Cerebral Infection and Parasitic Infestation

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Abstract: Cerebral infection and infestation are devastating events that can invite many life-threatening complications. The management of such complications may need neurosurgical intervention. Common cerebral infections include acute bacterial meningitis, tubercular and fungal infection. Common complications of acute bacterial meningitis that need neurosurgical intervention are hydrocephalus, brain abscess and subdural empyema. Tubercular and fungal infection usually complicate with granuloma or abscess formation, especially in immunocompromised or diabetic patients; however, hydrocephalus is also frequent in tubercular infection. Neurocysticercosis and hydatidosis are common parasitic infestations of the CNS. In this chapter, acute bacterial meningitis, viral meningitis, brain abscess, subdural empyema, fungal and tubercular infections are discussed, including their neurosurgical management. Parasitic infestations, neurocysticercosis, hydatidosis and cerebral malaria are discussed in brief. Finally, an important neurosurgical infection "shunt infection" is discussed in the last part of the chapter.

Abbreviations

ABM	acute bacterial meningitis	ADA	adenosine deaminase
AFB	acid-fast bacillus	AIDS	acquired immunodeficiency syndrome
ATT	anti-tubercular therapy	BCG	bacillus Calmette–Guerin
CD	Chagas disease	CFP	culture filtrate protein
CT	computed tomography	GIT	gastrointestinal tract
ELISA	enzyme-linked immunosorbant assay	EMB	ethambutol
ESAT6	early secreted antigenic target 6	FLAIR	fluid-attenuated inverse-recovery
HCP	Hydrocephalus	^{1}H-MRS	proton magnetic resonance spectroscopy
HAT	human African trypanosomiasis	HIV	human immunodeficiency virus
HSV	herpes simplex virus	ICSOL	intracranial space occupying lesion
INH	Isoniazid	IT	intrathecal
IVT	Intraventricular	IFN	interferon
ICP	intracranial pressure	IICP	increased intracranial pressure
IGRA	interferon-γ release assays	MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy	MTB	mycobacterium tuberculosis
NAA	n-acetyl acetic acid	NCC	neurocysticercosis
NHL	non-Hodgkin's lymphoma	PCO2	partial pressure of oxygen
PCR	polymerase chain reaction	PPD	purified protein derivative
PZA	Pyrazinamide	RIF	rifampicin
SOL	space-occupying lesion	SDE	subdural empyema
SIADH	syndrome of inappropriate antidiuretic hormone	TOF	Tetrology of Fallot
TB	Tuberculosis	TIWI	T1-weighted image
T2WI	T2-weighted image	TBA	tubercular brain abscess
TBM	tubercular meningitis	WHO	World Health Organization
WNV	West Nile virus	VZV	varicella-zoster virus

1. Introduction

A cerebral infection is a common condition encountered in neurological and neurosurgical practice. Because of the protective barrier of its bony components (skull and spinal column), the meninges, as well as the blood–brain barrier (BBB), the central nervous system (CNS) is particularly resistant to infection by bacteria and other pathogens. The CNS, on the other hand, is more vulnerable to infections than most other tissues once infection has begun. In the CNS, host defensive systems that are ordinarily observed in other parts of the body are insufficient to prevent bacterial reproduction and disease progression (Beatriz and Lopez 2019). The intensity of a bacterial CNS infection is heavily influenced by preexisting and/or predisposing factors. Respiratory and systemic infections, head trauma, past neurosurgical surgeries, cancer, alcoholism and other immunodeficiency conditions are also examples (Beatriz and Lopez 2019).

An intracranial infection affects the brain and meninges, and intraspinal infection affects the spinal cord and its meninges. Infections of the CNS are caused by viral, bacterial, fungal, protozoal and prionic agents.

Bacterial infections can affect diverse parts of the CNS, leading to a variety of clinical and pathologic symptoms. Meningitis, encephalitis and abscess are the three major infectious disorders based on the location and form of the inflammatory reaction. TB meningitis, tubercular abscess and tuberculoma are examples of tuberculous infection lesions.

2. Acute Bacterial Meningitis

Acute bacterial meningitis (ABM) is an emergency condition in neurology that can be fatal. It is characterized by a purulent infection in the subarachnoid spaces, which is frequently accompanied by meningeal inflammation, inflammation of the cerebral tissue and cerebral vasculature (LaPenna and Roos 2019). It affects the brain's leptomeninges. The term "meningitis" points to inflammation of the meninges in general. Meningitis can be due to a wide range of infectious as well as noninfectious diseases (Dorsett and Liang 2016). Acute bacterial meningitis, often known as purulent meningitis, is a serious sickness marked by purulent cerebrospinal fluid (CSF); it progresses quickly and is lethal if left untreated (Beatriz and Lopez 2019). The complication and mortality rates are both extremely high. As a result, early detection of clinical symptoms, early initiation of empiric antibiotic/s, correct diagnostic investigations and awareness of typical consequences are critical in the treatment of bacterial meningitis patients (LaPenna and Roos 2019). ABM occurs when bacteria reach the subarachnoid spaces via bacteremia (typically from an upper respiratory tract source), contiguous extension from dental or paranasal sinus infections, traumatic or congenital external communications or neurosurgical treatment (Dorsett and Liang 2016; Tintinalli and Stapczynski 2011).

2.1. Epidemiology

The most frequent purulent CNS illness is bacterial meningitis. Because of the introduction of conjugate vaccinations in the 1990s, occurrences of community-acquired bacterial meningitis have decreased significantly, although the fatality rates remain high (LaPenna and Roos 2019; Thigpen et al. 2011). Bacterial meningitis is much more common in developing nations, particularly in Sub-Saharan Africa, than it is in developed countries (LaPenna and Roos 2019).

Prior to the introduction of vaccines, the most common causes of ABM were reported to be Hemophilus influenza type b (Hib), Streptococcus pneumoniae and Neisseria meningitides, with their relative contributions differing by location, time and age group in different regions of the Earth (Jayaraman et al. 2018; McIntyre et al. 2012; Ramakrishnan et al. 2009). Since the 1980s, the frequency of community-acquired bacterial meningitis among American children has decreased dramatically because of the introduction of efficient vaccines against Hemophilus influenzae type b and Streptococcus pneumoniae (Honda and Warren 2009; Adams et al. 1993; Centers for Disease Control and Prevention 2005). The incidence rate of community-onset bacterial meningitis (3–6 cases per 100,000 people) among adults, on the other hand, has remained constant over the last decade (Honda and Warren 2009; Choi 2001; Short and Tunkel 2000).

2.2. Etiology and Pathophysiology

Bacteria enter the CNS after direct introduction of the cerebral tissue or from an infective focus external to the CNS. The route of entry of the microorganisms is (1) hematogenous, (2) direct spread from adjacent area infection, (3) direct inoculation by penetrating wound or during operation. The most prevalent route of infection is hematogenous transmission, and the upper respiratory tract is the most common entry point for microorganisms (Beatriz and Lopez 2019).

When the pathogenic bacteria settle and colonize the nasopharyngeal mucosa and enter the bloodstream through epithelial cells, meningitis develops. The bacteria must replicate and survive the host's defenses in the bloodstream in order to get direct entry to the CNS via the choroid plexus or microvasculature; pass the BBB; and survive and grow in the CSF (Beatriz and Lopez 2019; Kim 2003). Most bacteria get entrance to the CSF through mechanisms that are nor totally understood. Because the CSF lacks key host defense mechanisms, including lower concentrations of immunoglobulins and complement, bacterial proliferation is aided once the bacteria are present. The immune condition of the host, as well as the virulence of the bacteria, will undoubtedly play a part in the infection's development (Beatriz and Lopez 2019; Kim 2003). Once bacteria enter the CSF fluid,

their multiplication causes the BBB to become more permeable by releasing proinflammatory and toxic chemicals (Kim 2003).

Meningitis can also be caused by germs being transmitted directly from neighboring tissues to the brain, such as the (a) paranasal air sinuses, (b) middle ear cavity and mastoid sinuses, or (c) via an emissary vein from the scalp and face. Pathogen inoculation can also occur as a result of direct trauma implantation in penetrating traumas and compound skull fractures, as well as subsequent surgical operations and invasive investigation and therapeutic interventions, including due to congenital abnormalities like myelomeningoceles (Beatriz and Lopez 2019).

The three primary agents that cause ABM are N meningitides, S pneumoniae and H influenzae (Thigpen et al. 2011). Most surveillance studies in the USA revealed that S pneumoniae (61%), N meningitides (16%), group B streptococcus (14%), H influenzae (7%), and Listeria monocytogenes were the most common causative pathogens of bacterial meningitis (2%) (Dery and Hasbun 2007). A study conducted in Bangladesh revealed a similar picture (Gurley et al. 2009). Pneumococcal meningitis is caused by immune deficiencies (such as asplenia or agammaglobulinemia). Meningococcal meningitis is more likely in people who have asplenia or terminal complement insufficiency (Honda and Warren 2009; Overturf 2003). Escherichia coli, Streptococcus, Staphylococcus aureus and Moraxella were among the less frequent organisms discovered (Gurley et al. 2009).

Those who have recently undergone neurosurgical surgery, suffered head trauma or had endocarditis should be tested for Staphylococcus aureus species. Gram-negative bacilli can generate meningitis in persons who have had neurosurgery. Streptococci species and Gram-negative anaerobic organisms can cause meningitis in patients with otitis, sinusitis or mastoiditis (Beatriz and Lopez 2019; LaPenna and Roos 2019).

Purulent exudates might be detected in the subarachnoid space during the acute phase of the disease. There may be significant congestion of the leptomeningeal arteries, as well as cerebral edema. The meninges have an abundance of cellular infiltrates made up of neutrophils, as well as fibrin exudate. Bacteria can be found both within and outside the cell. Subacute and chronic stages may begin with a shift in cellular inflammatory infiltrates to mononuclear cells, such as lymphocytes, plasma cells and macrophages, once the infectious sequences have been brought under control by therapy (Beatriz and Lopez 2019). Fibroblast growth can be variable, resulting in leptomeningeal fibrosis. Inflammatory vasculitis with microthrombosis and cortical infarctions can be found in this stage of the disease. Purulent ventriculitis develops when an infection spreads into the ventricles, resulting in purulent collections that obstruct the ventricular system's foramina, preventing CSF passage and causing obstructive hydrocephalus. Communicating hydrocephalus can also be caused by leptomeningeal fibrosis, which causes poor CSF reabsorption (Beatriz and Lopez 2019). The infected process can spread to the cranial nerves, particularly the cochlear nerves, resulting in hearing impairment, which is one of the most common meningitis complications in children (Beatriz and Lopez 2019; Edwards and Baker 1981). Other cranial nerve palsies can result from basal meningitis.

2.3. Clinical Features

The classical triad of ABM is fever, headache and a stiff neck (LaPenna and Roos 2019). Some authors have included an altered state of consciousness instead of a headache in the classic triad. Although each of these signs/symptoms is common, the trio may not be present. Vomiting, a lowered degree of consciousness and photophobia are some of the other indications and symptoms. Temperatures greater than or equal to 37.7 °C/100 °F are the most sensitive of these symptoms, appearing in 95% of individuals at presentation and 99% within 24 h (LaPenna and Roos 2019; Durand et al. 1933). Headache, fever, altered sensorium and neck stiffness are symptoms that nearly all individuals with ABM will have (LaPenna and Roos 2019; van de Beek et al. 2004). Seizures were identified in 15% of adult cases (Weisfelt et al. 2006). In extreme cases, ABM can cause coma, seizures and focal neurologic impairments, all of which are linked to a poor prognosis (Honda and Warren 2009; Aronin et al. 1998; Flores-Cordero et al. 2003). Age, anatomic anomalies, concurrent illness, immunological function and the causative agent can all influence the severity of symptoms (Honda and Warren 2009). A full neurologic examination, as well as a general examination with a focus on the head, nose, ear and nasopharynx, should be performed on a suspected meningitis patient. Meningitis-specific movements, including Kernig's sign, jolt accentuation of headache and Brudzinski's sign can all indicate the existence of meningeal irritation (Honda and Warren 2009). Nuchal stiffness, which affects about 80% of people, should be tested during physical examination (LaPenna and Roos 2019; van de Beek et al. 2004; Weisfelt et al. 2006). Kernig's and Brudzinski's signs are traditional signs; however, their sensitivity is limited and their diagnostic value is dubious (LaPenna and Roos 2019; Thomas et al. 2002). A petechial rash, which is very symptomatic of meningococcemia, should be evaluated

on the skin of patients (LaPenna and Roos 2019). The anterior fontanelle bulges in babies. Papilledema may be present in some patients. When tapping your lumbar region, it will be noticed that the opening pressure is higher.

