aseptic meningitis. Viral culture is insensitive, so if a viral etiology is suspected, send for molecular testing by polymerase chain reaction from the cerebrospinal fluid.[4] Polymerase chain reaction testing is available for HSV, enterovirus, and other viral organisms.

DISPOSITION AND FOLLOW-UP

There can be overlap of cerebrospinal fluid findings with early bacterial meningitis and partially treated bacterial meningitis, making specific diagnosis for some cases of viral meningitis difficult in the ED. Although supportive care is the mainstay of treatment for viral meningitis, it is appropriate to admit the toxic-appearing patient to the hospital for empiric antibiotic therapy until culture results return in situations of diagnostic uncertainty. HSV-2 meningitis can cause necrotizing encephalitis and neurologic deficits.[4] Admit patients with diagnosed or suspected HSV-2 meningitis after beginning treatment with acyclovir 10 milligrams/kg IV every 8 hours.[8]

FUNGAL CNS INFECTIONS

Over the past 30 years, the incidence of fungal CNS infections has been increasing, likely due to acquired immunodeficiency syndrome as well as an increase in patients on immunosuppressants due to stem cell and organ transplants.[24] The most common cause of fungal meningitis is *Cryptococcus neoformans*, followed by *Coccidioides immitis*, which can be seen in immunocompetent hosts as well as the immunocompromised.[4,21] *Aspergillus* and *Candida* are most often discovered in immunocompromised hosts. Mucormycoses can be seen especially in diabetics from direct extension of sinus infection.

LABORATORY TESTING

The cerebrospinal fluid analysis of fungal meningitis shows lymphocytic predominance, an elevated opening pressure, low glucose, and slightly increased protein.[5,25] Significant elevations in opening pressure are often seen in cryptococcal meningitis. Gram stain is negative, and WBC is usually <500/mm^3. Consider fungal testing especially for immunocompromised patients where fungal etiologies are suspected, including India ink staining and serum cryptococcal antigen testing, cytology, and histopathology.[5] Send cerebrospinal fluid for *Borrelia* antibodies in patients with suspected Lyme disease and for acid-fast stain and culture for suspected mycobacteria in tuberculous meningitis.

Patients often have a prolonged symptom course. Use fungal stain and culture for diagnosis if a fungal etiology is suspected, and look for elevated opening pressure during LP. Consider CT or MRI to search for intracranial complications such as granulomas or abscesses.

TREATMENT

Treatment for fungal infections is dependent on diagnosis through LP. Amphotericin is the agent of choice in cryptococcal meningitis. Use fluconazole or itraconazole for *C. immitis*. Treat *Candida* meningitis with amphotericin B and flucytosine.[5]

VIRAL ENCEPHALITIS

Viral CNS infections can also cause viral encephalitis, which is an infection and inflammation of the brain parenchyma.[4] Viral encephalitis is clinically distinguished from viral meningitis with presence of neurologic findings such as altered level of consciousness, focal weakness, or seizures, although the two often coexist.

The causes of viral encephalitis vary year to year and across geographical locations, with an incidence of 3.5 to 7.5 per 100,000 people.[26] Immune status, exposure to insects or animals, and travel history play a key role in determining the etiology. An underlying cause, however, is found in only about a third of cases.[25] HSV accounts for 40% to 50% of cases where a cause is determined. HSV-1 is responsible for most cases of HSV encephalitis; HSV-2 frequently causes aseptic meningitis but is not usually associated with development of encephalitis.[26] Other viral pathologic agents in North America include Epstein-Barr virus, cytomegalovirus, and rabies. Common arboviral encephalitides include La Crosse encephalitis, St. Louis equine encephalitis, Western equine encephalitis, and West Nile virus.

PATHOPHYSIOLOGY

Immunocompromised patients such as those with organ or stem cell transplants are susceptible to new or reactivated infections with HSV and varicella-zoster virus. Impaired immune status also plays a role in cytomegalovirus encephalitis. The arboviruses are transmitted by mosquitoes and ticks. Rabies is transferred by the bite of an infected animal and leads to severe encephalitis and a very high mortality rate.[4] Common to all is preliminary viral invasion of the host at a site where replication takes place that is outside the CNS. Most viruses then reach the nervous system hematogenously during viremia. However, at least three important viruses—rabies, HSV, and herpes zoster virus—reach the spinal cord and

eventually the brain by traveling backward within axons from a distal site, where they gain access to nerve endings. Once in the brain, disruption of neural cell functions by the virus and by the effects of the host's inflammatory responses ensue. Gray matter is predominantly affected, resulting in cognitive and psychiatric signs, lethargy, and seizures.

