Intensive Care Unit Management of Meningitis and Encephalitis

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KEYWORDS

• Meningitis • Encephalitis • Intracranial pressure management • Hydrocephalus
• Cryptococcus • Rhombencephalitis

KEY POINTS

- Meningitis and encephalitis are uncommonly encountered infections that are associated with significant morbidity and mortality.
- Though the classic triad of fever, meningismus, and headache may be present, clinical features may vary by pathogen and may be associated with unique risk factors that could facilitate empirical antimicrobial administration.
- In addition to antibiotics, steroids, and anti-seizure medications, management of elevated intracranial pressure (ICP) and hydrocephalus may necessitate a stepwise approach that could culminate in the need for decompressive surgical craniotomy.
- In patients with elevated ICP, cerebrospinal fluid diversion via intracranial devices, lumbar drains, or serial lumbar punctures has demonstrated improved clinical outcomes and decreased morbidity.

INTRODUCTION

Meningitis and encephalitis are uncommon causes of infections that can lead to critical illness and represent 2.9% of all cases in the ICU.[1] Meningitis is an inflammation of the membranes that surround the brain and spinal cord, called the meninges, while encephalitis is an inflammation of the brain itself. Despite the low prevalence, CNS infections cause high rates of long-term neurological sequelae and, mortality. Mortality rates for bacterial meningitis vary from 10% in high-income countries to 58% in low-income countries with up to 25% with residual focal neurologic deficits.[2]

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Abbreviations	
ABC	airway, breathing, and circulatory support
ASM	anti-seizure medication
CMV	cytomegalovirus
CSF	cerebrospinal fluid
CT	computed tomography
EEG	electroencephalography
FLAIR	fluid-attenuated inversion recovery
GCS	Glasgow Coma Scale
HIV	Human Immunodeficiency Virus
HOB	head of bed
HSV	Herpes Simplex virus
ID	Infectious Diseases
IDSA	Infectious Diseases Society of America
LD	lumbar drains
LP	lumbar puncture
MRI	magnetic resonance imaging
NCS	Neurocritical Care Society
TB	tuberculosis
TBM	tuberculous meningitis
VZV	Varicella Zoster virus

Encephalitis mortality rates are similarly elevated at 5.6% to 39.3% with survivors suffering profound neurologic deficits like memory, attention, and vision impairments.[3] When treating meningitis and encephalitis, prompt recognition, identification of the pathogen and management are crucial in decreasing the risk of neurologic injury and death. In this article, we will review clinical presentations and evidence-based management strategies for meningitis and encephalitis.

CLINICAL PRESENTATIONS AND RISK FACTORS

The hallmark features of meningitis and encephalitis include altered mental status, fever, headache, and meningismus. In bacterial meningitis, these symptoms may present in isolation or in combination with one another. Several studies have reported at least two of these symptoms being present in at least 72% to 95% of patients, with only 44% having the classic triad of fever, headache, and meningismus.[4,5] Seizures as a presenting symptom is more common in encephalitis.[5,6] Other non-specific symptoms may be lethargy, photophobia, nausea, vomiting, and rash. In some cases, unique clinical features alongside close identification of risk factors may aid in diagnosis and management. **Table 1** highlights pathogen-specific risk factors and unique clinical features.

The most common causes of bacterial meningitis include *Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenza* type b, Group B Streptococcus (GBS), *Escherichia coli*, *Salmonella sp., Klebsiella, sp. Staphylococcus aureus, Listeria monocytogenes*, and *Mycobacterium tuberculosis.*[7] On the other hand, viruses—including Herpes Simplex virus (HSV), Varicella Zoster virus (VZV), enteroviruses, and arboviruses—are the most common cause of infectious encephalitis, ranging from 1.4 to 13.8 cases per 100,000 persons per year worldwide.[8,9] Risk factors for viral encephalitides are poorly understood but extremes of age and an immunocompromised state have been frequently reported. HSV encephalitis may present with temporal lobe hemorrhages, focal changes on electroencephalography (EEG), and hyponatremia.[9,10]

Severe manifestations of fungal infections include meningitis and one of the most common fungal etiologies being *Cryptococcus neoformans.*[11] Of one million cases