Based on the seriousness of the disease, signs of brain dysfunction such as confusion, delirium and lethargy might progress to a coma. Clinical signs can differ depending on the individual's age. For example, newborns rarely show signs of meningismus and are more prone to septicemia-like symptoms. Acute meningitis in the elderly can have a more subtle beginning, manifesting as tiredness and disorientation rather than the symptoms of a more severe feverish infection. Clinical signs and symptoms (Table 1) differ depending on the bacterial pathogen. For example, meningococcus meningitis is often grave, and even when the condition is detected early and appropriate treatment is administered, 5 to 10% of people die within 24 to 48 h of the start of symptom (Beatriz and Lopez 2019; Bilukha and Rosenstein 2005).

Table 1. Presenting clinical features of cases with ABM.

Sign or Symptom	Approximate Frequency (%)
Fever	>90
Headache	>90
Altered level of consciousness	>80
Meningismus	>85
Convulsion/seizures	~30
Vomiting	~35
Focal neurological deficit/s	10~20
Papilledema	<5

Source: Authors' compilation based on data from Honda and Warren (2009).

2.4. Laboratory Investigations

2.4.1. CSF: Opening Pressure, Chemistries and Cell Count

Meningitis is diagnosed by analyzing the cerebrospinal fluid because there may be no identifiable symptoms or physical signs. To avoid a misdiagnosis, the CSF must be interpreted carefully, the opening pressure is generally higher, in ABM, but the range might vary. For cryptococcal meningitis, measuring the opening pressure is very crucial because a high opening pressure (>250 mm Hg) is a poor prognostic sign (Honda and Warren 2009; Saag et al. 2000). Pleocytosis (100 cells/mm^3 to 10,000 cells/mm^3) is commonly detected in individuals with ABM, with neutrophil-predominant pleocytosis accounting for 80 to 95% of cases (Honda and Warren 2009; van de Beek et al. 2004; van de Beek et al. 2006). Up to 10% of patients with ABM have a normal or modestly raised CSF leukocyte count, which indicates a bad prognosis (Honda and Warren 2009; van de Beek et al. 2004). Although lymphocyte-predominant pleocytosis is common in viral, tuberculous or fungal meningitis, the presence of lymphocytes in the CSF does not exclude the potential of ABM. Almost all cases with bacterial meningitis have an increase in protein (Honda and Warren 2009; Tunkel et al. 2004). A lower glucose level in the CSF (less than 40 mg/dL) suggests the diagnosis of bacterial meningitis (Honda and Warren 2009; Tunkel et al. 2004). Other biochemical indicators, such as a high amount of lactate in the CSF or a high level of serum procalcitonin may help identify ABM from other causes of meningeal inflammation/irritation (Honda and Warren 2009; Genton and Berger 1990; Viallon et al. 1999).

2.4.2. Gram Stain and Cultures

As the sterilization of CSF may occur as early as 15 min following parenteral antibiotic therapy, a rapid Gram stain of the CSF can produce the rapid detection of the causal bacteria (Honda and Warren 2009; Kanegaye et al. 2001). A Gram stain of the CSF may show the pathogenic bacterium even if the CSF culture is negative. In bacterial meningitis, the sensitivity of a Gram stain varies from 60 to 90%, based on the number of bacteria in the CSF (Honda and Warren 2009; van de Beek et al. 2004). A positive Gram stain for bacterial meningitis is extremely specific. The yield of a Gram stain may be increased by centrifuging the samples. The culture of the CSF is crucial in the diagnosis of ABM (Honda and Warren 2009).

2.4.3. Serology, PCR and Latex Agglutination

The use of PCR assays in the detection of viral meningitis has been very beneficial (Honda and Warren 2009; Kupila et al. 2006). For both bacterial (N meningitidis, S pneumoniae and H influenzae) and viral (HSV, VZV and

enteroviruses) meningitis, PCR has a specificity and sensitivity of above 90% (Honda and Warren 2009; Radstrom et al. 1994; DeBiasi and Tyler 1999). Despite the fact that PCR assays are the gold standard for detecting viral meningitis, clinical matching is always recommended because false positive/negative results are possible (Honda and Warren 2009).

2.4.4. Cranial Imaging

Despite the low incidence (2%) of the existence of space-occupying lesions or mass effect in the common patient population, a CT scan is routinely conducted before lumbar puncture (Honda and Warren 2009; Hasbun et al. 2001). Prior to lumbar puncture, defined clinical criteria can help eliminate unnecessary cranial imaging. When a CT scan is recommended, the first dose of antimicrobials should be given before the cranial imaging (Honda and Warren 2009; Tunkel et al. 2004).

The findings of neuroimaging in acute meningitis differ according to the stage of the meningitis. In the early stages, imaging findings may be normal. On MRI, diffuse meningeal enhancement is seen with infrequent involvement of the perivascular Virchow–Robin spaces in the course of more advanced disease. Cerebral edema is also present, along with communicating hydrocephalus. On T2W or fluid attenuation inversion recovery (FLAIR) scans, hyperintensity of the cortical ribbon, most commonly representing an incipient infarction secondary to localized vasculitis, can be detected (Beatriz and Lopez 2019; Grossman and Yousem 2003).

2.4.5. Hematology

Neutrophilic leukocytosis with a high ESR is found in bacterial meningitis. Viral and fungal meningitis shows non-specific findings.

Investigations should also be carried out for evaluation of the source of infection.

2.5. Treatment

2.5.1. Antimicrobial Therapy

Though the management of meningitis patients is akin to that of other infectious disorders, empiric antibiotic therapy should be initiated soon after clinical diagnosis. Antimicrobials should be chosen empirically based on their action against the most possible pathogens, age, epidemiologic information, patient immunological status or other predisposing variables (e.g., history of the base of skull fracture or penetrating injury). Because the concentration of antimicrobials in the CSF is changeable, a bactericidal antibiotic is significantly preferred over one with bacteriostatic activity. Because S pneumoniae and N meningitidis cause nearly 80% of community-onset meningitis, third-generation cephalosporins (e.g., ceftriaxone, cefotaxime) have been utilized as first-line medicines (Honda and Warren 2009; van de Beek et al. 2004; Schuchat et al. 1997).

Antibiotic treatment should be adjusted once a causal bacterium has been detected. The selection of pathogen-targeted treatment is based on antimicrobial susceptibility in vitro and antimicrobial agent penetration into the cerebrospinal fluid (Honda and Warren 2009). However, if clinical improvement with an empiric antimicrobial agent has been demonstrated at this time, the empiric treatment that has already been provided should be continued.

Antimicrobial treatment should be prescribed for at least 5 days following the start of symptoms, including fever. Some authors advised that all patients receive treatment for at least 14 days (Greenberg 2010).

Antimicrobial agents should be administered intravenously. Antimicrobial drugs can be given intraventricularly or intrathecally in the case of postsurgical meningitis or ventriculitis (Remeš et al. 2013). In post-surgical individuals with meningitis and ventriculitis, intraventricular (IVT) or lumbar intrathecal (IT) antibiotics can result in very rapid CSF sterilization. Individuals treated with IVT/IT antibiotics have a very low relapse incidence of meningitis and/or ventriculitis. Antibiotics administered intraventricularly/lumbar intrathecally appear to be an efficacious and safe therapy for CNS infections produced by multidrug-resistant bacteria (Remeš et al. 2013).

Because the etiologic organisms vary from those shown in community-onset meningitis, broader-spectrum antibiotic drugs are necessary to treat nosocomial meningitis. Vancomycin in combination with 3rd or 4th cephalosporins or a carbapenem is an effective empiric antimicrobial treatment. Newer antistaphylococcal medicines (e.g., linezolid or daptomycin) were seen to be efficacious in the treatment of staphylococcal meningitis

(Honda and Warren 2009). In situations of nosocomial meningitis, removal of retained foreign bodies (e.g., contaminated bone fragment, intraventricular catheter, dirty debris in compound depressed fracture) is indicated.

Sinusitis, upper respiratory tract, CSOM, endocarditis and other causative factors should be treated.

2.5.2. Adjuvant Therapy

Corticosteroids have been utilized for ABM in pediatric cases, according to a controlled, randomized study in the 1980s. Dexamethasone treatment in the pediatric patient with ABM is accompanied with a lower death rate, as well as reduced frequency of neurological or audiological sequelae dues to a decrease in the host inflammatory reaction in the subarachnoid spaces (Honda and Warren 2009; Lebel et al. 1988; Odio et al. 1991; Schaad et al. 1993).

2.5.3. Supportive Care

In the treatment of meningitis, extensive supportive care is essential. It is critical to provide appropriate circulatory resuscitation. To avoid negative neurologic outcomes caused by dehydration, many specialists suggest euvolemic states over restricted volume states (Honda and Warren 2009; Maconochie et al. 2008). Periodic mental status evaluations are beneficial for assessing the recovery and early detection of fresh focal neurological abnormalities or seizures. Aggravation of meningeal inflammation, cerebral abscess with adjoining edema, hyponatremia and fever due to the syndrome of inappropriate antidiuretic hormone (SIADH), or toxicity due to high doses of antibiotics, particularly beta-lactams or carbapenems, can all cause mental status changes in individuals with meningitis (Honda and Warren 2009).

2.6. Complications and Treatment

The frequent complications of bacterial meningitis include the following:

1. Raised intracranial pressure is a frequent complication of bacterial meningitis;
2. Hyponatremia is a condition in which there is a lack of sodium (25%);
3. Affliction of a seizure (13–15%);
4. Hydrocephalus (acute) (3–8%);
5. Encephalitis is a disease that affects the brain and hearing loss is the most prevalent symptom of cranial nerve palsy;
6. Cortical insufficiency;
7. Effusion of the subdural space;
8. Abscess in the brain;
9. Dystonia;
10. Paralysis in a specific area;
11. Mental retardation, etc. (Honda and Warren 2009; Vasudeva 2019).

Increased intercranial pressure is seen in more than half of cryptococcal meningitis patients (Honda and Warren 2009; Saag et al. 2000). To manage acute hydrocephalus or increased intracranial pressure, repeated lumbar punctures, ventriculostomy, lumbar CSF drain or ventricular shunt insertion should be explored (Honda and Warren 2009; Saag et al. 2000).

The most common consequences of meningitis are hyponatremia and seizures. Hyponatremia affects about 25% of cases of bacterial meningitis (Honda and Warren 2009; Genton and Berger 1990). Hyponatremia can be caused by different factors, including salt depletion, SIADH, vigorous hydration or hypoadrenalism. Serial electrolyte monitoring should be used to ensure that serum electrolytes are properly adjusted. Seizures occur in 13–15% of ABM cases (Honda and Warren 2009; van de Beek et al. 2004; Aronin et al. 1998). Electroencephalographic monitoring should be undertaken in individuals with a history of seizure or variable mental status (Honda and Warren 2009; van de Beek et al. 2006). Seizures should be managed with IV anticonvulsants like lorazepam, midazolam, barbiturate or phenytoin as soon as possible. Though the necessity for anticonvulsants as a seizure prophylaxis in all cases of ABM is unclear, anticonvulsants should be used whenever clinical proof of seizure or a mass lesion is discovered (Honda and Warren 2009). In the condition of severe encephalitis, cerebral edema can occur, requiring ICP control with mannitol (1 g/kg first dose, 0.25–0.5 g/kg q6h), IV dexamethasone, or endotracheal intubation and mild hyperventilation, with arterial PCO2 of about 28–30 mm Hg. In these circumstances, an ICP monitor with transduced intraparenchymal pressure should be placed (Wan 2018).

