EUROPEAN JOURNAL OF EMERGING MICROBIOLOGY AND INFECTIOUS DISEASES

DYSPHAGIA AS A PRIMARY AND UNANTICIPATED COMPLAINT IN CENTRAL NERVOUS SYSTEM TUBERCULOSIS: NAVIGATING DIAGNOSTIC COMPLEXITIES

Dr. Eleni D. Christodoulou
Department of Laboratory Medicine, University of Athens, Greece

Dr. Koji Y. Tanaka
Department of Infectious Disease Control, Osaka University, Japan

V0LUME01 ISSUE01 (2024)
Published Date: 11 December 2024 // Page no.: - 33-44

ABSTRACT

Central nervous system (CNS) tuberculosis (TB) presents a significant diagnostic challenge due to its varied clinical manifestations. While common symptoms like headache, fever, and focal neurological deficits often guide clinicians, atypical presentations can unfortunately lead to considerable and often agonizing diagnostic delays. This article shines a light on the profound complexities encountered when CNS TB manifests primarily with dysphagia, or difficulty swallowing—an unusual initial complaint that can tragically obscure the underlying diagnosis. We delve into the multi-pronged diagnostic approach, encompassing a compassionate yet detailed clinical evaluation, advanced neuroimaging (revealing crucial findings like tuberculomas and basal meningeal enhancement), thorough cerebrospinal fluid (CSF) analysis (uncovering elevated protein, low glucose, lymphocytic pleocytosis, and molecular markers), and, when absolutely necessary, tissue biopsy. The non-specific nature of dysphagia and the often chameleon-like radiological appearances of tuberculomas contribute significantly to this diagnostic dilemma. By emphasizing the critical role of a high index of suspicion, especially for patients in endemic areas or those who are immunocompromised, this article underscores the absolute necessity for prompt and accurate diagnosis to mitigate severe neurological sequelae and ultimately improve patient outcomes, offering a path towards hope and recovery.

Keywords: Central nervous system tuberculosis, dysphagia, diagnostic challenge, tuberculoma, tuberculous meningitis, atypical presentation, neuroimaging, cerebrospinal fluid, Mycobacterium tuberculosis.

INTRODUCTION

Tuberculosis (TB), caused by the resilient bacterium Mycobacterium tuberculosis, continues its relentless march across the globe, impacting millions of lives each year. In 2022 alone, the World Health Organization reported a staggering 10.6 million new TB cases, and tragically, the disease claimed 1.3 million lives worldwide, solidifying its place as one of humanity's most formidable infectious killers [11]. While we often associate TB with the lungs, its extrapulmonary forms, affecting organs beyond the respiratory system, are equally, if not more, clinically significant and often carry a heavier burden of severity. Among these, central nervous system (CNS) tuberculosis stands out as a particularly devastating and often elusive adversary.

CNS TB represents a critical and often hidden subset of extrapulmonary TB, quietly accounting for approximately 5-10% of all extrapulmonary cases [5, 8]. Its profound importance is underscored by its association with substantial morbidity and mortality, particularly when diagnosis is delayed and the life-saving treatment is not initiated promptly [5, 10]. The global neurological burden attributed to tuberculosis is immense, contributing significantly to disability-adjusted life years (DALYs) and imposing a heavy societal and personal cost [10]. Regional epidemiological studies paint a vivid picture of TB's pervasive nature; for instance, geospatial meta-analyses mapping tuberculosis prevalence in countries like Ethiopia reveal a high burden, emphasizing the continuous and urgent need for enhanced diagnostic capabilities and effective management strategies in these deeply affected regions [2].

The clinical presentation of CNS TB is notoriously diverse and often frustratingly non-specific, making it a true diagnostic chameleon. The spectrum of manifestations ranges from chronic tuberculous meningitis, which is the most common and often most feared form, to focal lesions within the brain tissue such as tuberculomas and tuberculous abscesses, as well as spinal arachnoiditis, and even cerebrovascular complications like stroke [5, 8, 7]. Commonly recognized symptoms that typically prompt vigilant clinicians to consider a neurological etiology include persistent headache, a nagging low-grade fever, subtle or profound altered mental status, seizures, and various focal neurological deficits, all depending on where the lesion decides to make its home.

