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# Tuberculosis: A More Than One Pathophysiology to Induce Neurological Disorder

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**Abstract:** Tuberculosis (TB) is an infectious disease which can infect all body organs including the central nervous system (CNS). TB has a higher mortality rate worldwide and is a frequent cause of neurologic sequelae. Approximately 10% of TB patients also have a CNS involvement. CNS-TB can take several clinical forms; Therefore, this review concentrates on the most prevalent types of CNS-TB because it is one of the most severe forms of extrapulmonary tuberculosis. Tuberculous meningitis is the most common type of CNS tuberculosis. The patient presents with insidious chronic meningitis or acute fulminant meningitis. Hydrocephalus is usually associated, especially in children, Intracranial vasculopathy, which is a serious complication of Tuberculous meningitis that can cause stroke. CNS tuberculomas is a hard-granulomatous mass that is commonly presented with focal neurologic impairments depending on its location, along with symptoms and signs of increased intracranial pressure. Tubercular Brain Abscess and Tuberculous Encephalopathy are uncommon clinical presentations of CNS tuberculosis; they usually affect children and HIV patients. Spinal TB (Pott illness) is a common form of skeletal TB that usually affects the thoracic and lumbar spines; if the cervical spine is affected, potentially fatal neurological consequences can occur. The definitive diagnosis of CNS tuberculosis is usually based on examining the CSF (as with TB meningitis) and being evaluated by neuroimaging are often the two main components of the final diagnosis of CNS tuberculosis (CT, MRI). Empirical anti-tuberculous medication, steroids, and only in exceptional circumstances, surgery, are used to treat patients.

**Keywords:** Tuberculosis, Extra-Pulmonary Tuberculosis, Pott's Disease, Tuberculomas, Tuberculous Meningitis

## 1. Introduction

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis, which is an acid-fast bacillus. TB is a significant global public health issue with an expected 9.9 million cases of the disease and 1.5 million deaths in 2020 [1]. About 95% and 98% of TB-related infections and deaths occur in underdeveloped nations [2]. TB mainly affects the lungs, causing pulmonary tuberculosis (PTB), but it can also affect extra-pulmonary tissues, causing extra-pulmonary tuberculosis (EPTB), which accounts for 21% of all TB cases, It can also affect extra-pulmonary tissues in addition to the lungs, where it causes pulmonary tuberculosis (PTB) [3]. The most severe form of EPTB is CNS involvement, which makes up more than 10% of EPTB patients but only around 1% of all TB cases [4]. According to Canadian cohort study found that TB patients had a 1.0% probability of acquiring CNS TB among 82,764 TB patients between 1970 to 2001 [5]. many factors, including young age, HIV infection, use of immunosuppressive medications, poor nutritional condition, and alcoholism, are reported to have an impact on the development of CNS TB [6-8]. In contrast to non-HIV persons, TB patients with HIV have a five-fold increased risk of developing CNS involvement [9]. This paper highlights the major neurological patterns of EPTB, including: tuberculous meningitis (TBM), CNS tuberculomas, tubercular brain abscess (TBA), tuberculous encephalopathy (TE), and Pott's disease.

## 2. Tuberculous Meningitis (TBM)

TBM is the most common form of CNS tuberculosis. Its manifestations range from insidious chronic meningitis to acute fulminant meningitis. The cascade of events starts with the hematogenous spread of tuberculosis bacteria from a primary source, typically the lungs, but they are unable to pass

the blood-brain barrier. Additionally, the bacilli are dispersed throughout the meninges and brain tissue, generating tiny granulomatous foci (tubercles). These tubercles join together to form larger caustic foci, which can burst into the subarachnoid space and result in meningitis [10]. This discharging caseous lesion is called "Rich focus". A thick exudate is present that leading to hydrocephalus by obstructing the basal cisterns or the cerebral aqueduct, particularly in young infants [11].

### *2.1. Clinical Picture*

Although there are many different clinical manifestations, most patients experience fever, headaches, and altered mental status and consciousness. Because of the buildup of exudate in the basal cisterns, cranial neuropathies frequently affect the sixth and seventh cranial nerves [12, 13]. Children are more prone to experience seizures, nausea, and vomiting [6]. If they grow, tuberculomas can result in seizures, strokes, and localized neurological impairments. Intracranial vasculopathy, which is common in TBM, is frequently complicated by stroke [14, 15].

### *2.2. Diagnosis*

The diagnosis of TBM is difficult, and further testing involving neuroimaging and CSF analysis is required. MRIs performed at the time of presentation are extremely accurate and may detect hydrocephalus, leptomeningeal enhancement, infarcts, and tuberculomas [15]. Since MRI is frequently unavailable in regions with high TB prevalence, CT is the preferred imaging technique.

Common CT findings include [16]:

1. Hydrocephalus.
2. Deep infarcts.
3. Basal meningeal enhancement.
4. Tuberculomas.
5. Precontrast basal hyperdensity.

Typical CSF examination show [17]:

1. lymphocytic-predominant pleiocytosis.
2. high proteins (more than 100 mg/dl).
3. Low sugar.

### *2.3. Management*

Empirical anti-tuberculous medications should be taken as soon as TBM is detected because the condition is linked to high mortality and persistent neurological squeals, particularly in young children [18]. The WHO recommends two stages for the treatment of TBM: a two-month intense phase using the drugs rifampicin, ethambutol, pyrazinamide, and isoniazid. Continuation phase using isoniazid with rifampicin for (10 months) [19].