CLINICAL FEATURES

Consider encephalitis in patients exhibiting behavioral changes, new psychiatric symptoms, cognitive deficits, or seizures.[25] Although the triad of headache, fever, and altered mental status may be seen, it is not invariably present. Assess for signs of clinical syndromes outside the CNS. Rash or skin vesicles suggest herpes zoster, and skin vesicle culture may be useful for diagnosis. Lymphadenopathy or splenomegaly points to Epstein-Barr virus, which can be picked up on serologic testing. New onset of psychiatric symptoms and behavioral changes may be attributable to HSV. MRI, electroencephalogram, and polymerase chain reaction of the CSR could assist in making the diagnosis.

Physical Examination Examine for signs of meningeal irritation and increased intracranial pressure and for neurologic findings that reflect the areas of involvement. Carefully assess mental status and cognition. Encephalitis may show regional tropism. HSV involves limbic structures of the temporal and frontal lobes with prominent psychiatric features, memory disturbance, and aphasia. Some arboviruses predominantly affect the basal ganglia, causing choreoathetosis and parkinsonian movements. Involvement of the brainstem nuclei that control swallowing leads to the hydrophobic choking response characteristic of rabies encephalitis.[27]

DIAGNOSIS

Neuroimaging studies such as MRI or CT, electroencephalography, and LP are important in ruling out mass occupying lesions and making the diagnosis of encephalitis. MRI is more sensitive than CT. Obtain an MRI to help exclude lesions such as brain abscesses, and examine for findings suggestive of HSV encephalitis, such as involvement of the gray matter in the medial temporal and inferior frontal lobes (**Figure 174-2**). Electroencephalogram findings are generally nonspecific but can be useful in cases such as HSV encephalitis where an almost pathognomonic picture of periodic, asymmetric sharp waves is seen in the setting of acute febrile encephalopathy.[25] LP is the most useful diagnostic procedure in the ED once imaging studies exclude the increased intracranial pressure and the risk of uncal herniation.

Consider bacterial meningitis in the differential diagnosis when fever and meningeal symptoms predominate. A late-summer encephalopathy suggests the possibility of arbovirus encephalitis, and an animal bite for which no antirabies treatment was administered has relevance for rabies. Suspect subarachnoid hemorrhage with acute onset of severe headache as the presenting sign. Lyme disease, tuberculosis, and fungal and neoplastic meningitis are in the differential diagnosis in less fulminant cases. If focal neurologic signs are present, consider brain abscess, empyema, or cavernous sinus thrombosis as possible causes.

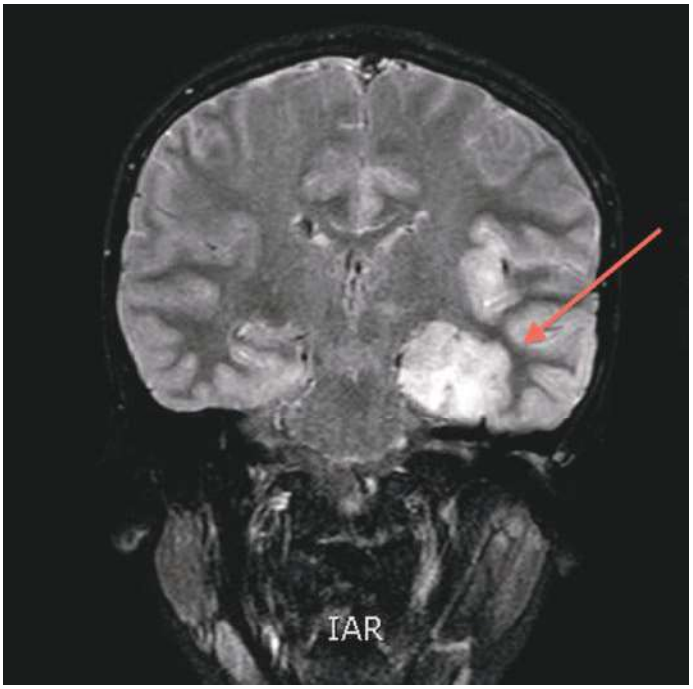

FIGURE 174-2. Fluid-attenuated inversion recovery hyperintensity in the left temporal lobe and left insula (arrow) suggests the diagnosis of herpes encephalitis. [Photo contributed by Elizabeth Yutan, Department of Radiology, Oregon Health & Science University.]