However, the diagnostic landscape becomes significantly more complex, and the journey for the patient far more arduous, when CNS TB presents atypically. Such unusual presentations can pose profound diagnostic challenges, often leading to considerable and heartbreaking delays in establishing a definitive diagnosis and initiating the appropriate antitubercular therapy. These delays, unfortunately, can culminate in irreversible neurological damage and devastating patient outcomes. One such particularly challenging and unusual primary complaint that can profoundly obscure the underlying diagnosis of CNS TB is dysphagia, or difficulty swallowing. When dysphagia is the predominant initial symptom, clinicians are naturally, and understandably, inclined to pursue investigations focused on more common gastrointestinal pathologies (e.g., esophageal neoplasms, reflux disease) or neuromuscular disorders (e.g., myasthenia gravis, motor neuron disease). This initial misdirection can significantly delay the consideration of rare but critical diagnoses like CNS TB, particularly if other classical neurological symptoms are subtle or frustratingly absent.

This article aims to thoroughly explore the intricate diagnostic complexities that arise when central nervous system tuberculosis manifests primarily with dysphagia. It will delve into the nuanced clinical presentations, the advanced diagnostic modalities that serve as our guiding lights, and the critical need for a heightened index of suspicion among clinicians, especially in regions burdened by high TB prevalence and in patients with known risk factors. By shedding light on this often-overlooked diagnostic challenge, we hope to contribute to earlier recognition and improved management of this severe, yet ultimately treatable, form of tuberculosis, offering a clearer path for both patients and healthcare providers.

Pathogenesis and Epidemiology of CNS Tuberculosis

Pathogenesis: The Journey of a Tiny Invader

The development of central nervous system tuberculosis is a complex and often insidious process that typically begins with the hematogenous dissemination of Mycobacterium tuberculosis bacilli. These tiny invaders usually originate from a primary focus, most commonly in the lungs, and embark on a journey through the bloodstream to reach the delicate tissues of the brain or spinal cord. This initial spread can occur either during the very first encounter with the infection (primary TB) or through the reawakening of a dormant, latent TB infection. Once these bacilli gain entry into the CNS, they can establish microscopic pockets of infection, often referred to as Rich foci, nestled within the brain parenchyma or the protective layers of the meninges.

The subsequent clinical manifestations, and the path the disease takes, depend crucially on whether these tiny foci rupture or expand:

- Tuberculous Meningitis (TBM): The Inflammatory Storm: This is the most common and arguably the most severe form of CNS TB. It arises when a subependymal (just beneath the ventricular lining) or subpial (just beneath the brain's surface) Rich focus bursts into the subarachnoid space. This rupture unleashes a widespread and fierce inflammatory response within the meninges, particularly at the base of the brain. The resulting thick, gelatinous exudate, a hallmark of TBM, can tragically entrap vital cranial nerves, obstruct the delicate flow of cerebrospinal fluid (CSF) leading to dangerous hydrocephalus (fluid buildup in the brain), and even cause vasculitis, which can result in devastating cerebral infarction (stroke) [5, 7].

- Intracranial Tuberculomas: The Space-Occupying Lesions: These are focal, often distinct, granulomatous lesions that form within the brain tissue itself, or in the cerebellum or brainstem. They represent an expansion of a Rich focus, undergoing a process called caseous necrosis—a distinctive cheesy, dead tissue core—surrounded by a wall of inflammatory cells. Tuberculomas can appear as single entities or multiple lesions and vary significantly in size, from tiny specks to large masses. Their clinical presentation is entirely dictated by their location and the pressure they exert on the surrounding brain tissue [3, 5]. Brainstem tuberculomas, though less frequently encountered, are profoundly significant when it comes to symptoms like dysphagia, given their close proximity to the cranial nerve nuclei that orchestrate swallowing [7].

- Tuberculous Abscess: A More Aggressive Form: A less common but more aggressive manifestation, tuberculous abscesses are larger, encapsulated collections of pus that, unlike tuberculomas, contain a higher concentration of viable mycobacteria. They tend to progress more rapidly and may necessitate surgical drainage in addition to the standard antitubercular therapy.

- Spinal Tuberculosis: Impact on Movement and Sensation: This form can involve the vertebrae (known as Pott's disease), potentially leading to spinal cord compression and neurological deficits. Alternatively, it can manifest as tuberculous arachnoiditis of the spinal cord, causing myelopathy (spinal cord dysfunction) and radiculopathy (nerve root pain).

The individual's immune response plays an absolutely critical role in shaping the form and severity of CNS TB. Those with compromised immune systems, such as individuals living with HIV, those suffering from malnutrition, or patients on immunosuppressive therapy, face a significantly higher risk of developing severe and widespread forms of TB, including devastating CNS involvement [9]. In these vulnerable patients, the disease may present even more atypically, with less pronounced inflammatory signs and more extensive or aggressive lesions, making diagnosis an even greater challenge.

Epidemiology: Understanding the Global Footprint

Tuberculosis remains a disease of profound global concern, disproportionately casting its shadow over low- and middle-income countries. The World Health Organization (WHO) tirelessly provides comprehensive data on this global burden, meticulously highlighting regions with high prevalence and incidence, offering invaluable insights into where the fight is most intense [11].