Table 1
Summary of risk factors and unique clinical features of common pathogens

Pathogen	Risk Factors	Clinical Features
Neisseria meningitidis	Complement pathway deficiencies, asplenia, chronic disease, large group gatherings, Human Immunodeficiency Virus infection, exposure to the African meningitis belt, and active or passive smoking[21]	Petechial rash → larger purpuric rash (42%–70%) → necrosis/ purpura fulminans (25%)[22] DIC, coma, adrenal hemorrhage, death[23,24]
Streptococcus pneumoniae	Immunocompromised states, HIV, splenectomy, DM, alcoholism[25]	Cerebrovascular complications—arterial stroke (30%), venous sinus thrombosis (9%), intracranial hemorrhage (9%) High risk of long-term neurological sequela, such as hearing loss (up to 50% of cases)[26] Death even with appropriate clinical management (20%)[27]
Listeria Monocytogenes	Consumption of contaminated soft cheeses, processed meats, livestock, raw produce, foods with a long shelf-half life[28] Chronic kidney or liver disease, pregnancy, age over 50[29]	Rhombencephalitis Asymmetric cranial nerve palsies, cerebellar signs, hemiparesis, hemisensory loss[30]
Mycobacterium Tuberculosis	Young age (especially < 5), HIV, immunosuppression[15–17] Farmers, miliary TB, malnutrition[18]	Three phases[19]: • Prodromal • Meningitic • Paralytic
Herpes simplex virus	Extremes of age, immunocompromise, HIV[9]	Temporal lobe hemorrhages, hyponatremia, focal EEG changes[9]
Varicella zoster virus	Older age, HIV, hematologic malignancies, glucocorticoids, chronic obstructive pulmonary disorder, DM, solid cancer, stroke, congestive heart failure[31]	Confusion, nausea, headache, gait disturbance, personality changes[32]
Cryptococcus neoformans	Immunocompromised state, HIV, chronic steroid use, chronic kidney, liver, lung disease, malignancy, transplants, iatrogenic[11,33]	Subacute to chronic onset Headache, intracranial hypertension, altered mental status, photophobia, seizures[3,12]
Coccidioides spp.	Filipino and African American descent, DM, and third trimester pregnancies, less commonly immunocompromise[33]	Intracranial hypertension, altered sensorium, neuropsychiatric symptoms[34]

(*continued on next page*)

Table 1
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Pathogen	Risk Factors	Clinical Features
Candida spp.	Infants Neurosurgical procedures, most commonly ventriculoperitoneal shunts, lumbar cistern peritoneal shunts, external ventricular drains, and ventriculostomies[35,36]	Neonates: systemic symptoms Post-surgical: meningeal signs and altered mental status[37]
Histoplasma spp.	Immunocompromise[38]	Subacute to chronic onset of meningeal symptoms
Naeglaria fowleri	Exposure to warm freshwater, nasal irrigation with contaminated water[39]	Rapidly progressive meningitis, high mortality
Balamuthia spp. *Acanthamoeba* spp.	Immunocompromise, diabetes, pregnancy, and liver disease[40]	Subacute onset of meningeal symptoms[40]
Toxoplasma gondii	Malignancy, HIV, immunosuppressive agents, pregnancy, primary ingestion of undercooked meat[41,42]	Subacute onset of focal neurologic deficits, seizures, and altered mental status Signs and symptoms of elevated intracranial pressure[43]

Data from refs.[3,9,11,12,15–19,21–30]

of cryptococcus globally, the incidence of cryptococcus meningitis has been reported at 223,000.[12] Other less common causes of fungal meningitis include *Coccidioides sp*., *Candida sp*., and *Histoplasma capsulatum*.

Finally, extremely rare causes of meningitis and encephalitis include protozoan parasites and typically follow a subacute onset of meningeal symptoms. These organisms include *Naeglaeria fowleri, Acanthamoeba sp.*, *Balamuthia sp.,* and *Toxoplasma gondii* and are also included in **Table 1**.

Tuberculosis (TB) is one of the most prevalent diseases in the world, affecting 10 million people a year.[13,14] Of these, 2% to 5% may develop tuberculous meningitis (TBM).[15] Risk factors include young age, Human Immunodeficiency Virus (HIV) infection, a previous history of miliary TB, malnutrition, and other causes of immunosuppression.[15–18] Though symptoms of TBM may be variable and non-specific, three phases have been described. The prodromal phase begins with the subacute onset of cough, fever, malaise, weight loss, and the gradual onset of headache. Within a few weeks, the meningitic phase emerges, with symptoms characterized by meningismus, headache, cranial nerve palsies, and confusion.[19] Unfortunately, by this stage, a rapid deterioration into the third paralytic phase of TBM occurs, which is defined by coma, seizure, hemiplegia, and death.[16,19] Atypical presentations may include progressive dementia and personality changes.[16,20]