3. Viral Meningitis

Meningitis, encephalitis and myelitis are frequent viral infections of the CNS found in clinical practice around the world (Abid et al. 2018; Big et al. 2009). Aseptic meningitis is a kind of viral meningitis. In adults, enteroviruses like coxsackieviruses and echoviruses are the most common etiology of viral meningitis (Honda and Warren 2009; Connolly and Hammer 1990). In western and south Asian countries, enteroviruses are by far the most common pathogens associated in viral meningitis (from 85 to 90% from all viral etiologies) (Abid et al. 2018; Rotbart et al. 1998; Caballero et al. 2011). Herpes viruses, such as HSV1/HSV2 and varicella-zoster virus, are infamous globally as the causes of viral encephalitis and meningitis (Abid et al. 2018; Tan et al. 2014). HSV-1 causes herpes simplex virus (HSV) encephalitis, which has an occurrence rate of 1 case per 250,000 people in the USA (van de Beek et al. 2006). HSV encephalitis has a bimodal age distribution, with cases younger than 20 years and older than 50 years of age being the most prevalent. HSV-2 is a common etiologic agent of meningitis, responsible for 17% of aseptic meningitis cases. In the USA (Honda and Warren 2009; Kupila et al. 2006), arboviruses, including the West Nile virus (WNV), have emerged as common causes of meningoencephalitis (Honda and Warren 2009). Aseptic meningoencephalitis is a complication of acute HIV infection (Honda and Warren 2009; Newton et al. 2002).

The clinical features of viral meningitis are akin to those of bacterial meningitis.

In viral, tuberculous, fungal meningitis, lymphocyte-predominant pleocytosis is common (Honda and Warren 2009).

The management of viral meningitis treatment is mainly supportive. Rest, fluids, antipyretics and analgesic or NSAID drugs can be administered as necessary. The most important decision is whether or not to initiate antibiotic treatment for bacterial meningitis on an empirical basis while waiting for the causes to be detected. If bacterial meningitis is suspected, intravenous (IV) antibiotics should be initiated as soon as possible (Wan 2018; Nigrovic et al. 2013). Several antiviral drugs are currently being evaluated in the general population; however, their effectiveness in precluding the potentially fatal complications of viral meningitis is yet to be determined. In herpetic viral infections, acyclovir is remarkedly beneficial solely if given very early in the course of the illness (Wan 2018). Seizure and encephalitis should be treated accordingly.

4. Fungal Infections

Fungal infections of the CNS can be fatal, and they are virtually often a clinical surprise. They have a mild presentation with few diagnostic features, and they are frequently misdiagnosed as pyogenic abscess, tuberculous meningitis or brain neoplasms (Sheikh and Amr 2010).

There are two types of fungal species that can harm the central nervous system (Sheikh and Amr 2010):

I. Pathogenic fungi: Infectious fungus that can infect healthy hosts.

(i) Cryptococcus neoformans is a kind of cryptococcus. (ii) Histoplasma capsulatum is the second kind of histoplasma. (iii) Coccidioides immitis is a kind of coccidioid. (iv) Paracoccidioides Braziliensis, (v) Sporothrix schenckii is a species of Sporothrix. (vi) Blastomyces dermatides is the sixth species in the Blastomyces genus.

II. Opportunistic fungi: Commonly generate infections in immunocompromised people.

1. Aspergillosis 2. Zygomycosis (Mucormycosis) 3. Cerebral Phaeohyphomycoses 4. Candidiasis (*C. albicans*, *C. tropicalis*, *C. lusitaniae*, *C. viswathii*) 5. Penicillioses

Meningitis can be caused by any of the major fungal infections. Meningitis can be due to a variety of fungi, ranging from relatively frequent cryptococcal meningitis to uncommon meningitis caused by filamentous or dimorphic fungi. CNS infections can be caused by Cryptococcus, Aspergillus, Candida and a variety of molds. Brain abscesses can be caused by many of the etiologic pathogens of fungal meningitis. *Candida* spp. are the most common etiologic pathogen, followed by *Aspergillus* spp.; however, Cryptococcus neoformans and other fungi can also be responsible for meningitis (Sheikh and Amr 2010).

Generally, a fungal infection of the CNS can result in one or more of the symptoms listed below (Sheikh and Amr 2010):

- Encephalitis;
- Chronic and sub-acute meningitis;
- Granulomas parenchymal or brain abscesses;
- Vascular thrombosis resulting in stroke, infarction or myelopathy;
- Vasculitis.

The most common variety of the disease is intraparenchymal abscesses or basal meningitis caused by fungal pathogens.

Clinical manifestations of fungal infection lack specific findings but present as other meningitis of more insidious onset, not responding to usual antibiotics. A CSF culture and PCR provide the diagnosis. The detection of cryptococcal meningitis and cryptococcal antigen latex agglutination of the CSF show excellent sensitivity and specificity (sensitivity: 93–100%; specificity: 93–98%) (Honda and Warren 2009). When present with a fungal granuloma, it mimics ICSOL or brain abscesses. It presents with features of the site of involvement. Cavernous sinus syndrome, cranial nerve palsy, hemiparesis and seizure may be the clinically presenting feature. Cranial imaging by a CT or an MRI is not specific. Postoperative histopathology can provide an answer. Specific antifungal agents, excision of the granuloma and reversal of immunosuppression, and immunomodulation state are the treatments (Sheikh and Amr 2010). Polyenes (amphotericin B), triazoles (itraconazole, voriconazole, isavuconazole and posaconazole), echinocandins (micafungin, caspofungin and anidulafungin) and flucytosine are four primary types of antifungal drugs that can be used to treat CNS infections (5-FC) (Sheikh and Amr 2010).

5. Brain Abscess

The localized intraparenchymal collection of pus in any part of the brain, e.g., cerebrum, cerebellum or brainstem, is called a brain abscess.

Brain abscesses are widespread in affluent countries and considerably more so in impoverished countries (Chowdhury et al. 2015; Bernardini 2004). Despite the introduction of modern neurosurgical innovation such as stereotactic aspiration and biopsy, improved culturing methods for detecting the infectious agent and new antibiotics, as well as noninvasive imaging methods, brain abscesses remain a public health concern, particularly in underdeveloped countries (Chowdhury et al. 2015). In impoverished countries, brain abscesses account for roughly 8% of intracranial space-occupying lesions, but in Western countries, the figure is closer to 2% (Chowdhury et al. 2015; Bernardini 2004; Zhang et al. 2014; Loftus et al. 1996; Sharma et al. 2000).

5.1. Etiology and Pathogenesis

The risk factors for brain abscess formation are multifactorial, including (a) pulmonary abnormalities (infection, A–V fistula, etc.), (b) cardiac pathology (congenital cyanotic heart disease, bacterial endocarditis, etc.), (c) nearby infections (CSOM, sinusitis, etc.), (d) penetrating head trauma, (e) AIDS, etc.

Brain abscesses are generally the outcome of a secondary infection from an extracerebral original source that disseminates to the CNS via (1) hematogenous spread or (2) contiguous extend from nearby structures (Beatriz and Lopez 2019).

Abscesses caused by hematogenous dissemination from a distant focus, responsible for roughly 20% to 25% of all cases (Beatriz and Lopez 2019; Brown and Gray 2009). Pulmonary infections, like bronchiectasis and lung abscesses, are the most prevalent primary causes in adults, followed by dental infections. Infections of the pelvis and abdomen, septicemia and bacterial endocarditis are some of the other causes. Congenital heart disorders with a right-to-left shunt owing to paradoxical emboli are the most prevalent primary causes in children (Beatriz and Lopez 2019; Frazier et al. 2008). About 20% of patients have abscesses caused by the contiguous extension of a local infection into the brain (Carpenter et al. 2007). Sinusitis, chronic and acute otitis, and mastoiditis are all common causes of an infection in children. Sinusitis and osteomyelitis of neighboring skull anatomical structures are the typical causes of an infection in adults. The direct insertion of germs in penetrating head injuries and postsurgical treatments can also cause brain abscesses. Certain abscesses can occur anywhere from 2 to 37% of the time in these situations (Beatriz and Lopez 2019; Honda and Warren 2009; Carpenter et al. 2007). In roughly 25% of brain abscesses, the cause of infection is idiopathic; a comprehensive work-up for cardiac shunts is required in the case of cryptogenic abscesses. Most brain abscesses are single lesions that develop in areas near the infection's initial source. Abscesses caused by direct extension from the odontogenic foci or frontal sinuses are mainly seen in the frontal lobe; abscesses caused by otogenic infections, on the other hand, are generally cerebellar or temporal. Multiple abscesses are caused by hematogenous dissemination and while they can occur anywhere in the brain, most are frequently seen in the region of the middle cerebral artery.

Regarding their spread from the nasopharynx and oropharynx, streptococci are the most common etiology of pyogenic brain abscesses. Another common reason for brain abscesses is anaerobic bacteria, which commonly

occur as part of a multi-microbial infection. Brain abscess microbiology is influenced by the initial location of the infection.

In individuals with lung abscesses, *Streptococcus* spp. and anaerobic microbes are frequently isolated. Individuals with brain abscesses caused by endocarditis frequently have Staphylococcus aureus or viridians-group streptococci (Honda and Warren 2009). Gram-negative enteric bacilli are frequently seen in conjunction with a genitourinary or intra-abdominal source. Brain abscesses due to otitis externa or otitis media can contain *Pseudomonas* spp. (Honda and Warren 2009; Mathisen and Johnson 1997). Brain abscesses that result from neurosurgical treatments or head trauma typically contain *Staphylococcus* spp. and aerobic Gram-negative bacilli (Honda and Warren 2009). Bacterial agent and sources in bacterial brain abscess are shown in Table 2.

Table 2. Bacterial brain abscess: bacterial agent and source.

Location of the Primary Infection	Bacterial Pathogen(s)
Hematogenous Spread	
Congenital cyanotic cardiac disease	*Haemophilus* spp., *Streptococcus* spp., *S. aureus*
Bacteremia and endocarditis	*Streptococcus* spp., *S. aureus*
Lung infections	*Streptococcus* spp., anaerobic Gram-negative, *Fusobacterium*, *Nocardia*, *Actinomyces*
Genitourinary and intra-abdominal infection	Enteric Gram-negative bacilli
Spread of Contiguous Infection	
Odontogenic and sinuses infections	*Streptococcus* spp., *S. aureus*, *Bacteroides*, *Enterobacteriaceae*, *Haemophilus* spp.
Mastoid and ear infections	*Streptococcus* spp., *Enterobacteriaceae*, *Pseudomonas*, *Bacteroides* spp.
Penetrating head trauma	Staphylococci, *Bacteroides* spp., *Enterobacteriaceae*, *Clostridium*
Post-surgical procedures	*S. aureus*, *Pseudomonas*

Source: Authors' compilation based on data from Honda and Warren (2009).

5.1.1. Stages of Cerebral Abscess

There are four well-recognized stages of a cerebral abscess (Table 3).

Table 3. Histologic staging of cerebral abscesses.