TREATMENT

The antiviral of choice for HSV encephalitis is high-dose acyclovir at 10 milligrams/kg IV.[8,26] Initiate treatment as soon as possible because the prognosis of HSV encephalitis is correlated with neurologic condition at the time antivirals are initiated. Treat varicella-zoster virus with acyclovir, 10 to 15 milligrams/kg IV. Patients with herpes zoster virus encephalitis may also benefit from acyclovir therapy. Treat patients with cytomegalovirus encephalitis with ganciclovir, 5 milligrams/kg IV.[27] There are no known treatments for arbovirus encephalitis; consider initiating treatment with acyclovir empirically until a cerebrospinal fluid diagnosis is made.[8] Rabies encephalitis is rare but neurologically devastating, and once symptomatic, it is usually fatal.

DISPOSITION AND FOLLOW-UP

Prognosis of viral encephalitides depends on the causative virus and host factors. Older adults and those who are immunocompromised are more likely to have an adverse outcome. Admit patients with encephalitis to the hospital. Patients may require intensive care unit care if they have signs of altered mental status or coma.

BRAIN ABSCESS

INTRODUCTION

A brain abscess begins as a focal area of cerebritis, which develops into a central pus-filled cavity ringed by a layer of granulation tissue and an outer fibrous capsule in a period of about 14 days.[28] It is surrounded by edematous brain tissue infiltrated with inflammatory cells. A brain abscess is a pathologic response typical of a relatively competent immune system against a bacterial invader. Focal brain infections from other organisms, such as granulomas due to tuberculosis, necrotic lesions of toxoplasmosis in immunocompromised patients, or cystic lesions of cysticercosis, are not abscesses in the pathologic sense.

PATHOPHYSIOLOGY

Organisms reach the brain hematogenously, from direct contiguous infection, or by direct seeding by neurosurgery or penetrating trauma. Hematogenous spread accounts for 15% to 30% of cases, direct spread from infection accounts for 25% to 50%, and trauma or surgery for 8% to 20%. The route is unknown in 15% to 20% of cases.[28,29] Direct spread usually results in an isolated brain abscess, whereas hematogenous seeding results in multiple abscesses.

Investigate for the source of the brain abscess in order to determine the likely bacterial etiology and to treat the source itself. Otogenic brain abscesses are often caused by gram-negative rods and are located adjacent to the temporal lobe or cerebellum. Sinogenic or odontogenic abscesses are often caused by anaerobic and microaerophilic streptococci and are commonly located in the frontal lobes. Abscesses formed from hematogenous spread are usually polymicrobial, with anaerobic and microaerophilic streptococci commonly represented. Direct implantation or traumatic injuries yield staphylococci, with Gram-negative rods also seen in cases related to neurologic surgery.[25]

CLINICAL FEATURES

History Presenting features of brain abscess are nonspecific, and patients are generally appear nontoxic. Headache is the most common feature, with fever as a close second. Although most patients present with one or more findings of headache, fever, altered mental status, focal neurologic symptoms, seizures, or balance changes, the classic triad of headache, fever, and focal neurologic deficit is present in <25% of all patients.[28,29] The nonspecific presentation contributes to both severity and outcome of brain abscesses because diagnosis and treatment are often delayed.[30] Symptoms reflect the infectious and neurologic (focal and mass-effect producing) aspects of the disease and are often present for 1 to 8 weeks.[28] The presentation may be dominated by the origin of the infection (e.g., ear or sinus pain). Seizure occurs in 25% to 34% of patients.[31]

Physical Examination Examine for focal neurologic signs that demonstrate the site of the lesion; for example, a frontal lobe lesion presenting with hemiparesis, a temporal lobe lesion presenting with homonymous superior quadrant visual field deficits or aphasia, or a cerebellar lesion presenting with limb incoordination or nystagmus. Focal signs are present in approximately 60% of patients. Assess for potential sites of origin, which may raise suspicion of brain abscess when the presentation is otherwise nonspecific (e.g., otitis media, sinus tenderness, evidence of pulmonary suppuration, or right-to-left shunting) in a patient with subacute headache and lethargy.