DIAGNOSTIC WORKUP

Diagnosing meningitis and encephalitis promptly is imperative for instituting targeted treatments. The first step is obtaining a detailed history for symptoms and identification of pathogen-specific risk factors. Additionally, key physical examination findings

include meningismus, focal neurologic deficits, papilledema, rashes, and altered sensorium. In cases with high clinical suspicion, empiric treatment for meningitis/encephalitis must be instututed with broad spectrum antimicrobials with or without steroids depending upon the clinical suspicion for bacterial, viral versus fungal or tuberculous meningits.

Laboratory Workup

Serum and cerebrospinal fluid (CSF) testing, highlighted in **Table 2**, should be sent promptly as part of the workup but should not delay initiation of empirical antibiotics. A lumbar puncture (LP), which is the gold standard for diagnosis, should also be pursued as soon as possible.[44] **Table 3** summarizes normal and abnormal CSF profiles by pathogen.[45–53] These values are not absolute and may vary among patients, especially in partially treated infections. Of note, if done in the early acute phase of meningitis or encephalitis, an LP may yield negative results. If the suspicion remains high, it is important to repeat the LP. For HSV encephalitis, false negatives are not uncommon when an LP is performed within 72 hours of illness. In a retrospective multicenter center study of critically ill patients admitted for possible encephalitis, 4% of patients tested negative within 4 days of symptom onset, leading to delayed treatment.[54] The Infectious Diseases Society of America (IDSA) therefore recommends re-testing CSF within 3 to 7 days and continuation of antibiotics during this time.[55] Additionally, broadening the workup is sometimes required to identify the causative agent. Of note, limitations do exist with multiplex PCR panels. Firstly, they include the most common pathogens for meningitis and encephalitis; and, individualized evaluation of a patient's risk factors should warrant a more expanded workup for pathogens not included in the multiplex panel. Secondly, in a meta-analysis, multiplex panels were found to have moderate sensitivities but excellent specificities for both bacteria and viruses.[56] As such, these panels are excellent for ruling in pathogens but are not as effective for ruling out pathogens. More specifically, for bacteria, the sensitivity and specificity were 89.5% and 97.4%, respectively. For viruses, the sensitivity and specificity were at least 75.5% and 99%, respectively.[2,56] Moreover, for specific pathogens, such as *Listeria monocytogenes, Hemophilus influenzae,* and *Escherichia coli,* the validity of the multiplex PCR panel was suboptimal.[56] Additionally, in another meta-analysis of 113 studies by Tansarli and colleagues, HSV-1 and 2, enterovirus,

Table 2
Laboratory diagnosis of meningitis and encephalitis

Basic Serum Studies	Basic CSF Studies:
• Complete blood count with differential	• Cell count and differential
• Basic metabolic panel	• Protein
• Blood cultures	• Glucose
• Erythrocyte sedimentation rate	• Culture and gram stain
• C-reactive protein	• Meningitis/Encephalitis panel
• HIV	Expanded
Expanded:	• 1,3-Beta-D-glucan
• 1,3-Beta-D-glucan	• Aspergillus Galactomannan antigen
• Aspergillus Galactomannan antigen	• Cryptococcus antigen and fungal culture
• Venereal Disease Research Laboratory	• HSV, VZV, Cytomegalovirus PCR
	• West Nile Virus IgM and IgG antibody
	• Toxoplasma CSF PCR, IgM, and IgG

Data from Ref.[3]

Table 3
Cerebrospinal fluid profiles in meningitis and encephalitis

	Normal	Bacterial	Viral	Fungal	TB	Parasitic[a]
Color	Clear	Cloudy, purulent	Clear	Clear	Clear	Clear
Opening Pressure (cm H2O)	6–25	Elevated	Normal	Variable	Variable	Variable
WBC Count (cells/μL) and Differential	0–5 Rare PMNs	Elevated (typically > 1000) PMN predominance	Normal to mildly elevated (typically < 150) Lymphocytic predominance	Elevated (typically 100–500) Lymphocytic predominance	Elevated (typically 100–500) Lymphocytic predominance	Elevated May have eosinophilia
Protein (mg/dL)	15–45	Elevated	Normal to mildly elevated	Elevated	Elevated	Elevated
Glucose (mg/dL)	45–80 60%–80% of serum glucose	Reduced	Normal	Significantly reduced	Significantly reduced	Low normal-normal

[a] Of note, some parasitic infections, such as primary amebic meningoencephalitis, cannot be distinguished from acute bacterial meningoencephalitis by CSF profile alone and will require a history of freshwater exposure to further delineate.