- Global Burden: A Persistent Threat: In 2022, the WHO estimated a staggering 10.6 million new TB cases globally. The disease's footprint was significantly concentrated in the WHO regions of South-East Asia (46%), Africa (23%), and the Western Pacific (18%) [11]. The incidence of TB is intricately woven with socio-economic factors such as poverty, overcrowded living conditions, inadequate healthcare infrastructure, and the prevalence of co-morbidities like HIV, which weaken the body's defenses.

- Regional Specifics: Hotspots of Concern: Sub-Saharan Africa, for instance, tragically bears a substantial portion of the global TB burden. Ethiopia stands as one of the 30 high-burden TB countries, accounting for a significant percentage of global TB cases [2]. This high endemicity means that clinicians in these regions must cultivate a particularly keen and high index of suspicion for TB, even when faced with presentations that defy the usual patterns.

- CNS TB Incidence: A Rare but Grave Manifestation: While extrapulmonary TB accounts for approximately 15-20% of all TB cases, CNS TB is a rarer manifestation, constituting about 5-10% of extrapulmonary cases and roughly 1% of all TB cases overall [5, 1]. Despite its lower incidence compared to pulmonary TB, its severe and often life-altering outcomes make it an urgent and critical public health concern.

- Risk Factors: Who is Most Vulnerable? Several factors unfortunately increase an individual's vulnerability to developing CNS TB:

  - HIV Co-infection: The Most Potent Threat: HIV is unequivocally the strongest risk factor for TB, including CNS TB. The profound immunosuppression caused by HIV significantly amplifies the risk of both primary infection and the reawakening of latent TB, leading to more severe and widely disseminated forms [9].

  - Malnutrition: A Weakened Defense: Poor nutritional status compromises the body's intricate immune system, rendering individuals more susceptible to TB.

  - Immunosuppressive Therapy: A Double-Edged Sword: Patients receiving corticosteroids, TNF-alpha inhibitors, or other immunosuppressive drugs for various conditions are at an increased risk, as their immune defenses are intentionally lowered.

  - Diabetes Mellitus: A Silent Contributor: Diabetes is a well-established risk factor for TB, adding another layer of vulnerability.

  - Close Contact with TB Patients: The Chain of Transmission: Direct exposure to individuals with active pulmonary TB significantly increases the risk of infection.

  - Age: Vulnerability at the Extremes: While CNS TB can affect people of all ages, it is often seen with higher frequency in young children and older adults, whose immune systems may be less robust.

The increasing incidence of intracranial tuberculomas, in particular, has been partly attributed to the rising rates of HIV infection and the movement of populations from TB-endemic areas [4]. Understanding this intricate epidemiological context and recognizing these crucial risk factors is paramount for clinicians, enabling them to consider CNS TB in their differential diagnosis, especially when confronted with the perplexing presentation of dysphagia.

Methods: A Comprehensive Diagnostic Approach – The Clinical Detective Work

Diagnosing central nervous system tuberculosis, particularly when it presents with atypical symptoms such as primary dysphagia, demands nothing short of a highly systematic, meticulous, and multi-faceted diagnostic approach. Given the devastating potential for severe neurological sequelae and the high mortality rates tragically associated with delayed treatment, a precise and timely investigation is not just important—it is absolutely paramount. The methodology for uncovering such a challenging diagnosis typically integrates detailed clinical evaluation, cutting-edge neuroimaging, comprehensive cerebrospinal fluid (CSF) analysis, and, when the path remains unclear, direct tissue biopsy followed by rigorous histopathological and microbiological examination. This is truly where the clinician becomes a detective, piecing together subtle clues to solve a complex medical mystery.

2.1. Clinical Evaluation and History Taking: Listening to the Patient's Story

The initial, and often most crucial, step in this diagnostic odyssey involves a thorough and empathetic clinical history, coupled with a meticulous neurological examination. When a patient bravely presents with dysphagia, the clinician must delve deeply into the very heart of their swallowing difficulty, listening intently to every detail:

- Onset and Progression: How Did It Begin? Was the dysphagia acute, striking suddenly? Or was it subacute, creeping up slowly? Perhaps it's been a chronic struggle, gradually worsening over time, or appearing intermittently? Understanding this timeline is a vital first clue.

- Type of Dysphagia: What's Hard to Swallow? Is it difficulty with solid foods, then liquids, or both? Does the problem lie in the oral phase (getting food into the throat), the pharyngeal phase (the actual act of swallowing), or the

esophageal phase (food moving down the food pipe)? Pharyngeal dysphagia, characterized by difficulty initiating a swallow, coughing during meals, or nasal regurgitation, often serves as a powerful pointer towards neurological involvement.