Stage	Pathology	Resistant to Inserting a Needle
Stage 1: Early cerebritis Days: 1–3	Early infection, perivascular infiltration of inflammatory cells around the central core of coagulation necrosis, poorly demarcated from the surrounding brain.	Intermediate resistance
Stage 2: Late cerebritis Days: 4–9	Pus generation in necrotic center which is encircled by inflammatory cells, a fibroblast.	No resistance
Stage 3: Early capsule development Days: 10–13	Neovascularity, necrotic center, a capsule is better formed on the cortical side than on the ventricular side of the lesion.	No resistance
Stage 4: Late capsule formation Days: >14	Dense collagenous capsule with well-defined necrotic center, gliosis around the capsule.	Firm resistance, "pop" on entering

Source: Authors' compilation based on data from Greenberg (2010).

5.2. Clinical Features and Diagnosis

None of the symptoms are specific (Greenberg 2010). The clinical signs of people with brain abscesses differ depending on where the abscess is located and how virulent the germs are. Fever, headaches and altered mental status are the most classical symptoms (Beatriz and Lopez 2019). Focal neurological impairments and other

features of a space-occupying mass (hemiparesis, seizure, etc.) may also be present based on the site of the abscess, as well as clinical features of a raised ICP (vomiting/nausea, headache, lethargy, etc.) (Beatriz and Lopez 2019).

5.3. Imaging

The widespread availability of imaging tests has assisted in the detection of brain abscesses. In the case of a well-developed or chronic brain abscess, a contrast CT scan may show single- or multiple-ring-enhanced lesions (Figure 1). To identify a brain abscess, a contrast MRI is more specific and sensitive than a contrast CT scan (Figure 2) (Honda and Warren 2009).

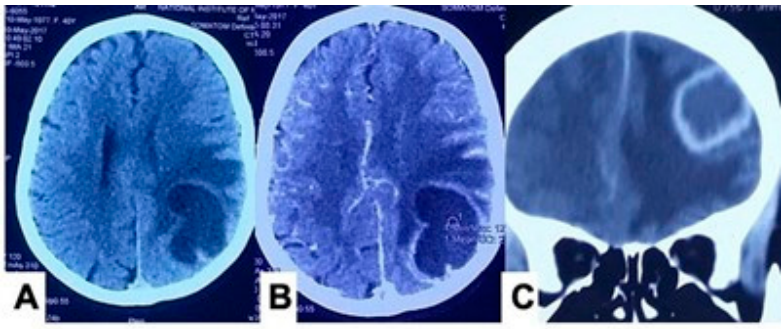

Figure 1. Plane (**A**) and contrast (**B**,**C**) CT scan of a head with a parieto-occipital brain abscess. Source: Figure by authors.

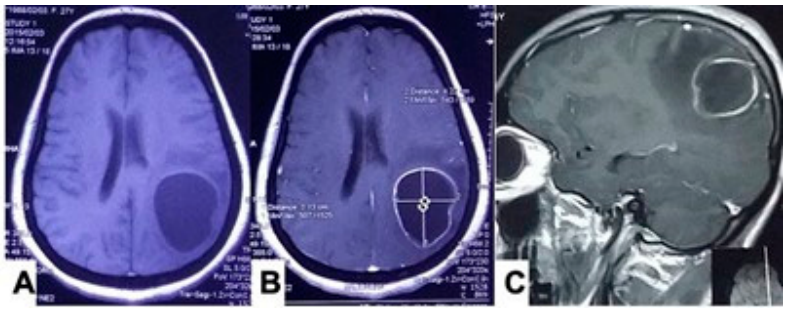

Figure 2. Plane (**A**) and contrast (**B**,**C**) MRI of a brain with parieto-occipital abscess. Source: Figure by authors.

MR spectroscopy is helpful for differentiating from other SOL-like metastases, GBM, etc. Lactate and acetate are increased in abscess. On in vivo MR spectroscopy, pyogenic and tuberculous abscesses can be distinguished by their distinct metabolite patterns, with detection of amino acids, succinate and acetate in pyogenic abscesses and a lipid peak in tuberculous abscesses (Figure 3) (Mohindra et al. 2016).

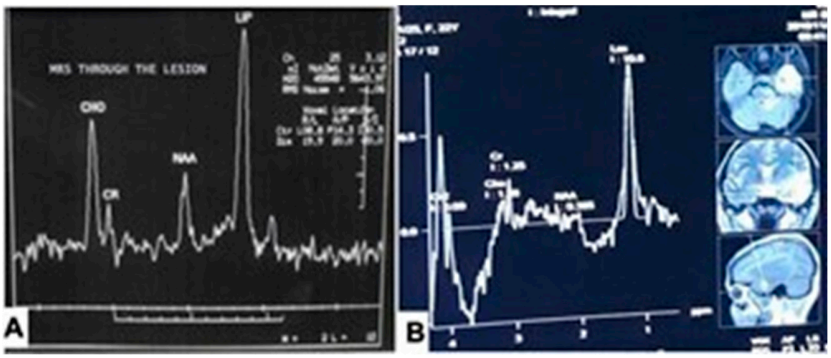

Figure 3. (**A**,**B**) MRS through a tuberculous brain abscess showing increased lipid and lactate peaks. Source: Figure by authors.

The differential diagnosis of brain abscesses is necrotic neoplasms such as glioblastomas multiforme and metastasis, which are sometimes hard to differentiate by a conventional CT scan and MRI. Combined proton

magnetic resonance spectroscopy (^{1}H-MRS) and diffusion-weighted magnetic resonance imaging (DWI) are utilized for the diagnosis of brain abscesses and glioblastoma. DWI shows the brain abscess as a homogeneous hyperintense mass and ^{1}H-MRS shows the presence of acetate, lactate and amino acids, as well as the absence of normal brain elements. DWI sometimes shows glioblastoma multiforme as a hyperintense mass; however, ^{1}H-MRS shows a significantly elevated lactate and reduced N-acetyl-aspartate. A combination of the findings of DWI and ^{1}H-MRS can differentiate brain abscessse and glioblastomas (Nakaiso et al. 2002).

Hematological studies are non-specific and may be normal. Investigations for the primary source of infection should be carried out.

5.4. Treatment

The successful care of a brain abscess necessitates a comprehensive approach. The management team's nucleus is a neurosurgeon who collaborates closely with an infectious disease specialist, a neurologist and a neuroradiologist. Neuroradiological examination, surgical intervention, antibiotic usage and elimination of primary infected foci are all part of this strategy (Alvis Miranda et al. 2013). There is no one-size-fits-all approach to treating a brain abscess. It involves long-term antimicrobial treatment, surgical drainage or excision, and correction of the primary source of infection (Greenberg 2010).

5.4.1. Medical Therapy

While empiric antibiotic therapy should be initiated, particularly in cases with sepsis or eminent herniation, effort should be employed to obtain a tissue or microbiologic diagnosis as soon as possible (Honda and Warren 2009; Cunha 2001). Empiric antibiotics should cover Gram-negative, Gram-positive and anaerobic germs, since brain abscesses are typically polymicrobial (Honda and Warren 2009). In general, an empiric antibiotic combination includes the following (Greenberg 2010):

(1) Third- or fourth-generation cephalosporin;
(2) Vancomycin;
(3) Metronidazole.

Carbapenems may be used instead of cephalosporins and metronidazole in some cases (Honda and Warren 2009).

Antibiotic therapy can be adjusted if a causal bacterium has been identified. But if clinical improvement is shown with empiric treatment, it should be continued.

Antibiotics should be administered by an intravenous route and continued for at least 6–8 weeks (Greenberg 2010).

Sole medical management is indicated in the following conditions:

Early stage (cerebritis) of the disease before encapsulation;
Small lesion (<2.5 cm);
Multiple lesions;
Abscess in critical location (deep-seated, dominant hemisphere and eloquent area, brain abscess);
Poor surgical candidate;
Concomitant meningitis/or encephalitis;
Duration of symptoms <2 weeks;
Patient showing definite improvement within the first week of initiation of antibiotics.

In cases with brain abscesses, seizures are a common consequence which occur in 13 to 25% of cases. Though seizures may have little effect on the overall mortality, an anticonvulsant should be provided at an early stage of treatment to preclude seizures (Honda and Warren 2009). Dexamethasone has been utilized to lower intracranial pressure in patients who are at the risk of brain herniation. The effectiveness of steroids in the management of a brain abscess is unknown (Honda and Warren 2009).

5.4.2. Surgical Treatment

The indications for surgical treatment include the following (Greenberg 2010):

(1) Remarkable mass effect produced by the abscess seen on CT or MRI;
(2) Diagnostic dilemma;
(3) Near the ventricle (likelihood of an intraventricular rupture);
(4) Signs of remarkedly raised intracranial pressure;
(5) Grave neurologic status;
(6) Traumatic brain abscess accompanied by foreign material;

(7) Multiloculated abscess;
(8) Fungal abscess;
(9) Failure of medical treatment (neuro-deterioration increasing in size after 2 weeks of treatment, progressing toward the ventricle and no reduction in size after 4 weeks of treatment);
(10) No facility for follow-up by a CT scan every 1–2 weeks.

The following are the guiding principles for surgical care according to the British Society for Antimicrobial Chemotherapy's "Infection in Neurosurgery" Working Party (Alvis Miranda et al. 2013; Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy 2000):

- To reduce raised intracranial pressure urgently;
- Diagnosis confirmation;
- To get pus for microbiological studies;
- To potentiate the effectivity of antibiotic therapy;
- To preclude the ventricular extension of an infection iatrogenically.

The surgical procedures utilized are (1) needle aspiration via a bur hole, (2) total resection after craniotomy and (3) stereotactic aspiration.

Most surgical treatment is needle aspiration. If necessary, it can be carried out under local anesthetic. Irrigation with antibiotics and regular saline can be combined. In roughly 70% of cases, it is needed to repeat the procedure. Surgical excision may be required in some cases (Greenberg 2010).

Abscesses that expand after 2 weeks of antibiotic medication or fail to diminish after 3 to 4 weeks of antibiotics are usually treated with craniotomy and excision. Multiloculated abscesses and bigger lesions with a noticeable effect which are superficial and situated in non-eloquent areas of the brain are also candidates for a craniotomy (Figure 4) (Moorthy and Rajshekhar 2008). Repeated pus collection following aspiration can result in abrupt neurological deterioration; hence, the removal of abscesses in the cerebellum is also suggested (Moorthy and Rajshekhar 2008). A craniotomy may be required to remove bone chips or foreign material from a traumatic brain abscess (Honda and Warren 2009).

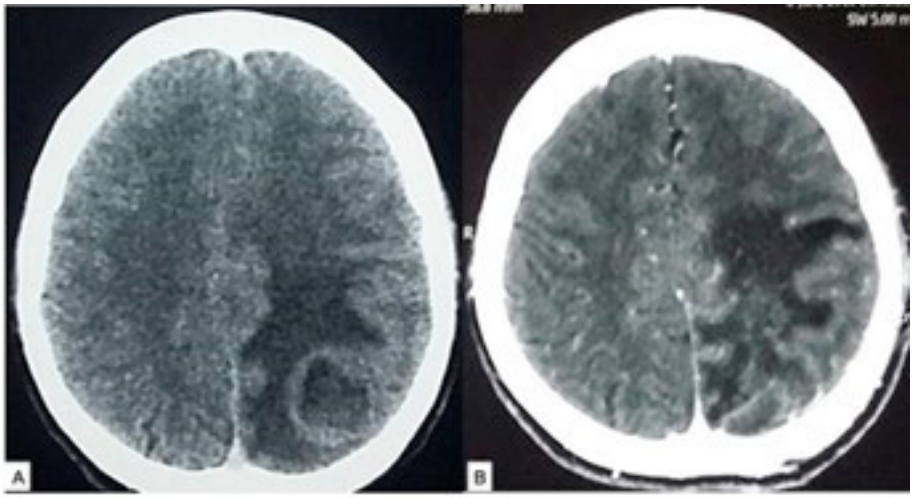

Figure 4. Pre- (**A**) and (**B**) postoperative (craniotomy) CT of a brain abscess. Source: Figure by authors.