Data from refs.[45-53]

and *Cryptococcus* spp. had the highest proportions of false negatives when sending multiplex PCR panels.[57] In clinical practice, if multiplex panels return negative but the suspicion for certain bacterial, viral, and fungal meningitides and encephalitides persist, de-escalation of antimicrobials should occur only after dedicated PCR testing of the specific pathogen.

Head Imaging

Prior to an LP, head imaging should be pursued to rule out mass lesions or other causes of elevated ICP that could place a patient at risk for herniation. A computed tomographic (CT) scan is generally adequate for this screening.

The IDSA recommends pursuing head imaging if a patient meets any of the following:

- Immunocompromised state
- History of CNS disease
- New-onset seizure
- Papilledema
- Altered mental status
- New focal neurologic deficit.

Despite these guidelines, one observational study demonstrated over-utilization of head imaging, citing the use in 65% of patients who did not meet criteria.[2]

MRI may also be a helpful diagnostic tool. In patients with meningoencephalitis, almost 50% of patients will have MRI findings of abnormal meningeal enhancement on post-contrast T1 sequences and hyperintensity on fluid-attenuated inversion recovery (FLAIR) sequences.[58,59] A common misconception is delaying an LP to obtain

Table 4
MRI findings in meningitis and encephalitis by pathogen

Mycobacterium tuberculosis	Leptomeningeal Enhancement, Hydrocephalus, Vasculitis, Tuberculomas
Cryptococcus neoformans	Leptomeningeal enhancement, Pseudocysts, Cryptococcomas
Candida albicans *A. fumigatus*	Abscesses, Vascular lesions
HSV-1	T2 and FLAIR hyperintensities in the medial temporal lobes, sometimes associated with hemorrhagic foci
VZV	Leptomeningeal enhancement, Cerebellitis
CMV	Periventricular white matter T2 FLAIR hyperintensities
WNV	T2 and FLAIR hyperintensities in basal ganglia, thalamus, midbrain
Enterovirus	Rhombencephalitis
Listeria monocytogenes	Subcortical abscesses, Cranial nerve enhancement
Borrelia burgdorferi	Single or multiple small non-enhancing subcortical or periventricular white matter hyperintensities, most often supratentorial
Toxoplasma gondii	Multiple concentric and eccentric enhancing lesions, primarily in the basal ganglia, thalami, cortico-medullary junction

Adapted from Perillo T, Capasso R, Pinto A. Neuroimaging of the Most Common Meningitis and Encephalitis of Adults: A Narrative Review. Diagnostics 2024;14(11):1064. https://doi.org/10.3390/diagnostics14111064; with permission.
Data from refs.[41,59,61]