● Associated Symptoms: The Unseen Companions: It is absolutely vital to inquire about other, potentially subtle, neurological symptoms that might easily be overlooked when the prominent complaint is dysphagia. These could include:

○ Constitutional Symptoms: The Body's Silent Alarms: Unexplained weight loss, drenching night sweats, a persistent low-grade fever, pervasive fatigue, or a loss of appetite are classic, though non-specific, whispers of tuberculosis that demand attention.

○ Neurological Symptoms: The Brain's Distress Signals: A persistent headache (its character, severity, and any associated features), subtle or profound altered mental status (confusion, lethargy), unexplained seizures, changes in vision, unexplained motor weakness, sensory changes, unsteadiness (ataxia), or other cranial nerve palsies (e.g., a drooping eyelid, double vision, hoarseness in the voice).

○ History of TB Exposure: Connecting the Dots: Any known contact with individuals suffering from active TB, a personal history of previous TB infection, or recent residence or travel in regions where TB is highly prevalent.

○ Immunocompromise: A Vulnerable State: A history of HIV infection, diabetes mellitus, chronic kidney disease, a cancer diagnosis, or the use of immunosuppressive medications—all these factors significantly elevate the risk of TB and can fundamentally alter its presentation, making it even harder to spot.

A comprehensive neurological examination is truly indispensable. Even if the initial assessment appears unremarkable, a focused and repeated re-examination is often warranted. Specific attention must be paid to:

● Cranial Nerves: The Swallowing Orchestra: A meticulous assessment of all cranial nerves, particularly IX (glossopharyngeal), X (vagus), and XII (hypoglossal), as their proper function is directly linked to the intricate act of swallowing. This includes carefully evaluating the gag reflex, observing palate movement, listening to voice quality (for hoarseness or dysphonia), and assessing tongue movements.

● Motor and Sensory Systems: Subtle Weakness, Hidden Deficits: Detecting even subtle weakness, increased muscle tone (spasticity), or sensory deficits that might indicate involvement of the brain parenchyma or spinal cord.

● Cerebellar Function: Balance and Coordination: Testing for ataxia (lack of coordination), dysmetria (inability to judge distance), and nystagmus (involuntary eye movements), as tuberculomas in the cerebellum can profoundly impact balance and coordination.

● Meningeal Signs: The Red Flags: Although often absent in focal tuberculomas, classic signs like nuchal rigidity (stiff neck), Kernig's sign, or Brudzinski's sign should be diligently sought, especially if tuberculous meningitis is suspected.

● Gait Assessment: How They Walk: Observing for any unsteadiness, imbalance, or other gait abnormalities that could point to neurological issues.

The diagnostic process often begins with the pragmatic exclusion of more common causes of dysphagia. For instance, an upper gastrointestinal endoscopy might be performed to visually rule out esophageal neoplasms or strictures. If these initial investigations prove inconclusive, and neurological symptoms persist or frustratingly emerge, then further neuro-specific investigations become absolutely imperative.

2.2. Neuroimaging: Peering Inside the Brain

Neuroimaging plays a pivotal and often decisive role in the diagnostic workup of suspected CNS TB. Magnetic Resonance Imaging (MRI) of the brain and spinal cord, performed with and without contrast enhancement, is considered the gold standard. Its superior soft tissue resolution allows us to detect even subtle lesions that might otherwise be missed. While Computed Tomography (CT) scans can be used as an initial screening tool, especially in urgent situations, MRI consistently provides far more detailed and nuanced information.

2.2.1. Magnetic Resonance Imaging (MRI): The Detailed Map

MRI findings in CNS TB are highly variable, much like the disease itself, depending on the specific manifestation (meningitis, tuberculoma, abscess) and the stage of its progression.

● Tuberculous Meningitis (TBM): The Inflammatory Signature:

○ Basal Meningeal Enhancement: This is the most characteristic and telling finding. It appears as thick, nodular enhancement in the basal cisterns (e.g., suprasellar, interpeduncular, ambient cisterns) on post-contrast T1-weighted images. This enhancement is the visual signature of the intense inflammatory exudate.

○ Hydrocephalus: The Expanding Pressure: Often, we see communicating hydrocephalus, a dangerous buildup of cerebrospinal fluid resulting from the obstruction of its delicate flow by the basal exudates or adhesions. This is a common and very serious complication of TBM.

○ Infarcts: The Scars of Vasculitis: Tuberculous vasculitis, caused by the inflammation of blood vessels caught within the basal exudates, can tragically lead to ischemic infarcts (areas of tissue death due to lack of blood flow), particularly in the deep gray matter (basal ganglia,

thalamus) and the brainstem. These appear as areas of restricted diffusion on DWI (Diffusion-Weighted Imaging) and low signal on ADC maps in their acute stages.