Corticosteroids reduce mortality and relapse, and they can be used as an adjuvant therapy for TBM, particularly in cases when IRIS is present or in people who have PTB and HIV [20]. Presently, host-directed therapies (HDTs) are receiving attention, and numerous medications are being developed as supplements to current anti-tuberculous treatments. In experimental settings, HDTs lessen tissue necrosis and inflammation as well as aid in drug penetration and granuloma dissociation [21]. Hydrocephalus in TBM patients can be treated medically with diuretics or surgically with serial lumbar punctures or a ventriculoperitoneal shunt operation [22]. Only in cases of obstructive hydrocephalus is surgery recommended. Early shunt surgery can improve outcomes for hydrocephalus-affected kids by lowering mortality and morbidity [23, 24].

## 3. CNS Tuberculomas

Tuberculomas are 2–8 cm in diameter, hard, avascular, granulomatous masses that have zones of caseous necrosis where TB bacteria can be noticed. Although it can arise anywhere in the CNS, intracranial tuberculomas are far and away the most frequent. And they can happen even if there is no evidence of TB infection outside the CNS [25]. According to Nelson CA and Zunt JR 10% of patients with TBM also have tuberculomas [26].

*Clinical Picture and Diagnosis*

The most frequent clinical presentation is focal neurologic impairments depending on the location of the lesion, along with fever, headaches, seizures, and papilledema. The primitive diagnosis is typically based on neuroimaging; a CT scan may reveal the presence of low- or high-density masses with strong homogeneous or ring enhancement with contrast. On a CT scan, the presence of a central calcification "target sign" surrounded by ring enhancement is pathognomonic for tuberculoma [27].

Management of tuberculomas is the same as for TBM, but there is considerable debate over how long it should last since some doctors advise delaying therapy until there is no longer any contrast enhancement on a CT scan and because persistent tuberculoma is linked to ongoing neurologic impairments [28]. The role of surgical in treating some conditions is unclear, and neurosurgical resection is only used to address serious problems such obstructive hydrocephalus.

## 4. Tubercular Brain Abscess (TBA)

TBA is a rare form of CNS tuberculosis characterized by a pus-filled encapsulation that may or may not show signs of a tubercular granuloma and which includes viable TB bacteria. Up to 7.5% of CNS tuberculosis patients without HIV in impoverished nations have TBA [29]. TBA make up 4% of all intracranial abscess cases [30]. Compared to tuberculomas, abscesses are more isolated, bigger, and grow more quickly. Images from MRIs and CT scans are diagnostic. Bacterial superinfection can happen in rare occasions [31].

*Clinical picture*

Clinical presentation includes seizures, a focal neurological deficit, increased intracranial pressure. Surgical exploration or pus drainage may influence excellent long-term outcomes [32].

# 5. Tuberculous Encephalopathy (TBE)

TBE is an uncommon clinical manifestation of CNS tuberculosis that predominantly affects children. It is believed to be caused by an immune system acting without an actual bacterial invasion.

*Clinical Picture and Diagnosis*

Clinical manifestations might range from a minor condition to a deadly one. TBE should be diagnosed if focal neurologic abnormalities, convulsions, stupor, and coma start to occur. Normal or somewhat aberrant CSF often has elevated protein levels. It is possible to see a pattern resembling hemorrhagic leukoencephalopathy or post-infectious demyelinating encephalomyelitis [33]. To reduce morbidity and mortality rate, early diagnosis and treatment with anti-tuberculous medications and steroids are essential.

# 6. Pott's Disease

Spinal TB (Pott illness) accounts for 50% of all skeletal TB cases, which represent 10% of all EPTB cases [34]. All parts of the spine, including the bones and the extradural and intradural regions of the spinal cord, are susceptible to TB. Although TB predominantly affects the thoracic and lumbar spines, the illness can also damage the cervical spine and cause potentially fatal neurological consequences [35]. The cancellous bone under the periosteum of the vertebral body anteriorly or close to the intervertebral disc is where the involvement of the vertebral bodies with TB begins. A paraspinal abscess that compresses the spinal cord, granulation tissue in the dura that causes compression, vertebral disintegration and collapse, or anterior spinal artery vasculitis that results in vascular insufficiency can all cause neurological impairments.

### *6.1. Clinical picture*

The clinical presentation is usually nonspecific and includes back pain, kyphosis, sensory symptoms, and paraparesis. Acute neurological impairments develop from compression of the spinal cord caused by a vertebral fracture or abscess.

### *6.2. Diagnosis*

In impoverished nations, spinal X-rays are the only form of neuroimaging available. Even though they may be normal in the early stages, plain radiographs can detect spondylitis with a sensitivity of 70% [36]. Early signs of spondylitis include radiolucency and plate border loss, which are followed by destruction of the vertebral body, sclerosis, and paravertebral masses. When one is available, an MRI can accurately diagnose the condition.

### *6.3. Management*

Before beginning empirical anti-tuberculous therapy (for 9 to 12 months) and corticosteroids, a presumptive diagnosis based on clinical manifestations and x-ray findings (or MRI, if available) is necessary for all kinds of spinal TB. Spondylitis surgical alternatives, including as decompression, fixation, and deformity correction, are taken into account on a case-by-case basis [37].

# 7. Conclusion

CNS tuberculosis is a global health problem, especially in areas with a high HIV burden. This disease can result in major neurological consequences. A 12-month course of therapy is suggested and is thought to be an important determinant of the outcome. The integration of CNS tuberculosis detection and therapy into national TB control programs is needed to ensure a better response.

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