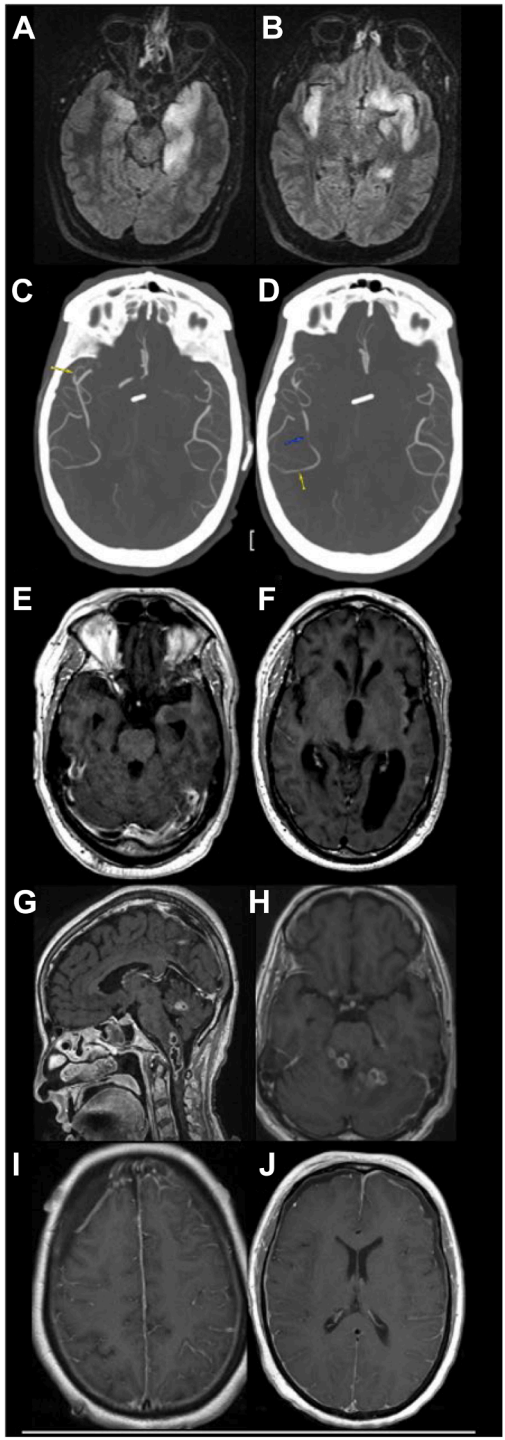

Fig. 1. Neuroradiology findings of meningitis and encephalitis caused by various pathogens. (*A–B*) T2 FLAIR hyperintensities of the L medial temporal lobe and the bilateral insula in HSV

an MRI so as to avoid iatrogenic meningeal enhancement. Studies have shown that *unexplained* meningeal enhancement after LP is very rare and not more common than in cases with no prior LP. If an LP is performed before MRI and meningeal enhancement is found, it should only be attributed to the LP after all other causes have been ruled out.[60] Key MRI findings of common pathogens, summarized by Perillo and colleagues, are highlighted in **Table 4** and **Fig. 1**.[41,59,61]

Seizures are a common complication of encephalitis and, less frequently, meningitis.[62] Clinical and electrographic seizures, the latter may be difficult to detect on bedside assessment, lead to worse outcomes both during hospitalization and long-term for affected patients.[63] In a retrospective cohort study by Carrera and colleagues on patients with CNS infection and persistent altered mental status, 33% of patients with CNS infection had electrographic seizures, most without any clinical correlate. Of note, 86% of these patients had evidence of a clinical seizure prior to EEG monitoring.[62] The utilization of EEG monitoring is thus important for prevention of secondary neurologic injury. EEG monitoring should also be pursued in patients with prior evidence of a clinical seizure or persistently poor mental status.

DIFFERENTIAL DIAGNOSIS

Though meningitis and encephalitis have characteristic clinical features, such as nuchal rigidity, there are a variety of other conditions that can mimic the clinical features of meningitis and encephalitis. These are outlined in **Table 5** along with their associated workup.

DISCUSSION OF MANAGEMENT

The first step in managing CNS infections is ensuring a stable airway, breathing, and circulatory support (ABCs).

Antimicrobials

Once ABCs are addressed, prompt initiation of antimicrobials should ensue. Empirical antimicrobials should be tailored toward patient risk factors (**Table 1**). As previously mentioned, antibiotics should not be delayed for imaging or an LP. With delays, the morbidity and mortality in these patients increases. A retrospective case study of 123 cases of adult bacterial meningitis found an adjusted odds ratio of 8.4 for mortality in patients who received antibiotics over 6 hours after presentation.[64] Empirical antibiotics include vancomycin and ceftriaxone or cefotaxime.[47,53] Ampicillin for *Listeria monocytogenes* coverage is recommended in immunocompromised adults or adults older than 50 years of age.[65] For empirical coverage of HSV encephalitis, acyclovir should be added.[66] **Table 6** lists additional common pathogens and their associated treatments based on IDSA guidelines.[2,25,47,50,66,67]

encephalitis. (*C–D*) Multifocal luminal irregularity and stenosis of the right middle cerebral artery and its branches in a patient with CMV meningoencephalitis. (*E–F*) Left medial temporal lobe and insular enhancement in a patient with *Candida auris* meningitis. (*G–H*) Multifocal ring-enhancing lesions in the cerebellum and brainstem in a patient with *Listeria monocytogenes* meningitis. (*I*) Leptomeningeal enhancement in a patient with *Streptococcus pneumoniae* meningitis. (*J*) Pachymeningeal enhancement in the same patient with *S pneumoniae* meningitis. CMV, cytomegalovirus; HSV, Herpes Simplex virus.