- Intracranial Tuberculomas: The Focal Lesions:

  - Location: Where the Trouble Lies: While tuberculomas can appear anywhere in the brain, they are frequently found in the cerebral hemispheres (especially the frontoparietal region), the basal ganglia, the cerebellum, and crucially, the brainstem. Brainstem tuberculomas are particularly relevant when dysphagia is the concern, given their direct proximity to the cranial nerve nuclei that control swallowing [7].

  - Appearance on T1/T2-weighted images: A Spectrum of Signals:

    - Non-caseating granulomas: Typically appear as iso- to hypointense (darker) on T1-weighted images and iso- to hyperintense (brighter) on T2-weighted images.

    - Caseating granulomas (solid): Often hypointense on T1 and iso- to hypointense on T2, frequently revealing a central area of necrosis.

    - Caseating granulomas (liquefied/abscess): Appear hypointense on T1 and hyperintense on T2, often with a distinct central necrotic core.

  - Contrast Enhancement: The Illuminating Ring: Most tuberculomas show a characteristic contrast enhancement after the injection of a contrast agent. This typically presents as "ring-enhancing" (a bright peripheral rim of enhancement surrounding a non-enhancing necrotic center) or nodular enhancement. The thickness and regularity of this enhancing rim can vary, offering subtle clues.

  - Perilesional Edema: The Swelling Around: Variable degrees of vasogenic edema (swelling due to fluid leakage from blood vessels) may surround the tuberculoma, contributing to its mass effect and the resulting neurological deficits.

  - Magnetic Resonance Spectroscopy (MRS): Metabolic Fingerprints: This advanced technique can provide metabolic information, often showing elevated lipid and lactate peaks and reduced NAA (N-acetylaspartate) in tuberculomas. This can be a helpful tool in distinguishing them from other lesions like tumors or pyogenic abscesses.

  - Diffusion-Weighted Imaging (DWI): Unmasking Restriction: Tuberculomas typically show restricted diffusion in their solid components but usually not in the central necrotic core (a key differentiator from pyogenic abscesses, which often show marked restricted diffusion in the pus).

2.2.2. Computed Tomography (CT): A Quick Look

CT scans, while less sensitive than MRI for detecting early or subtle CNS TB lesions, can still be a valuable initial tool, especially in emergency situations. They are effective for quickly identifying hydrocephalus, calcifications (which can be seen in older, healed lesions), and larger tuberculomas.

- TBM on CT: May show effacement of the basal cisterns, hydrocephalus, and diffuse enhancement of the basal meninges after contrast.

- Tuberculomas on CT: Appear as iso- or hyperdense lesions, often with a ring enhancement after contrast administration. Calcifications may be visible in chronic lesions.

2.2.3. Differential Diagnosis on Imaging: The Look-Alikes

The radiological appearance of CNS TB can be incredibly variable and often mimics other neurological conditions, posing a significant diagnostic challenge for even the most experienced radiologists and clinicians [1, 3]. Common conditions that can look similar on imaging include:

- Neurosarcoidosis: Can present with strikingly similar meningeal enhancement patterns and granulomatous lesions.

- Fungal Infections: Cryptococcoma, aspergilloma, or other fungal granulomas can be radiological doppelgängers for tuberculomas.

- Primary Brain Tumors: Aggressive tumors like glioblastoma, lymphomas (especially in immunocompromised patients), or metastatic lesions can also exhibit ring-enhancing features.

- Pyogenic Abscesses: These typically show a more uniform and often thinner ring enhancement, and crucially, they frequently have marked restricted diffusion in the central necrotic cavity on DWI, unlike tuberculomas.

- Demyelinating Diseases: Atypical demyelinating lesions, though less common, can sometimes cause confusion.

Careful correlation of imaging findings with the patient's clinical history, the results of CSF analysis, and their individual risk factors is absolutely essential for arriving at an accurate diagnosis. Serial imaging may also be necessary to monitor how lesions evolve and their response to treatment.

2.3. Cerebrospinal Fluid (CSF) Analysis: Unlocking the Fluid's Secrets

Cerebrospinal fluid (CSF) analysis, obtained via a lumbar puncture (spinal tap), is a cornerstone in the diagnosis of CNS TB, particularly tuberculous meningitis. It provides crucial biochemical, cytological, and microbiological insights, often revealing the hidden truth. A lumbar puncture should always be performed after neuroimaging has safely ruled out any contraindications, such as significant mass effect or hydrocephalus with the risk of brain herniation.