DIAGNOSIS

Neuroimaging is essential to the diagnosis of brain abscess and is one instance where a contrast-enhanced head CT scan is preferred over a noncontrast study in the ED. A noncontrast CT scan may only show a hypodense low-attenuation abnormality with mass effect, but later in the course, CT may show a peripheral ring.[28] A head CT with IV contrast shows one or several thin, smooth rings of enhancement surrounding a low-density central area and surrounded by edema (**Figure 174-3**). MRI usually demonstrates a ring whether or not gadolinium enhancement is used. Both CT and MRI are highly sensitive; CT is often more readily available in the ED. Avoid LP if clinical suspicion is high or focal neurologic deficits are present to prevent potential herniation in the case of increased intracranial pressure. If possible, obtain cultures of blood and other sites of infection to guide future management.

The differential diagnosis is broad because of the nonspecific symptoms of brain abscess. A sudden onset with focal features may suggest cerebrovascular disease. Prominent fever, stiff neck, and altered mental status may suggest meningitis or encephalitis. A protracted course with features of increased intracranial pressure may suggest neoplasm. Brain neoplasm, subacute brain hemorrhage, and other focal brain infections, such as toxoplasmosis, may mimic the imaging findings of brain abscess.

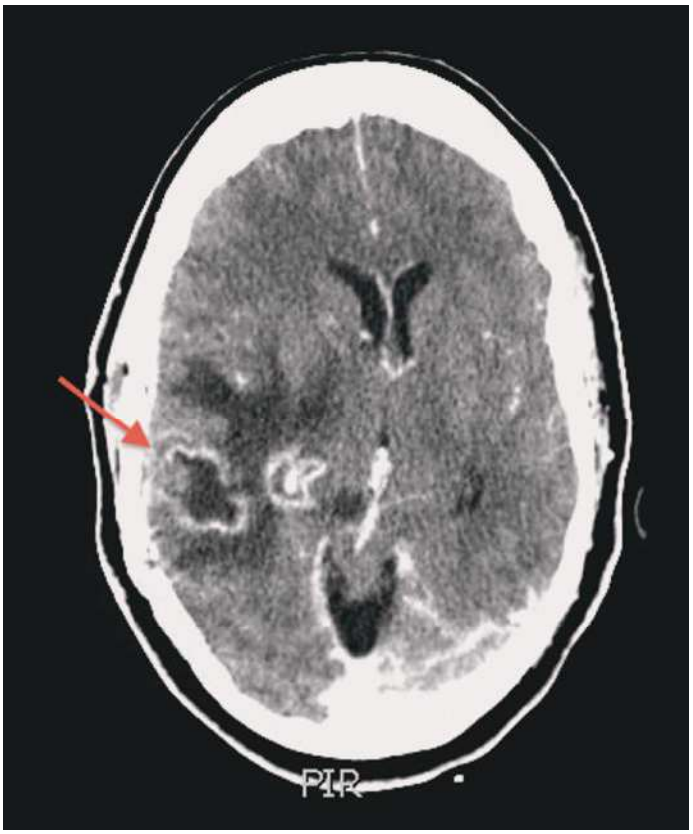

FIGURE 174-3. Ring-enhancing brain abscess with surrounding edema (arrow). [Photo contributed by David Peterson, Department of Radiology, Oregon Health & Science University.]

TREATMENT

Early combination empiric antibiotic therapy is important (**Table 174-4**). A multidisciplinary approach with neurosurgery and infectious disease consultations will help guide treatment selection. Aminoglycosides, macrolides, and first-generation cephalosporins are not effective treatment for brain abscess. Treatment with steroids is controversial.