Table 5
Differential Diagnoses and Workup

Chemical and Drug Induced Meningitis	Medication Review for drugs Such as intravenous immunoglobulin, Non-Steroidal Anti-Inflammatory drugs, intrathecal Administration of Chemotherapy or Antibiotics
Autoimmune Meningitis	Subacute onset, associated movement and mood disorders. Serum and CSF autoimmune and paraneoplastic panels MRI brain demonstrating temporal lobe enhancement or T2 hyperintensity
Toxidromes	Medication and history review for alcohol and drug intoxication or withdrawal, serotonergic and anti-cholinergic medications, baclofen withdrawal
Subarachnoid Hemorrhage	Presents similarly with meningismus and headache Stat CT Head and CT Angiography to rule out aneurysmal rupture Lumbar puncture for xanthochromia
Posterior Reversible Encephalopathy Syndrome	MRI Brain demonstrating bilateral T2 Hyperintense lesions EEG to rule out concurrent seizures
Reversible Cerebral Vasoconstriction Syndrome	CT angiography for MR angiography for assessment of vessel abnormalities Digital Subtraction Angiography as the gold standard Medication review of culprit medications
Cerebral Venous Sinus Thrombosis	CT or MR venogram

Corticosteroids

Given the association of bacterial lysis and inflammation in the subarachnoid space with poor outcome, adjuvant treatment with corticosteroids has been added to meningitis regimens to reduce this inflammation and neurological sequelae from meningitis. In a prospective, randomized multicenter trial, dexamethasone 10 mg every 6 hours was compared with placebo in adults with bacterial meningitis. Results demonstrated a significantly lower rate of unfavorable outcomes in the dexamethasone group.[68] IDSA guidelines recommend the use of dexamethasone in adults with suspected or proven pneumococcal meningitis, ideally before or with the first dose of antibiotics.[47]

Elevated Intracranial Pressure and Hydrocephalus

Patients with bacterial, fungal, and rarely, viral meningitis may develop hydrocephalus and elevated intracranial pressure (ICP). This is due to the loss of cerebrovascular autoregulation with increased vasodilation, venous thrombophlebitis producing venous congestion, and the development of hydrocephalus due to impaired CSF flow and reabsorption.[69] Hydrocephalus will be evident on head imaging, while an LP can identify patients with elevated ICP. Elevated ICP in adults is defined as a measurement above 20 mm Hg. Additionally, physical examination findings include a worsening mental status, pupillary changes or papilledema, posturing, or decreased Glascow Coma Scale (GCS) score. If not addressed, these patients will be at risk for increased morbidity and mortality. At present, there is no consensus on whether to monitor ICP or how to manage ICP elevation in these patients.[69] Frequent

Table 6
Antimicrobial treatment of meningitis and encephalitis based on common pathogens

Bacterial	
Streptococcus pneumoniae	Vancomycin and ceftriaxone or cefotaxime
Neisseria meningitidis	Ceftriaxone or cefotaxime
Listeria monocytogenes *Streptococcus agalactiae*	Ampicillin or penicillin G (*may also consider addition of gentamicin)*
Hemophilus influenzae	Ceftriaxone or cefotaxime
Escherichia coli	Ceftriaxone or cefotaxime
Mycoplasma pneumoniae	Azithromycin, doxycycline, or a fluoroquinolone may be considered
Mycobacterium tuberculosis	Isoniazid, rifampin, pyrazinamide, ethambutol x 2 mo Isoniazid and rifampin for additional 10 mo
Borrelia burgdorferi	Ceftriaxone, cefotaxime or penicillin G
Treponema pallidum	Penicillin G
Viral	
HSV-1, 2	Acyclovir
VZV	Acyclovir or ganciclovir
CMV	Ganciclovir and foscarnet
EBV	Supportive, may consider steroids if benefits outweigh risks
Fungal and Protozoa	
Coccidioides spp	Fluconazole Alternatives include itraconazole, voriconazole and amphotericin B
Cryptococcus neoformans	Amphotericin B and flucytosine
Histoplasma capsulatum	Amphotericin B followed by itraconazole
Acanthamoeba	Trimethoprim-sulfamethoxazole plus rifampin plus ketoconazole can be considered
Naegleria fowleri	Amphotericin B and rifampin can be considered
Toxoplasma gondii	Pyrimethamine plus either sulfadiazine or clindamycin is recommended

Data from[2,25,47,50,66,67]

neurologic examinations, a high clinical index of suspicion, and multidisciplinary involvement of Neurocritical Care, Neurosurgery, and Infectious Diseases (ID) teams is crucial.