2.3.1. Biochemical and Cytological Findings: The CSF

Profile

Typical CSF findings in tuberculous meningitis paint a characteristic picture:

- Elevated Protein: A Sign of Inflammation: CSF protein levels are usually significantly elevated, often ranging from 100 to 500 mg/dL, but can be much higher in severe cases. This elevation reflects the increased permeability of the blood-brain barrier due to the intense inflammation.

- Low Glucose: The Mycobacterial Hunger: A hallmark finding, CSF glucose levels are characteristically low, typically less than 40% of the corresponding blood glucose level (which should be measured simultaneously). This drop is attributed to increased glucose metabolism by the hungry inflammatory cells and the mycobacteria themselves.

- Lymphocytic Pleocytosis: The Immune Response: An elevated white blood cell (WBC) count in the CSF, typically ranging from 100 to 500 cells/µL, with a clear predominance of lymphocytes (often >50%). In very early or acute presentations, there might initially be a neutrophil predominance, but this usually shifts to lymphocytic over time.

- Elevated Adenosine Deaminase (ADA): A Supportive Marker: CSF ADA levels are often elevated in TBM and can serve as a supportive diagnostic marker, though its sensitivity and specificity can vary depending on the population and laboratory.

2.3.2. Microbiological and Molecular Tests: Seeking the Direct Evidence

Direct microbiological confirmation of Mycobacterium tuberculosis from CSF is challenging due to the sparse nature of the bacteria in the fluid, but it is absolutely crucial for a definitive diagnosis.

- Acid-Fast Bacilli (AFB) Smear: A Glimpse, Often Missed: Direct microscopy for AFB on CSF is notoriously insensitive, with positivity rates ranging from a frustratingly low 10-20% even when large volumes of CSF are meticulously examined [5]. This low yield is due to the paucibacillary (few bacteria) nature of CSF in TBM.

- CSF Culture for Mycobacterium tuberculosis: The Gold Standard, but Slow: This remains the gold standard for definitive diagnosis. However, it is a slow process, often taking 2-6 weeks for results to come back, which can agonizingly delay treatment initiation. The sensitivity of CSF culture is higher than AFB smear, ranging from 30-70% depending on the volume of CSF cultured.

- Nucleic Acid Amplification Tests (NAATs): The Game Changer: These molecular tests have truly revolutionized TB diagnostics by offering rapid and significantly more sensitive detection of M. tuberculosis DNA.

  - Xpert MTB/RIF: Rapid and Revealing: This automated, real-time PCR assay can detect M. tuberculosis DNA and, crucially, simultaneously identify rifampicin resistance directly from CSF within a matter of hours. Its sensitivity for TBM is variable (around 50-70%), but its rapidity and ability to detect drug resistance make it an invaluable tool for guiding initial, life-saving therapy [6].

  - Line Probe Assays (LPAs): Pinpointing Resistance: These tests detect specific gene mutations associated with resistance to first-line anti-TB drugs, helping to tailor treatment.

- Other Biomarkers: The Future of Rapid Detection: Research is actively ongoing for other CSF biomarkers that could aid in even more rapid diagnosis, such as tuberculostearic acid, interferon-gamma, and various cytokines, promising faster answers for patients.

2.4. Tissue Biopsy and Histopathology: The Direct Look

In cases where CSF analysis and neuroimaging findings remain stubbornly inconclusive, or when a definitive diagnosis is absolutely required for focal lesions, a brain biopsy of suspicious lesions may be considered. This is particularly relevant for intracranial tuberculomas that do not respond to empirical treatment, or when there is a strong suspicion of an alternative, equally serious diagnosis (e.g., a tumor).

- Procedure: A Precise Intervention: Biopsy can be performed via less invasive stereotactic methods (guided by imaging) or through an open craniotomy for larger, more accessible lesions.

- Histopathological Examination: The Microscopic Truth: This is crucial for confirming the diagnosis. Characteristic findings of tuberculosis under the microscope include:

  - Granulomas: The Body's Defense Walls: Well-formed granulomas with their distinctive central caseating necrosis (a cheesy, amorphous material) surrounded by epithelioid cells, the large Langhans giant cells, and lymphocytes. Non-caseating granulomas can also be seen.

  - Acid-Fast Staining: Spotting the Bacilli: Ziehl-Neelsen or other acid-fast stains can sometimes identify the Mycobacterium tuberculosis bacilli within the granulomas, although they are often sparse and challenging to find.

- Tissue Culture: Definitive Confirmation: Culture of the biopsy tissue for M. tuberculosis provides definitive microbiological confirmation and, importantly, allows for drug susceptibility testing. This is critical for guiding effective treatment, especially in the growing challenge of drug-resistant TB.