There are some advantages in removing a brain abscess in a patient who is otherwise neurologically sound. As a result, the risk of recurring pus collection is virtually completely minimized, and the cost of repeated imaging is reduced. The length of stay in the hospital is also shortened (Moorthy and Rajshekhar 2008). As the capsule is frequently attached to the neighboring white matter, the neurosurgical procedure may inflict an unintentional extensive injury to adjacent viable brain tissue. Primary resection of a brain abscess carries the risk of severe damage to the adjacent brain, with a greater probability for neurological impairment and epilepsy (Alvis Miranda et al. 2013).

Stereotactic aspiration is used to treat deep-seated abscesses and lesions of the brainstem that do not respond to antibiotics alone.

Multiple abscesses are effectively treated by aspirating the largest one and then starting antibiotic therapy which may be needed for up to 3–6 months (Moorthy and Rajshekhar 2008).

Ventricular drainage is utilized to manage brain abscesses that burst into the ventricles, along with intravenous and/or intrathecal antimicrobials (Brook 2017).

5.4.3. Treatment of the Primary Source of Infection

A middle ear infection can be surgically managed at the same time or shortly after an otogenic brain abscess is treated (Moorthy and Rajshekhar 2008). Tetralogy of Fallot (TOF) should be corrected as soon as possible. Other sources should be treated according to their merit.

6. Subdural Empyema

Despite rigorous neurosurgery therapy, the subdural empyema (SDE), i.e., a purulent infection of the area between the cerebral dura and the arachnoid mater, is a neurosurgical emergency with a 10–13% fatality rate (Honda and Warren 2009). Subdural abscess, circumscript meningitis and pachymeningitis interna are all terms used to describe this condition (Agrawal et al. 2007). It is generally unilateral and spreads quickly through the subdural area until it is stopped by particular restrictions (e.g., tentorium cerebelli, falx cerebri, base of the brain and the foramen magnum). It accounts for 20% of all intracranial abscess cases. Men are more likely to contract the infection, accounting for up to 80% of the cases (Agrawal et al. 2007).

Subdural empyema has a pathophysiology that is akin to that of a cerebral abscess: direct spread from a nearby focus (e.g., paranasal air sinus infections, otitis media, cranial trauma or cranial osteomyelitis) or hematogenous dissemination from distant foci (Honda and Warren 2009; Agrawal et al. 2007). SDE is usually a consequence of purulent meningitis in babies (Greenberg 2010; Agrawal et al. 2007; Segun 2017; Rich et al. 2000; Barkovich 2000). Hematogenous dissemination from a distant target, especially the lungs, is rare (Honda and Warren 2009). An SDE can develop following cranial trauma or surgery, especially if there is an open depressed fracture with penetrating injuries (Greenberg 2010; Agrawal et al. 2007). Retrograde septic thrombophlebitis can potentially spread the illness (Agrawal et al. 2007; Tewari et al. 2004). Subdural empyema, which is linked to thrombophlebitis and venous sinus thrombosis, may result in a cerebral abscess or an infarction (Agrawal et al. 2007).

Subdural empyema has a microbiology profile that is similar to that of brain abscesses. Staphylococci, anaerobes and aerobic streptococci, Streptococcus pneumoniae, Hemophilus influenzae and other Gram-negative bacteria are common causal organisms (French et al. 2014).

6.1. Presentation

The most frequent clinical presentation features are a triad of sinusitis, fever and neuro-deficits, with a fulminant, as well as a swift downhill course (Agrawal et al. 2007). The common clinical features are summarized in Table 4.

Table 4. Clinical features of SDEs.

History	Physical Examination
Fever	Altered mental status: drowsiness, confusion, stupor and coma
Headache	Meningeal irritation signs or meningismus
Recent history (<2 week) of sinusitis, mastoiditis, meningitis, otitis media, cranial trauma or surgery, sinus surgery or respiratory infection	Hemiparesis or hemisensory deficits
Drowsiness, confusion, stupor or coma	Aphasia or dysarthria
Hemiparesis or hemiplegia	Seizure
Seizure-generalized or focal	Swelling, sinus tenderness or inflammation
Nausea or vomiting	Papilledema and other features of a raised ICP like vomiting/nausea, gait disturbance and altered mental status
Blurring of vision (amblyopia)	Homonymous hemianopsia

Table 4. *Cont.*

History	Physical Examination
Dysphasia	III, V or VI cranial nerves palsies; particularly if the abscess is close to the petrous portion of the temporal bone, generating facial pain and 6th nerve palsy
Recent H/O brain abscess	Fixed and dilated pupil on the same side as a result of compression of the oculomotor nerve

Source: Authors' compilation based on data from Agrawal et al. (2007).

6.2. Evaluation

As clinical findings are nonspecific for the diagnosis, laboratory data and neuro-imaging studies are helpful to reach the diagnosis.

6.2.1. Laboratory Data

The WBC count, ESR and C-reactive protein level can all be significantly high, and these tests can help determine which patients should be scanned (Agrawal et al. 2007).

Regarding the risk of cerebral herniation, lumbar puncture is not recommended if intracranial pressure is elevated. When increased intracranial pressure has been ruled out, lumbar puncture will be useful in ruling out meningitis. Findings in the CSF may indicate the existence of infection (Agrawal et al. 2007).

6.2.2. Imaging

The neuroimaging diagnosis of an SDE has traditionally relied on CT and MRI. The primary procedure for the rapid and noninvasive detection of an SDE is carried out via high-resolution, contrast CT scanning. A lenticular or crescentic extracerebral hypodense region over the hemisphere or along the falx can be seen on a contrast CT of the head in the coronal and axial planes. The infusion of contrast material improves the delineation of the edges (Figure 5) (Greenberg 2010; Agrawal et al. 2007).

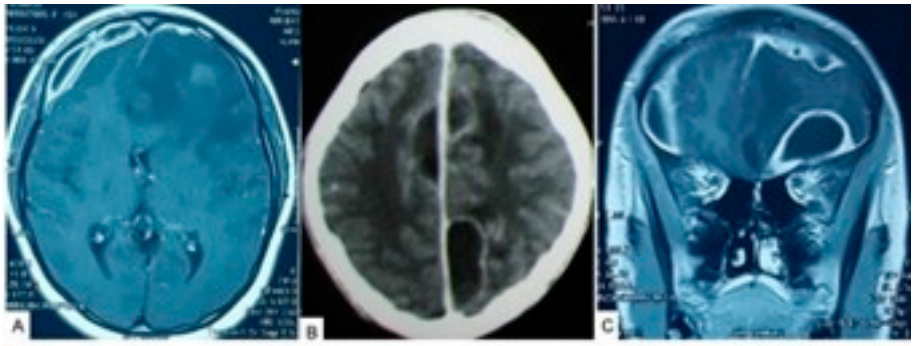

Figure 5. Subdural empyema; (**A**) interhemispheric; (**B**) convexity; (**C**) subfrontal and convexity. Source: Figure by authors.

MRI with gadolinium contrast is the preferred diagnostic technique for an intracranial SDE. SDEs are characterized by fluid collection encircled by a contrast-enhancing rim. Extra-axial fluid and its rim enhancement are better visualized with an MRI than with a CT. T1WI exhibits a modest signal, while T2WI shows a reasonably high signal (Agrawal et al. 2007).

6.3. Treatment

The keys to better clinical results are early and correct diagnosis, quick neurosurgical intervention and adequate antibiotic medication. Surgical drainage and antibiotic treatment are the principal forms of treatment. SDE pus should always be sent to the lab for anaerobic and aerobic culturing. Wide craniotomy with irrigation improvises the result in an SDE by permitting wide exposure, satisfactory exploration and better drainage of

subdural pus material. Neuroimaging can precisely localize the pus which can be removed through a burr hole; however, wide craniotomy, evacuation and irrigation are the methods of choice, as they allows for wide exposure, appropriate exploration and better evacuation of subdural pus (debride and drain). The goal of therapy is to completely drain the pus and eliminate the source of illness (Greenberg 2010; Agrawal et al. 2007). Another technique is drainage and irrigation through stereotactic burr hole implantation, but this is less preferable due to reduced exposure and the possibility of incomplete purulent material evacuation (French et al. 2014). In critically unwell patients, bur hole evacuation is recommended.

Antibiotics should be initiated as soon as possible and changed as needed based on the culture, with sensitivity assessment.

7. Tuberculosis

Tuberculosis is generated by mycobacterium tuberculosis. It is highly prevalent in underdeveloped countries, but it is growingly threatening public health in advanced nations due to rising HIV epidemics, as well as migration from third-world countries (Hossain et al. 2017; Ertem et al. 2010). Tuberculosis persists as a serious global health issue. Globally, an estimated 10.4 million new cases of tuberculosis were notified in 2015. By 2030, 15 years after its declaration, the World Health Organization's "End TB Strategy" aims to a 90% decrease in TB-related mortality and an 80% decrease in TB occurrence (Davis et al. 2018). One of the most dangerous clinical presentations of tuberculosis is CNS involvement, which occurs in 5–10% of extrapulmonary tuberculosis cases and accounts for about 1% of all TB cases (Hossain et al. 2017; Cherian and Thomas 2011). Immunosuppression, whether caused by solid organ transplantation or HIV infection, increases the danger of contracting or reactivating tuberculosis which complicates the management of underlying immunosuppression, as well as CNS tuberculosis (Hossain et al. 2017; Nelson and Zunt 2011). HIV infection increases the likelihood of contracting tuberculosis, the rate at which the illness progresses from latent to active, and TB-related mortality and morbidity (Hossain et al. 2017; Nelson and Zunt 2011). HIV-positive people with tuberculosis are five times more likely than HIV-negative people to have CNS involvement (Nelson and Zunt 2011). Tubercular meningitis (TBM), tubercular abscesses and intracranial tuberculomas are all symptoms of CNS tuberculoma, the most serious form of extrapulmonary tuberculoma (Chou et al. 2012). Meningitis or no meningeal involvement can accompany intracranial tuberculoma. Tuberculomas are more commonly detected in the supratentorial space in adults, and multiple tuberculomas are more common than single tuberculoma (Chou et al. 2012; Bayındır et al. 2006).

7.1. Epidemiology

Although TB usually involves the lungs, it can occur in any organ or tissue. Extrapulmonary TB accounts for 20–25% of reported cases in countries with comprehensive diagnostic and reporting systems. Extrapulmonary cases (without concomitant pulmonary disease) accounted for 14% of all notified cases (new and relapse) worldwide in 2007 (WHO 2010). According to the WHO, 8.8 million new cases of active tuberculosis were reported per year in 2005, resulting in 1.6 million fatalities (Rock et al. 2008; WHO 2007). According to the WHO, 9.27 million new cases of tuberculosis (139/100,000 population) occurred in 2007, similar to the 9.24 million new cases (140/100,000 population) in 2006 (Cherian and Thomas 2011). Tuberculosis continues to be a global problem, with most new active tuberculosis infections occurring in emerging and poor countries (Rock et al. 2008; WHO 2007). Demographic factors like poverty, congestion, malnutrition and a weakened immune system account for 80% of new tuberculosis cases worldwide, whereas HIV accounts for the rest of the 20% tuberculosis cases in Sub-Saharan Africa (Rock et al. 2008; WHO 2007; Waaler 2002).

7.2. Pathogenesis

M. tuberculosis is an acid-fast bacillus (AFB) which infects predominantly humans and is aerobic, nonmotile and non-spore-forming. It has a sluggish doubling period (from 15 to 20 h) and takes many weeks to develop on traditional Löwenstein–Jensen media, where it usually grows in parallel groups, generating serpentine cording's colonial characteristic (Rock et al. 2008). CNS tuberculosis can also be caused by *Mycobacterium bovis* and atypical *Mycobacterium* spp. (Chowdhury et al. 2017).