DISPOSITION AND FOLLOW-UP

Neurosurgery involvement is paramount in the treatment and management decisions. Patients with small abscesses <2.5 cm, with good clinical condition with a Glasgow coma score >12, and who have an etiology that is known may be treated with IV antibiotics alone.[32] Aspiration may be done by the neurosurgical team to elucidate the causative organism. Total excision is less necessary with improved imaging, although it is preformed in the setting of increased intracranial pressure or after failed medical management or aspiration.[5]

EPIDURAL ABSCESS

INTRODUCTION AND EPIDEMIOLOGY

Spinal epidural abscess is a collection of pyogenic material that accumulates in the epidural space between the dura and vertebral periosteum and often leads to devastating neurologic outcomes.[33,34] Spinal epidural abscess is a rare diagnosis and accounts for 0.2 to 1.2 cases per 10,000 hospital admissions. The incidence has doubled in the past two decades, largely attributed to factors such as an increasing proportion of immunocompromised patients, more prevalent IV drug use, a larger number of spinal procedures being preformed, and improved imaging modalities for detection.[35,36] Despite improvement in diagnosis and treatment, mortality remains high at 2% to 20%.[33] *S. aureus* is the most commonly involved bacteria and is responsible for 70% of cases with a higher proportion of methicillin-resistant *S. aureus* seen in patients with implantable devices.[33,36] Other pathogens include *Staphylococcus epidermidis*, streptococcal species, and gram-negative bacilli, which is especially prevalent in IV drug users. Mycobacteria and fungi causing spinal epidural abscess are rare.

PATHOPHYSIOLOGY

Spinal epidural abscess arises from hematogenous spread through blood circulation 25% to 50% of the time, with soft tissue, urine, and respiratory infections contributing in the majority of cases. In general, hematogenously spread epidural abscesses are more likely to be found in the posterior epidural space. Ten to 30% of spinal epidural abscesses are caused by direct extension from infected adjacent tissue, such as psoas abscess, vertebral diskitis, or vertebral osteomyelitis. Direct extension often infects the anterior portion of the spinal column.[33,37] Fifteen to 22% of spinal epidural abscesses are caused iatrogenically from neurosurgical procedures, including percutaneous diagnostic and therapeutic techniques. Trauma contributes to a small proportion of spinal epidural abscesses, with the remainder of cases without an identifiable source.[35,36]

Most spinal epidural abscesses affect the thoracic and lumbar spine, where the epidural space is wider with a larger venous plexus.

TABLE 174-4 Guidelines for Empiric Treatment of Brain Abscess Based on Presumed Source

Presumed Source	Primary Empiric Therapy	Alternative Therapy
Otogenic	Cefotaxime 2 grams IV every 4–6 h or ceftriaxone 2 grams IV every 12 h PLUS metronidazole 500 milligrams IV every 8 h	Piperacillin/tazobactam 4.5 grams IV every 6 h
Odontogenic	Penicillin G 4 million units IV every 4 h	Ceftriaxone 2 grams IV every 12 h PLUS metronidazole 500 milligrams IV every 6 h
Sinogenic	Cefotaxime 2 grams IV every 6 h or ceftriaxone 2 grams IV every 12 h PLUS metronidazole 500 milligrams IV every 8 h	No recommendation
Penetrating trauma	Cefotaxime 2 grams IV every 6 h or ceftriaxone 2 grams IV every 12 h PLUS metronidazole 500 milligrams IV every 8 h ± rifampin 10 milligrams/kg every 24 h	No recommendation
After neurosurgical procedure	Vancomycin loading dose 25–30 milligrams/kg IV loading dose or linezolid 600 milligrams IV every 12 h PLUS ceftazidime 2 grams IV every 8 h ± rifampin 10 milligrams/kg every 24 h	Can substitute linezolid 600 milligrams IV every 12 h instead of vancomycin. Can substitute meropenem 2 grams IV every 8 h OR piperacillin/tazobactam 4.5 grams IV every 6 h OR cefepime 2 grams IV every 8 h for ceftazidime.
Unknown source	Cefotaxime 2 grams IV every 6 h PLUS metronidazole 500 milligrams IV every 6 h	No recommendation

Note: See also http://www.hopkins-abxguide.org; accessed June 18, 2014.