In any patient with elevated ICP, a stepwise approach for management may be followed. At minimum, this includes elevating the head of bed (HOB) to at least 30° and ensuring adequate sedation, analgesia, fever control, hyperosmolar therapy and discussions regarding surgical CSF diversion or decompression. Higher blood pressures may be observed during this time to maintain cerebral perfusion pressure. If blood pressure medications are required for severe hypertension, intravenous (IV) or short acting medications should be utilized. If a patient is mechanically ventilated, a brief period of hyperventilation for goal (partial pressure of arterial

Table 7
Management of Elevated Intracranial Pressure

Supportive Measures	HOB > 30° Head midline Brief course (<2 h) of hyperventilation for end-tidal CO2 goal 30–35 Sedation and analgesia Fever and pain control Seizure control
Hyperosmolar Therapy	Hypertonic saline (HTS) • 5 cc/kg bolus of 3% over 5–20 min • 3 cc/kg bolus of 5% over 5–20 min • 2 cc/kg bolus of 7.5% over 10–20 min • 30 cc of 23.4% over 5–10 min with close hemodynamic monitoring if acute herniation • Hold for sodium > 160 meq/L • Concentrations higher than 3% should be administered via central line or intraosseous line Mannitol 20% • Dose: 0.5–1 g/kg IV bolus up to 100g over 5–15 min • Place foley, given rapid diuresis, and administer additional isotonic intravenous fluids to prevent intravascular volume depletion • Avoid in end-stage renal disease and anuric patients • Hold for serum osmolality > 320 or osmolar gap > 20 mOsm/kg • Can be repeated every 4–6 h
Additional ICP Measures	CSF diversion Hypothermia or Targeted Temperature Management Pentobarbital Paralysis

Data adapted from Ref.[71]

carbon dioxide) $Paco_2$ 30 to 35 mm Hg is appropriate. If there is a concern for seizures, anti-seizure medications (ASMs) should be administered promptly.

Once all core measures are addressed, hyperosmolar therapy should be administered without delay guided by ICP or worsening physical examination findings, such as obtundation, pupillary changes, or posturing. Of note, Neurocritical Care Society (NCS) guidelines highlight the scarcity of literature addressing the use of hyperosmolar therapy for elevated ICP in the setting of meningitis. However, the panel recognized one study that demonstrated improved mortality with ICP control.[70] **Table 7** summarizes various types of hyperosmolar therapy recommended by NCS in the general management of intracranial hypertension.[71] In cases of acute herniation, 30 cc of 23.4% hypertonic saline should be administered promptly via either a central venous catheter or an intraosseous catheter. Other interventions in the step-wise ICP ladder include hypothermia or targeted temperature management, barbiturate therapy, paralysis, and surgical intervention, such as decompressive craniotomy, which could be utilized in cases of refractory ICP in meningitis.[72]

Presently, there is no algorithmic approach for when to pursue CSF diversion and surgical management. A systematic review of management strategies for raised ICP in meningitis and encephalitis included external ventricular devices, lumbar drains (LD), ventriculoperitoneal shunts, intraparenchymal monitors, and decompressive craniotomy. Despite variable approaches for detecting and managing elevated ICP, this review demonstrated that, in the adult population, CSF drainage, in addition to conventional therapy, reduced both morbidity and mortality.[69] Another study

highlighted similar findings and additionally found that it was rare to require barbiturate coma or decompressive craniotomies once patients were treated with CSF drainage.[73] A study utilizing LD in patients with acute bacterial meningitis found that LD drainage, when set at a maximum drainage of 10 cc/hr and ICP of 10 mm Hg, was associated with 0% mortality compared with 15% in the non-LD group.[74] In resource-limited settings, serial LPs, have been demonstrated to improve survival at least in patients with *Cryptococcus* meningitis, may be the only option for ICP monitoring and CSF drainage.[75]

Seizures

As previously mentioned, EEG monitoring is helpful in identifying electrographic seizures. Empirical initiation of ASMs is usually not necessary. If patients are in status epilepticus, either convulsive or non-convulsive, a stepwise escalation of ASMs based on American Epilepsy Society and NCS guidelines is recommended.