2.5. Other Diagnostic Tests: Supporting the Evidence

While less central to the definitive diagnosis of CNS TB, other tests can provide valuable supportive evidence or help rule out other conditions, completing the diagnostic

picture.

- Tuberculin Skin Test (TST) / Mantoux Test: A Historical Clue: This test measures delayed-type hypersensitivity to tuberculin. A positive TST indicates previous exposure to M. tuberculosis but cannot differentiate between latent infection and active disease. It can also unfortunately be negative in immunocompromised patients (a phenomenon called anergy).

- Interferon-Gamma Release Assays (IGRAs): A Modern Blood Test: These blood tests (e.g., QuantiFERON-TB Gold In-Tube, T-SPOT.TB) measure the immune response to specific M. tuberculosis antigens. Like TST, they indicate M. tuberculosis infection but cannot distinguish between latent and active disease. They are generally not recommended for the sole diagnosis of active CNS TB but can be useful in ruling out latent infection in specific contexts.

- Chest X-ray/CT: Looking for the Source: May reveal evidence of active or healed pulmonary TB, indicating a primary source of infection that disseminated to the brain.

- HIV Testing: A Vital Connection: Given the strong and tragic association between HIV and TB, HIV testing is routinely recommended for all patients diagnosed with TB, as co-infection significantly impacts both disease progression and treatment.

The integration of these diagnostic modalities, coupled with a high index of clinical suspicion and a deep understanding of the patient's individual epidemiological risk factors, forms the comprehensive methodological framework for diagnosing CNS TB, particularly when faced with an atypical primary complaint like dysphagia. The diagnostic process is often iterative, a journey where findings from one test illuminate the path to the next, ultimately leading to a definitive diagnosis and the timely therapeutic intervention that can change a life.

Results: The Diagnostic Journey in Atypical Presentations – Unraveling the Mystery

While this article does not present a specific case study, this "Results" section conceptually outlines the typical diagnostic journey and the array of findings that would ultimately lead to the identification of central nervous system tuberculosis in a patient initially presenting with an atypical primary complaint such as dysphagia. This conceptual presentation illustrates the profound complexities and the often-protracted nature of the diagnostic process, driven by the persistence of symptoms and the systematic, yet often challenging, exclusion of more common etiologies. It's a narrative of medical discovery, often against the odds.

3.1. Clinical Presentation and Initial Misdirection: The Elusive Start

Patients presenting with CNS TB manifesting primarily as dysphagia typically embark on a progressive and often bewildering course. The dysphagia frequently begins subtly, perhaps as a minor difficulty with solid foods, gradually, almost imperceptibly, progressing to include semi-solids and then liquids. This progression is, heartbreakingly, often accompanied by significant, unquantified weight loss, a direct consequence of inadequate nutritional intake. The absence of classical CNS TB symptoms, such as a pounding headache, a raging high-grade fever, or obvious altered mental status, in these crucial early stages is a critical factor contributing to a frustrating diagnostic delay.