The inhalation of droplet nuclei carrying *Mycobacterium tuberculosis* bacteria causes infection, which results in bacillus seeding in the respiratory unit of the lungs. The bacilli engage with alveolar macrophages through a variety of receptors once they reach the alveoli (Rock et al. 2008). Ingestion and direct contact with eroded mucosa

or skin can potentially lead to infection. When these innate immune cells are activated, a cascade of chemokines and cytokines is produced, a type 1 T-helper cell-mediated immune response is triggered and a granuloma form (Hossain et al. 2017). CNS tuberculosis is always a secondary infection that enters the CNS by a hematogenous pathway from a primary or secondary location.

7.3. Pathology

Tuberculosis is characterized by chronic granulomatous inflammation that results in a caseating granuloma, a foreign body variety of giant cell granuloma. The disease starts with the formation of tiny tuberculous foci (rich foci) inside the spinal cord, brain or meninges in CNS tuberculosis. The site of these foci, as well as the ability to regulate them, decides which type of CNS TB develops. Tuberculous meningitis (TBM) is the most prevalent form of CNS tuberculosis, followed by tubercular encephalitis, intracranial tuberculoma and a tuberculous brain abscess (Hossain et al. 2017; Rock et al. 2008).

7.3.1. TB Meningitis

The most prevalent symptom of neuro-tuberculosis is tuberculous meningitis (Beatriz and Lopez 2019). A dense gelatinous exudate arises after tubercle bacilli form a granuloma and is released into the subarachnoid space; it is most prominent anteriorly in the suprasellar area and interpeduncular fossa (Figure 6), and it may extend across the prepontine cistern and around the spinal cord. This exudate surrounds arteries and cranial nerves, causing a bottleneck in the circulation of the CSF at the tentorial aperture, resulting in hydrocephalus. RBC, neutrophils and macrophages are seen in the exudate, preceded by lymphocytes in more developed exudates. Rich foci are found in both the meninges and the brain, and they usually follow a vascular pattern (Rock et al. 2008). The genesis of vasculitis in the vessels of the circulus arteriosus, the vertebrobasilar system and the perforators of the middle cerebral artery, leading in infarctions in the supplying areas of these vessels, is the most significant consequence of TBM (Rock et al. 2008).

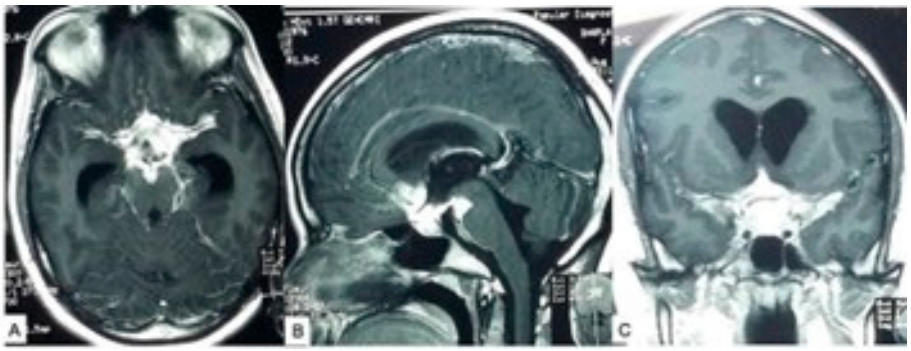

Figure 6. (**A**–**C**) Contrast MRI axial, sagittal and coronal image showing basal tubercular meningitis with a granuloma. Source: Figure by authors.

7.3.2. Tuberculoma

When tubercles in the tissue expand sans bursting into the subarachnoid space, tuberculomas form. As a result, they frequently take place in the absence of TBM, but they can also develop in the presence of TBM. Multiple tuberculomas are seen more frequently than solitary lesions. Around a central area of caseating necrosis, tuberculomas of the cerebrum show classic granulomatous responses composed of epithelioid cells and giant cells mixed with mainly lymphocytes. In contrast to pus, any liquefaction of the center area of necrosis produces straw-colored or clear fluid (Rock et al. 2008). Three forms of intracranial tuberculoma have been identified based on MRI findings: caseating or noncaseating with a solid core, and caseating with a liquid center (Hossain et al. 2017; Chou et al. 2012). Lesions in children are often infratentorial, but lesions in adults are typically supratentorial. Tuberculomas of the cerebrum, cerebellum and brainstem can arise in both infratentorial and supratentorial locations.

7.3.3. Tubercular Brain Abscess (TBA)

Abscess development is a rare symptom of CNS tuberculosis. TBA is identified by an encapsulated collection of pus containing alive bacilli, without indications of a characteristic tubercular granuloma, and must be recognized from granulomas with central caseation, as well as liquefaction-imitating pus. TBAs can appear as single or numerous lesions (Hossain et al. 2017; Rock et al. 2008; Chowdhury et al. 2017; Kumar et al. 2002). TBA might be monocular or multilocular in nature (Kumar et al. 2002). Tuberculous abscesses are larger than tuberculomas, often measuring more than 3 cm in diameter. Fever, headache and focal neurologic impairments are common symptoms of tuberculous abscesses, which are more severe than tuberculomas (Nelson and Zunt 2011). Patients with defective cell-mediated immunity, such as AIDS and other immunodeficiencies which prevent a granulomatous inflammatory response, are more likely to develop this lesion. Tuberculous abscess patients have a more grievous clinical presentation than tuberculomas patients (Beatriz and Lopez 2019).

7.4. Clinical Features

Most individuals with tubercular meningitis (TBM) have a history of vague ill health that lasts 2 to 8 weeks before meningeal irritation develops. Malaise, anorexia, weariness, fever, myalgias and headache are some of the nonspecific symptoms (Cherian and Thomas 2011). Adults with TBM frequently exhibit conventional meningitis symptoms like fever, headache and meningismus (stiff neck), as well as localized neurological impairments, behavioral abnormalities and changes in consciousness. Fever, convulsions, stiff neck and gastrointestinal symptoms like vomiting and nausea are frequent in children with TBM (Rock et al. 2008). In children, headaches are less frequent than in adults. Furthermore, because the meninges at the base of the brain are more likely to be involved, symptoms associated with cranial nerve dysfunction may be noted in a substantial proportion of individuals (up to 70%) (Beatriz and Lopez 2019). Usually, the most afflicted nerve is the sixth cranial nerve. When the optic nerve is involved, vision loss might be a dominant clinical manifestation. Vision loss in these patients could be caused by optochiasmatic arachnoiditis, 3rd ventricle compression of the optic chiasma (if hydrocephalus occurs) or an optic nerve granuloma. Papilloedema may be discovered through ophthalmoscopic examination. Choroid tubercles are yellow lesions with vague edges that can be found singly or in clusters on funduscopy (Cherian and Thomas 2011).

Patients with a tuberculoma or TBA frequently present with headaches, papilledema, seizures or other symptoms of increased intracranial pressure (IICP), depending on their site. With tuberculomas, the onset of symptoms is commonly measured in weeks or months.

TBA has a shorter incubation period (1–3 months) than tuberculoma, but a longer incubation period than pyogenic cerebral abscesses. It is characterized by headaches, fever and localized neurological impairments (Rock et al. 2008; Kumar et al. 2002). The involvement of long white fiber tracts can cause hemisensory deficit or hemiplegia, and engagement of cranial nerve nuclei result to cranial nerve palsy such as diplopia, facial palsy, gaze palsy, dysphagia, etc. The patient may have a low degree of consciousness as a result of the involvement of or pressure on the reticular activating system. Tuberculoma of the upper brainstem, primarily in the midbrain, obstructs CSF flow and results in hydrocephalus, with nausea, vomiting, headache, visual disturbances, papilledema and reduced awareness as the symptoms (Kumar et al. 2002; Sutlas et al. 2003). Different disorders can accompany a midbrain lesion. Weber's syndrome (Warembourg et al. 1960) is characterized by oculomotor nerve palsy and hemiparesis on the contralateral side. When the TBA affects the tegmentum of the midbrain with a red nucleus, Benedict's syndrome manifests as 3rd nerve palsy with contralateral hemiparesis, except for the arm, which displays ataxia, hyperkinesia and coarse intention tremor (Greenberg 2010).

Movement disorders such as parkinsonism, tremor, extrapyramidal syndrome, chorea, dystonia, myoclonus and hemiballismus can arise when the basal ganglia are involved. Behavioral abnormalities, cognitive impairment, pituitary hypofunction, cachexia, diabetes insipidus, precocious puberty and other symptoms of diencephalic involvement may occur (Chowdhury et al. 2017).

7.5. Diagnosis

7.5.1. Traditional CSF Analysis

Cytology

A typical CSF examination can reveal moderate lymphocytic pleocytosis, moderately increased protein levels and hypoglycorrhachia in cases with CNS TB (low glucose) (Rock et al. 2008).

The presence of tubercular bacilli in the CSF, either by smear examination or tubercular culture, is essential for a definitive diagnosis of TBM. Standard staining procedures applied to CSF samples, such as Ziehl–Neelsen, Kinyoun or auramine-rhodamine, have been reported to detect about 100 AFB/mL of the CSF. It has been proposed that if remarkable volumes of the CSF are studied arduously, the organism can be identified in over 90% of centrifuged CSF specimens, along with ventricular CSF, producing the greatest identification rates. CSF culture positivity rates for clinically confirmed cases range between 25% and 70% (Cherian and Thomas 2011).

Molecular and Biochemical Analysis

Commercially obtainable nucleic acid amplification (NAA) techniques and other polymerase chain reaction (PCR)-based techniques, antibody and antigen detection or chemical assays like adenosine deaminase (ADA), as well as tuberculostearic acid measurements are currently available molecular-based techniques (Cherian and Thomas 2011; Rock et al. 2008). Commercial nucleic acid amplification (NAA) assays (PCR) for the diagnosis of tubercular meningitis are 56% sensitive and 98% specific, and when significant volumes of the CSF are studied, the diagnostic yield of NAA increases (Cherian and Thomas 2011; Pai et al. 2003).

Skin tests that are positive for CNS TB have a diagnostic value of 10–20% (Cherian and Thomas 2011; Kilpatrick et al. 1996) to 50% (Cherian and Thomas 2011; Mahadevan et al. 2005). The efficiency of the tuberculin test for the diagnosis of tuberculosis varies depending on age, BCG vaccination, nutritional state, HIV infection and administration manner (Cherian and Thomas 2011; Joos et al. 2006).

ADA (adenosine deaminase) is a cell-mediated immune marker that is mostly associated with lymphocyte proliferation and differentiation (Cherian and Thomas 2011; Kashyap et al. 2006). The sensitivities and specificities of ADA in the CSF were measured to be between 44 and 100%, and 71 and 100%, respectively (Cherian and Thomas 2011; Rock et al. 2008). The development of T-cell-based interferon release assays have been a significant advancement in recent years (IGRAs). IGRAs are in vitro tests that rely on the release of interferon (IFN) after T-cell activation by antigens that are more specific to MTB than pure protein derivatives (PPD) (like early secreted antigenic target 6 (ESAT6) and culture filtrate protein 10 (CFP10)) (Cherian and Thomas 2011).

7.5.2. Imaging

Before starting or within the first 48 h of treatment, every case with tubercular meningitis should be examined using contrast CT imaging (Cherian and Thomas 2011; Thwaites et al. 2009). An early brain CT scan aids in the diagnosis of TBM and can offer crucial baseline information for surgical hydrocephalus treatments (Cherian and Thomas 2011). Hydrocephalus, contrast enhancement of basal meninges and infarctions in the cerebral hemisphere and brain stem are common neuroradiological findings in tuberculous meningitis (Beatriz and Lopez 2019) (Figure 6). In terms of identifying and assessing CNS TB, a contrast MRI is widely thought to be better than a CT. While an MRI is undoubtedly superior to a CT for detecting parenchymal and meningeal irregularities, its limited availability globally and the need for general anesthesia in youngsters imply that it may have a minimal influence on TBM detection globally (Rock et al. 2008).