The cervical spine is affected only 5% to 20% of the time, although morbidity and neurologic devastation are much greater in these cases.[38]

Mechanisms for spinal cord neurologic sequelae are uncertain and are thought to be from a combination of direct compression from the abscess itself, ischemia due to compression of spinal veins and arteries, and septic thrombophlebitis.[33]

CLINICAL FEATURES

Back pain is the most common presenting complaint and is seen in 70% to 90% of cases. Fever is another common symptom, followed by the presence of a neurologic deficit. However, the classic triad of back pain, fever, and neurologic symptoms is seen in a minority of patients (8% to 37%) on initial presentation.[33,36] Typically, patients with spinal epidural abscess progress through four stages in a period ranging from hours to days. Stage 1 consists of back pain, fever, and localized spinal tenderness. Stage 2 is composed of spinal irritation, including radicular pain, hyperreflexia, and nuchal rigidity. Stage 3 involves the bowel and bladder, with symptoms of fecal or urinary incontinence, as well as focal neurologic deficits such as motor weakness. Finally, in stage 4, paralysis ensues.[33,36]

HISTORY

Screen any patient presenting with back pain, fever, or neurologic complaint for spinal epidural abscess. Patients may have a history of chronic back pain or may offer a mechanism of mild trauma as an explanation for their symptoms, which can distract from a diagnosis of spinal epidural abscess. Similarly, neck pain or stiffness is often thought to be meningitis or encephalitis, causing cervical spinal epidural abscess to be overlooked.

Carefully search for back pain red flags in the patient's history, including immunocompromised states, such as human immunodeficiency virus or diabetes, and immunosuppressant medications, such as steroids or chemotherapy. Elicit a history of recent systemic illness or infection. Inquire about any current or former IV drug use, which can make patients higher risk for spinal epidural abscess development from *Pseudomonas* species. Solicit information about prior spinal surgeries or procedures, including LPs, epidurals, spinal injections, or anesthesia. Ask about any changes in bowel or bladder habits, specifically episodes of bladder fullness or urinary or fecal incontinence.[36,39]

PHYSICAL EXAMINATION

Perform a thorough physical examination starting with a general assessment of sources of infection, including observation of the skin and palpation of soft tissues for signs of infection. Palpate the spine searching for tenderness to palpation, especially in the midline, which may suggest spinal epidural abscess. Complete a full neurologic examination, including sensory dermatome testing and motor evaluation including ambulation. Check reflexes for hyper- or areflexia. Evaluate for symptoms of cauda equine syndrome. Perform a rectal examination looking for decreased rectal tone, which has a sensitivity of 60% to 80%, and an evaluation of perianal sensation for saddle anesthesia, which has a sensitivity of 75%.[40]

DIAGNOSIS

Diagnosis is delayed in many patients with spinal epidural abscess due to nonspecific presenting symptoms and the rarity of diagnosis. Send blood for laboratory studies including blood culture, CBC, erythrocyte sedimentation rate, and C-reactive protein. Leukocytosis is seen in only 60% to 75% of patients and is not sensitive or specific enough for a diagnosis of spinal epidural abscess. Erythrocyte sedimentation rate is much more sensitive and, in one study, was elevated in 110 of 117 patients diagnosed with spinal epidural abscess.[41] C-reactive protein has the advantage of rising faster than erythrocyte sedimentation rate and returns to normal sooner as well, but some labs have a delay in resulting C-reactive protein. Do not withhold further diagnostics and treatment pending C-reactive protein.[36] Blood cultures are positive in 40% of cases and may be helpful for inpatient teams. Do not perform LP if there is suspicion for spinal abscess. Cerebrospinal fluid culture is positive less than a quarter of the time, and LP poses the risk of traversing an abscess and causing meningitis or a subdural infection.[36]

MRI with gadolinium is the gold standard imaging study for the diagnosis of spinal epidural abscess and has a sensitivity and specificity greater than 90%.[37] If MRI is not available, consider emergent transfer to an appropriate referral center. In patients with contraindications to MRI, CT with myelography can be useful to localize epidural compression but is limited in its ability to distinguish abscess from other compressive lesions.[36] Plain radiographs are not sensitive or specific for diagnosis of spinal epidural abscess.[37]

TREATMENT

Once diagnosis has been established, prompt treatment is essential to reduce morbidity and enhance survival. Immediate consultation and evaluation with a spine surgeon are paramount, and if a spine surgeon is not available, emergent transfer to a referral center is appropriate.[36] Neurologic outcome is correlated with degree of neurologic deficit prior to treatment, so time is of the essence.

There are no conclusive data regarding surgery versus conservative antibiotic therapy, and practices vary considerably from immediate operative therapy to conservative IV antibiotic therapy.[37] Patients with