Hyponatremia

Another cause of morbidity and mortality in meningitis and encephalitis is hyponatremia, which may be caused by cerebral salt wasting, diabetes insipidus, and Syndrome of Inappropriate Anti-diuretic Hormone. Prompt recognition and management are crucial as hyponatremia, as well as its correction, may cause cerebral swelling, further adverse outcomes, and increased mortality for patients.[76] If severe, hyponatremia may cause further alterations in mental status, seizures, and—without treatment *or* inappropriately rapid correction—at worst, coma or death. For these patients, a pragmatic approach focusing on the etiology of hyponatremia will help with treatment. Close attention should be paid to the rate of correction to prevent secondary neurologic injury.

Vascular complications

Vascular complications could be seen in bacterial, fungal, tubercular meningitis. This could include septic cerebral sinus venous thrombosis, septic cortical vein thrombosis, vasculitis, cerebral ischemia, subarachnoid hemorrhage, and intracerebral hemorrhage. These complications vary in incidence depending upon the underlying organism and patient specific risk factors. For example, vasculitis maybe seen in up to 30% streptococcal meningitis patients and is associated with a high risk of morbidity and mortality.[77]

From their time of arrival to their discharge, patients with meningitis and encephalitis require multi-disciplinary team involvement, including Internal Medicine, ID, Neurology, Critical Care, Neurocritical Care, and Neurosurgery if there are any concerns for raised ICP. Disposition could be variable and may include a general floor, step-down unit, or an intensive care unit. However, the clinical course remains dynamic and escalation of monitoring can occur at any time.

PROGNOSIS

Prognosis of meningitis and encephalitis varies between the two and among pathogens as well. As previously mentioned, mortality rates in meningitis vary from 10% in high-income countries to 58% in low-income countries; in encephalitis, mortality rates are up to 39.3%, with nearly 50% of survivors suffering profound neurological deficits, including hearing loss, seizure disorders, and cognitive impairments.[2–4] Even with treatment in some cases and with certain pathogens, mortality and morbidity may remain high. For example, the mortality in HSV encephalitis with and without treatment has been documented as 19% and 70%, respectively.[78] Additionally, one case series showed that 30% to 70% of survivors have significant neurologic sequela.[78] Similarly,

in cases of treated tuberculous meningitis, short-term in-hospital mortality rates are up to 50% and increase to 58% for long-term 5 year mortality, with post-treatment disability varying between 29% and 50%.[79–81] The goal in these patients is to treat the primary neurologic disorder while preventing secondary neurologic injury. Post-ICU care of the patient should focus on ongoing monitoring of their neurologic status, gradual weaning of supportive therapies, and initiation of supportive rehabilitation to address any residual cognitive, sensory, coordinative, or motor deficits. These will include physical, occupation, and speech therapy, cognitive rehabilitation, audiology support, continued follow-up with epileptologists, and psychosocial support. Once medically stable for discharge, patients and families should be counseled about medication administration and adherence and symptom monitoring and management. In addition, they should be connected to an outpatient specialist for continued evaluation and care in the outpatient setting.

SUMMARY

Meningitis and encephalitis are conditions frequently associated with significant morbidity and mortality. Caused by a variety of pathogens, recognition and rapid initiation of treatment is crucial in decreasing neurological injury and preventing death. These interventions include antibiotics, steroids, targeted therapies toward reducing ICP, and, in severe cases, neurosurgical intervention. With timely recognition, intervention, multidisciplinary team coordination, and structured follow-up, hospitalized patients with meningitis and encephalitis can achieve meaningful neurologic recovery.

CLINICS CARE POINTS

- CSF studies are crucial to the diagnosis of meningitis. If an LP is done in the early acute phase of meningitis or encephalitis, it may yield negative results. If the suspicion of meningitis or encephalitis remains high, a repeat LP should be performed, and antibiotics should be continued.
- Head imaging prior to an LP is only recommended in certain patient populations. However, from a diagnostic perspective, it may provide additional information about the pathogen.
- Initiation of antibiotics should not be delayed by an LP. In acute bacterial meningitis, IDSA guidelines recommend administration of steroids alongside the first dose of antibiotics.
- In patients with a worsening mental status, pupillary changes or papilledema, posturing, or decreased GCS, empirical treatment of elevated ICP should be initiated promptly. This should be pursued in a stepwise fashion.
- CSF diversion, as well as therapeutic LPs, may reduce mortality in patients with hydrocephalus and elevated ICP.
- Early involvement of Infectious Disease, Critical Care, Neurocritical Care, Neurology, and Neurosurgery teams is important for high-quality multidisciplinary management of critically ill patients with meningitis and encephalitis.

DISCLOSURE

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