Tuberculomas are low-density, lobulated or spherical masses with uneven walls that display homogeneous or ring-enhancing uptake following contrast injection (Figures 7–9). They might appear as single or numerous nodules (Rock et al. 2008; Katti 2004). The extent of edema around the tuberculoma is assumed to be inversely proportional to the age of the tubercular lesion; the radiographic appearance of tuberculomas depends largely on whether the TB lesion is caseating, noncaseating, with a solid center or caseating with a liquid center (Rock et al. 2008; Bernaerts et al. 2003). T1-weighted images of tuberculoma are isointense to modestly hyperintense, while T2-weighted images are hypointense (Sanei Taheri et al. 2015; Sharma et al. 2008) (Figure 10). The gray–white matter interface is where most tuberculomas are found (Beatriz and Lopez 2019).

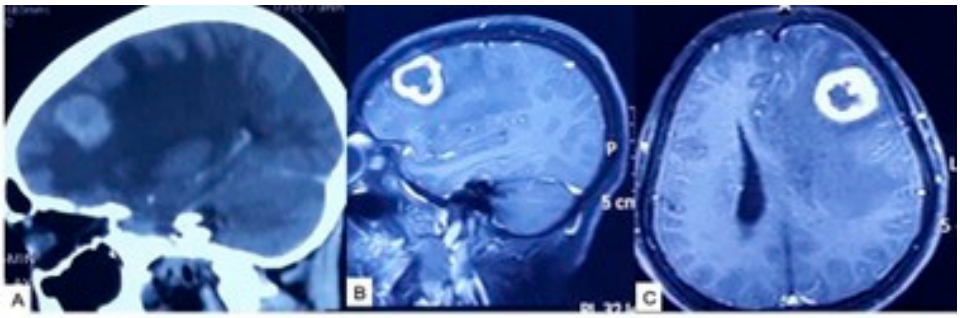

Figure 7. Contrast-enhanced CT (**A**) and MRI (**B**,**C**) showing lt. frontal tuberculoma. Source: Figure by authors.

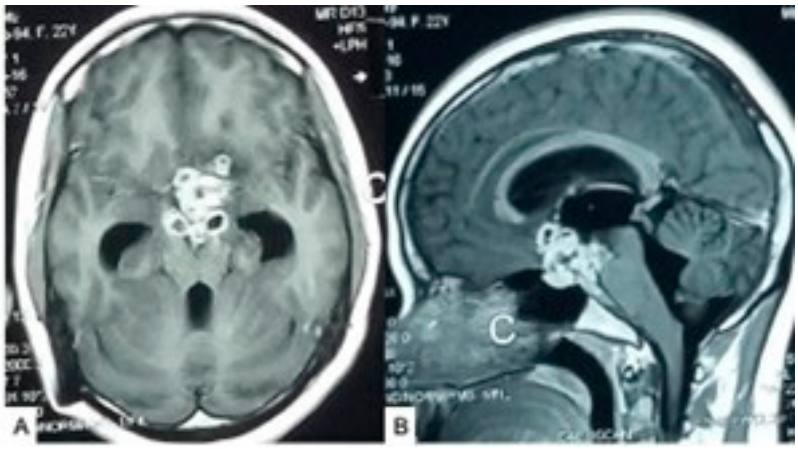

Figure 8. Multiloculated tuberculoma on a contrast-enhanced MRI (**A**,**B**). Source: Figure by authors.

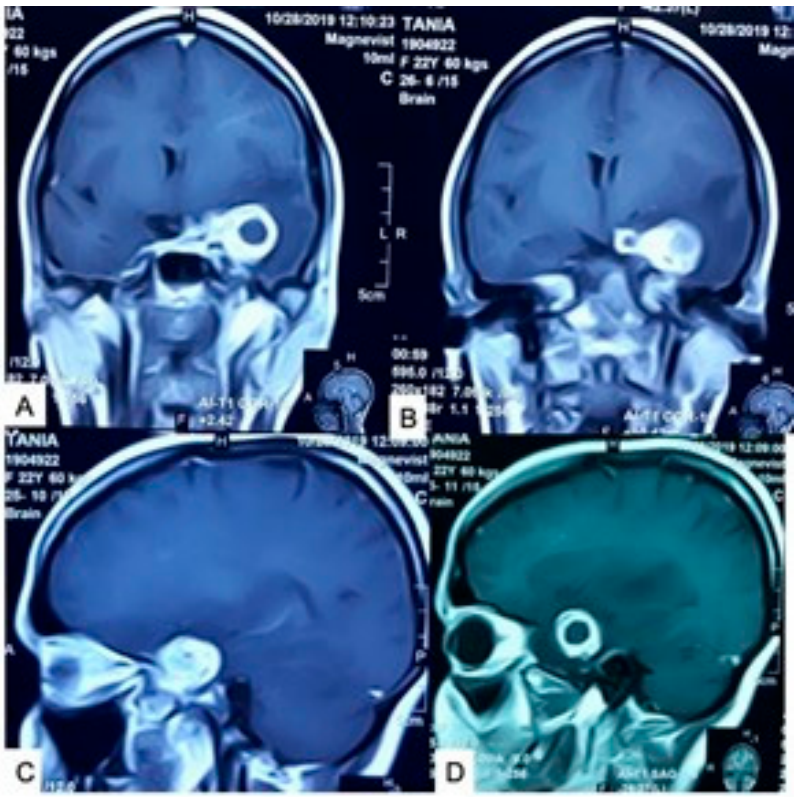

Figure 9. Tuberculoma in the medial temporal region on a contrast-enhanced MRI (**A–D**). Source: Figure by authors.

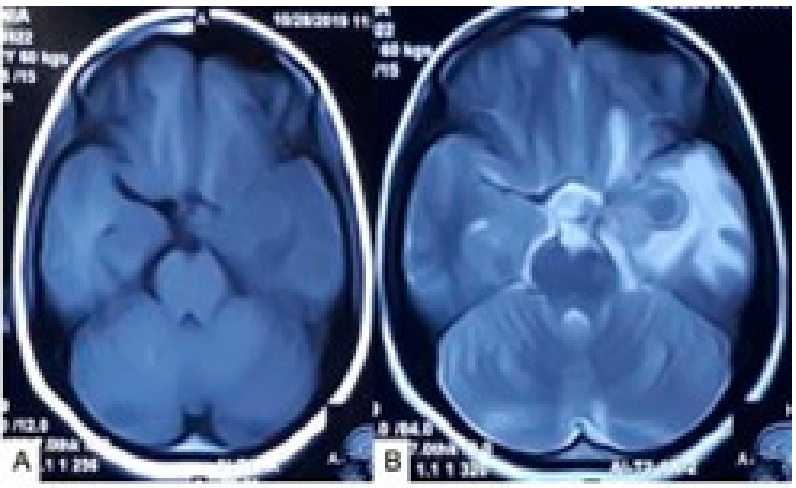

Figure 10. Tuberculoma on an MRI: (**A**) T1WI isointense; (**B**) T2WI hypointense. Source: Figure by authors.

A tuberculous abscess is a rare condition marked by liquefaction and pus in the center. It is often multiloculated and can be solitary or multiple. Tuberculous abscesses are distinct from tuberculomas, which include central caseation and liquefaction that resemble pus. On a CT scan, the tubercular abscess has a hypodense appearance with peripheral edema, as well as a mass effect. The central necrotic area exhibits increased signal strength on T2W imaging. Ring enhancement can be seen on postcontrast pictures, which is usually thin and consistent (Sanei Taheri et al. 2015). Other radiographic techniques, like magnetic resonance spectroscopy (MRS), have been found to differentiate tuberculomas from cysticercosis but not from CNS non-Hodgkin lymphoma (NHL). In tuberculoma (Hossain et al. 2017; Rock et al. 2008), an MRS indicates a higher lipid peak with lower N-acetyleaspartate and choline levels (Hossain et al. 2017; Sharma et al. 2008). An MRS uses a big lipid lactate peak to selectively identify tuberculomas (Cherian and Thomas 2011; Kingsley et al. 2006) (Figure 3).

7.6. Complications

Cortical infarcts and hydrocephalus are two significant consequences of tuberculous meningitis. The infarcts are caused by endarteritis obliterans, which causes severe vascular alterations. Because the basal perforating arteries are involved, the majority of the infarcts occur in the corpus striatum and internal capsule. The inflammatory exudate transforms to a more fibroblastic response as the disease and treatment proceed, which can result in meningeal fibrosis, CSF blockage and communicative hydrocephalus. Due to granulomatous ependymitis, obstructive hydrocephalus can be due to a focal blockage of the cerebral aqueduct or ventricular foramen (Beatriz and Lopez 2019).

7.7. Treatment

Tuberculosis is a systemic disease. Anti-tubercular chemotherapy is the treatment for TB according to the WHO guidelines. Along with anti-tubercular chemotherapy, other forms of treatment may be needed according to the site of involvement and type of pathology. The WHO categorizes the drugs according to different combinations of drugs. WHO-recommended anti-TB medication formulations and fixed-dose drug combinations have recently been included on the WHO Model List of Essential Medicines (WHO 2010). Isoniazide (INH), rifampicin (RIF), pyrizinamide (PZA), ethambutol (EMB) and streptomycin are the first-line anti-TB medications recommended. For all instances of tuberculosis (pulmonary and extrapulmonary), the WHO recommends a 6-month treatment program. Some specialists, however, advocate for a therapy period of 9–12 months (WHO 2010).

The present WHO recommendations for TBM depend on those used to treat pulmonary TB and recommend that all patients be treated with two months of rifampicin (RMP), isoniazid (INH), pyrazinamide (PZE) and ethambutol (ETB), followed by up to ten months of RMP and INH (Davis et al. 2018; WHO 2010). Although starting this regimen before the commencement of coma is the best predictor of survival from TB meningitis (Prasad et al. 2016), this regimen ignores the anti-tuberculosis medications' varied capacity to permeate the brain (Davis et al. 2018; Donald 2010).

The utilization of steroids as an additional therapy in the management of CNS tuberculosis dates back to the 1950s and is still a contentious topic today (Hossain et al. 2017; Rock et al. 2008). According to Prasad et al.'s meta-analysis, steroid use is linked to fewer deaths (Rock et al. 2008; Prasad et al. 2000). In cases of CNS TB, the current guidelines from the Infectious Diseases Society of America, the Centers for Disease Control and Prevention, and the American Thoracic Society recommend steroid therapy as an adjuvant therapy to regular anti-TB chemotherapy.

Dexamethasone, at a starting dose of 8 mg/day for children weighing less than 25 kg and 12 mg/day for children weighing 25 kg or more and adults, is the standard treatment. The starting dose is given for three weeks, then gradually reduced over the next three weeks (Hossain et al. 2017; Rock et al. 2008).

Since the discovery of efficient anti-TB chemotherapy, the main functions of surgery have been to treat serious complications, including hydrocephalus, the mass effect of tuberculomas and brain abscesses (Rock et al. 2008). Tuberculomas respond to anti-TB chemotherapy in the majority of cases, and surgery is not required. However, a huge tuberculoma that is having a significant mass effect, a tuberculoma that is enlarging paradoxically or a diagnostic difficulty necessitates surgical intervention. When a tuberculoma is superficial and easily accessible, surgical removal is also advised as a first-line treatment (Demetriou 2013).

Surgical draining or excision is required for large and chronic abscesses. In the case of smaller and more perplexing lesions, stereotactic biopsy may be used for tissue diagnosis (Hossain et al. 2017). TBA surgical intervention has three goals: (1) to lower the size of the space-occupying mass and relieve the elevated ICP; (2) to minimize the bacterial load; (3) to histopathologically investigate the TBA's wall to confirm the diagnosis of a TBA (Mohindra et al. 2016). Simple aspiration (one time), repeated aspiration via a burr hole, continuous drainage, fractional drainage, stereotactic aspiration and craniotomy followed by excision are some of the treatment possibilities. There are reports describing the complete cure of tuberculous abscesses with multiple aspirations and chemotherapy, but based on the results of Mohindra et al.'s series, large-sized (more than 3 cm in diameter) lesions invariably require excision and smaller ones resolve completely with adequate duration of appropriate ATT regimen (Mohindra et al. 2016).

8. Parasitic Infestations

Parasitic illnesses of the CNS persist to be a major etiology of morbidity, as well as mortality around the world. Millions of adults and children in low- and middle-income nations suffer from cognitive, neurological and mental health disorders caused by parasite infections (Carpio et al. 2016).

The CNS can be affected by any parasite that affects humans; nevertheless, cysticercosis is the most prevalent parasitic infestation of the CNS. Toxoplasmosis, echinococcosis and schistosomiasis are some of the less common illnesses. Paragonimiasis, toxocariasis, malaria, onchocerciasis, human African trypanosomiasis (HAT) and American trypanosomiasis (Chagas disease (CD)), as well as angiostrongyliasis are all rare parasitic disorders that involve the CNS. The causative parasites, vector or intermediary hosts, routes of transmission and endemic areas or geographic distributions of these diseases are all different (Carpio et al. 2016).

8.1. Neurocysticercosis

Cysticercosis is the most common parasitic infestation of the brain and spinal cord. Cysticercosis is caused by the larval stage of pork tape worm Taenia solium, which has marked predilection for neural tissue. The human GIT is the sole habitat for adult worms. When humans ingest food contaminated with viable eggs, the eggs hatch into a larva in the duodenum, enter into the circulation and gain access to the brain.

There are two types of cysts that develop in the brain: (1) cystercercus cellulosae are regular, round or oval, thin-walled, 3–20 mm size, and tend to develop in the parenchyma or subarachnoid space, producing mild inflammation; (2) cystercercus racemosus is larger (4–24 mm size), grows actively in a grape shape as clusters in the basal subarachnoid space, producing intense inflammation (Greenberg 2010).

The locations of cysts tend to fall in the following four groups: (a) meningeal, (b) parenchymal, (c) ventricular, and (d) mixed (Greenberg 2010). NCC has a wide variety of clinical symptoms that are largely influenced by the site of cysts and the host's immunological response. The most common signs of cysts in the brain parenchyma include seizures, headaches, focal impairments and cognitive problems, all of which are associated with an elevated ICP (Greenberg 2010; Carpio et al. 2016). The most common causes of this illness are acute hydrocephalus

caused by intraventricular cysts, or persistent hydrocephalus caused by arachnoiditis or ependymitis (Carpio et al. 2016). Cranial nerve palsies can occur with basal arachnoiditis (Greenberg 2010).

8.1.1. Diagnosis

Cysticercosis antibody titers determined by ELISA are considered significant at 1:64 in serum and 1:8 in the CSF. Mild peripheral eosinophilia and eosinophils in the CSF may be an indication (Schaad et al. 1993). The best option would be to look for parasite DNA in the CSF. The identification of parasite DNA using PCR is a relatively straightforward experimental method that is now garnering far more interest than the serological detection of viable parasite-released products (Carpio et al. 2016).

Neuroimaging is helpful in the detection of NCC because it allows for the identification of the parasite's stages of evolution, as well as the quantity and location of the lesions. Neuroimaging techniques enable observation of the parasite's vesicular, granular–nodular, colloidal and calcified phases in the CNS. For the identification of the scolex and the detection of extraparenchymal NCC, an MRI scan is more sensitive than a CT (Carpio et al. 2016). Ring-enhancing cystic lesions of various sizes in a parenchymal or extraparenchymal lesion with mild inflammatory change (edema) are present on MRI. Intraparenchymal punctate calcification can be seen on CT. Hydrocephalus can be seen in intraventricular cysts. A skull X-ray may show calcification in 13–15% of cases (Greenberg 2010).

8.1.2. Treatment

Medical treatment is the mainstay of treatment.

Antihelminthic drugs include the following:

- Albendazole, 15 mg/kg/d in 2–3 divided doses with corticosteroids, 16 mg/d for 3 months;
- Praziquantel, 50 mg/kg/d in 3 divided doses, with corticosteroids for 15 days;
- Albendazole/praziquantel plus corticosteroids if >2 active parenchymal cysts.

Surgery is sometimes needed for establishing the diagnosis. CSF diversion is needed in the HCP.

8.2. Hydatidosis

The parasite Echinococcus granulosus causes cystic echinococcosis or hydatid disease (cyst). Men are the intermediate host and are infected either by ingesting food contaminated with the ova or by direct contact with an infected dog. Ova hatches into a larva in the stomach; it then disseminates through systemic circulation from the stomach mucosa to the brain (few larvae bypass hepatic and pulmonary filtration). The infestation may be primary or subsequent to the burst of a primary cerebral cyst, either spontaneously or traumatically, or to the embolization of cardiac cysts (Carpio et al. 2016). Primary cysts are usually solitary and secondary cysts are multiple (Greenberg 2010).

Cysts may go unnoticed until they reach a size that causes a mass effect. Brain lesions affect 1 to 4% of cystic echinococcosis patients, with nonspecific clinical symptoms such as a raised ICP and seizure activities, similar to those of a space-occupying mass. There is one record of an infected cranial hydatid cyst in the literature reported by the author in 2010 (Hossain et al. 2010).

The detection of cerebral hydatid cysts relies heavily on imaging techniques like CT and MRI (Limaiem and Kchir 2014). In imaging examinations, hydatid cysts may appear as big, well-marked, smooth and thin-walled cystic lesions with a spherical or oval form and no edema. On CT, the cyst contents exhibit a CSF-like density, and all MR sequences show CSF-like signal patterns. A tiny rim of enhancement can be noticed on post-contrast photos. The existence of a daughter cyst within a cystic lesion is regarded as an echinococcus cyst that is pathognomonic (Carpio et al. 2016). Serological tests (ELISA or CFT) for the detection of antibodies can help in the diagnosis.

Treatment is surgical removal of an intact cyst by craniotomy, along with Albebdazole 400 mg bid for 28 days (Greenberg 2010).

8.3. Cerebral Malaria

Malaria is the most common parasite infection on the planet. It primarily affects African children, as well as Asian adults, with the overwhelming majority of instances (>90%) occurring in children aged 5 years and less. Plasmodium falciparum causes cerebral malaria, which can produce acute encephalopathy (fever and convulsions), which can be deadly or progress to diverse neurological sequelae. Headache, weakness, abdominal

discomfort, muscle aches and erratic fever are among the earliest symptoms of malaria. Nausea, vomiting and orthostatic hypotension are other common side effects. They can later develop into a severe headache followed by drowsiness, confusion, generalized seizures and coma. Residual neurologic impairments are typical in persons who survive cerebral malaria. Microscopy detection of the parasite is the gold standard for diagnosing malaria (Idro et al. 2010; Mohamed and Mansour 2017).

The treatment of cerebral malaria according to the WHO guidelines should be carried out by IV artesunate (2.4 mg/kg/dose) at 0, 12, 24 and 48 h.

9. Shunt Infection

Infection and malfunction are the most common complications of a ventricular shunt system, and both are interrelated. Because of the foreign bodies and direct communication with the CNS, shunt infections are difficult to treat. Infection is recorded in 4–30% of cases, depending on the patient's history, the presence of an external drainage and previous infection history (Stadler et al. 2019). Shunt infection rates per case range from 10–22% and roughly 6.0% every procedure, with 90% of infections happening within 30 days of surgery (Gutierrez-Murgas and Snowden 2014). Children with shunt infection have a higher rate of mortality and morbidity, with an increased risk of seizure. The time between surgery and infection presentation varies from 15 to 12 months (Stadler et al. 2019).

9.1. Etiology and Pathogenesis

The risk factors for shunt infection are as follows (Greenberg 2010; Gutierrez-Murgas and Snowden 2014; Stadler et al. 2019):

(1) Young age;
(2) Length of the procedure;
(3) Open neural tube defect;
(4) Timing of operation—early timing of the day decreases the chance of an infection;
(5) Failure to maintain adequate asepsis;
(6) Postoperative other site infection like RTI, abdominal infection, UTI, etc.;
(7) Low birth weight and prematurity;
(8) Relative immunosuppression;
(9) Number of aspirations or revisions;
(10) Length of hospital stay;
(11) Neurosurgeon's experience, skills and neurosurgical technique;
(12) Manipulation of the indwelling shunt tube during surgery.

The majority of shunt infections are due to Gram-positive bacteria, with coagulase- negative staphylococci (Staph epidermidis) detected in 17 to 78% of cases, and Staphylococcus aureus found in 4% to 30% of cases (Gutierrez-Murgas and Snowden 2014; Stadler et al. 2019).

Biofilm formation is an important issue in shunt infection and antibiotic resistance. Biofilms are self-contained populations of bacteria or fungi that develop a heterogeneous structure made of biological parts and a complicated self-produced matrix to cling to surfaces (Scherr et al. 2014). The first adhesion of an organism to an artificial or host surface is the first step in the development of a biofilm. Bacteria concentrate and grow on the bacterial device or host surface after attachment. This is a serious issue since biofilms can evade the immune system of the host and are more resistant to antimicrobial therapy (Gutierrez-Murgas and Snowden 2014; Hess et al. 2012). Maturation and detachment occur when bacteria attach and replicate on the medical device, allowing for biofilm-related illnesses and sepsis to develop and spread (Gutierrez-Murgas and Snowden 2014).

9.2. Clinical Manifestations

The range of clinical features include the following (Stadler et al. 2019):

(1) Wound infection: symptoms of inflammation and purulent discharge, with organisms identified by Gram stain or culture in an incision or shunt tract. Shunt infections should be managed as wound breakdown with exposed shunt tubing.
(2) Meningitis: meningismus, fever, CSF leukocytosis and organisms identified on Gram stain or culture are all symptoms of meningitis.

(3) Peritonitis: fever, abdominal rigidity and tenderness (abdominal pseudocyst and abscesses can both present with a mass and a fever), and organisms identified by Gram stain or culture. Fever, leukocytosis and a positive blood culture are all signs of vascular shunts, with or without shunt nephritis or cor pulmonale.
(4) Minimal evidence of CSF contamination with bacteria collected from purulent exudate in or on shunt material, Gram stain of CSF extracted from the shunt or positive culture on fluid aspirated from the shunt under sterile conditions are all signs of an infected shunt apparatus. Any end of the shunt tube can become clogged, resulting in symptoms of an elevated ICP.

9.3. Laboratory Data

Leucocytosis with a high ESR. Blood culture is positive in less than one third of the cases. Shunt tap and CSF study, including culture, are very important. Culture of the shunt device after removal is positive in >90% of cases.

9.4. Treatment

Shunt infections are currently treated by shunt removal, as well as systemic or intraventricular antibiotics. Shunt removal, along with antibiotic treatment and external ventricular drainage, was determined to be the most efficient method of eradicating shunt infection in children (Gutierrez-Murgas and Snowden 2014; Schreffler et al. 2002). Vancomycin for the wide spectrum coverage of staphylococci and other Gram-positive organisms, and cefepime, ceftazidime or meropenem for the coverage of Gram-negative bacteria are two empiric antibiotics advised by the Infectious Diseases Society of America (Gutierrez-Murgas and Snowden 2014; Prusseit et al. 2009). Rifampicin may be added for increased coverage (Greenberg 2010). After obtaining the culture report, antibiotics may be modified. Antibiotics should be continued 10–14 days after the CSF becomes sterile (Greenberg 2010).

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