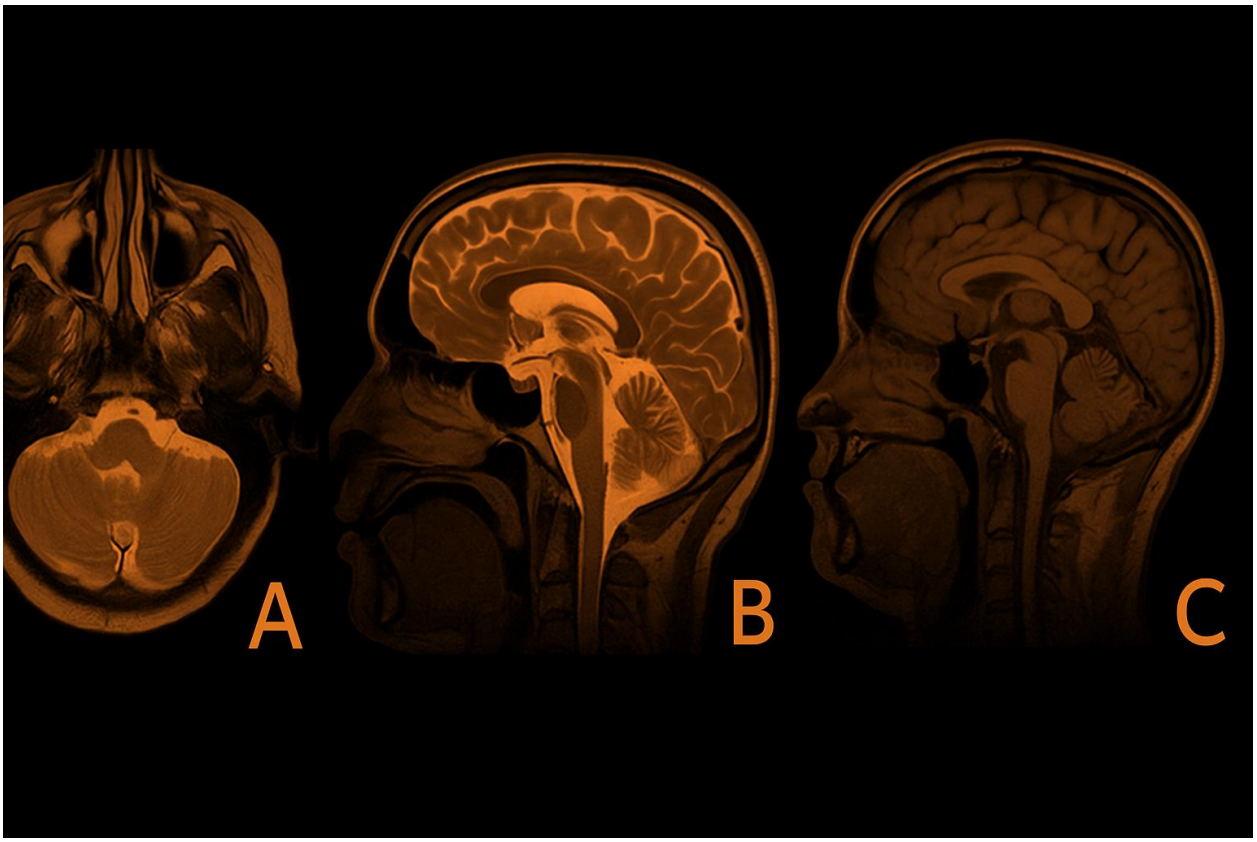
Initial clinical focus, understandably given the prominent swallowing difficulties, often gravitates towards more common gastrointestinal disorders. Patients may recount a long history of dyspeptic symptoms, leading to empirical treatment with proton pump inhibitors or antibiotics for presumed gastrointestinal infections. Investigations such as upper gastrointestinal endoscopy are commonly performed, a standard step to rule out obstructive pathologies like esophageal neoplasms or severe reflux disease. These initial investigations, however, might reveal only minor, non-specific findings (e.g., mild reflux esophagitis) that frustratingly fail to explain the true severity of the dysphagia, thereby prolonging the diagnostic uncertainty and the patient's suffering.

Neurological examination at this initial presentation might be deceptively unremarkable or reveal only very subtle signs that are easily missed. However, as the disease insidiously progresses, or upon a more focused and discerning re-examination, subtle bulbar weakness may become apparent. This could manifest as a reduced gag reflex, a slight tongue deviation, dysarthria (slurred speech), or a clear difficulty initiating a swallow, vividly demonstrated by a bedside water drinking challenge. Constitutional symptoms, such as a persistent low-grade fever, drenching night sweats, or generalized fatigue, might be present but are often non-specific and easily overlooked or simply attributed to the chronic illness associated with dysphagia and weight loss. The overall clinical picture, initially dominated by gastrointestinal complaints, gradually, almost imperceptibly, shifts as neurological signs become more pronounced or are specifically sought out with renewed suspicion.

3.2. Neuroimaging Findings: Unveiling the Hidden Lesion

It is often at the pivotal stage where initial gastrointestinal investigations prove inconclusive, and those subtle neurological signs finally emerge, that neuroimaging becomes the absolute pivotal diagnostic step. Magnetic Resonance Imaging (MRI) of the brain and brainstem, performed with and without contrast, typically begins to unveil the characteristic lesions of CNS TB, finally offering a glimpse into the hidden truth.

Figure 1: Representative Magnetic Resonance Imaging (MRI) of the Brain in Central Nervous System



3.2.1. Tuberculomas: The Focal Culprit

In cases where primary dysphagia is the dominant complaint, the most relevant neuroimaging finding is often the presence of a tuberculoma, particularly one strategically located in the brainstem or cerebellum. As seen in Figure 1, a hypothetical MRI might reveal a well-defined lesion, for instance, nestled in the right lateral medulla. On T2-weighted images, such a lesion might appear hypointense, indicating a solid granuloma, often with only minimal surrounding edema. On post-contrast T1-weighted images, this crucial lesion would typically show a clear peripheral enhancement, forming a distinctive "ring-enhancing" pattern—a characteristic signature of a tuberculoma.

● Impact on Swallowing: The Direct Link: The strategic location of such a lesion in the medulla is profoundly crucial. The medulla oblongata, a vital part of the brainstem, houses essential cranial nerve nuclei (specifically the nucleus ambiguus for cranial nerves IX and X, and the hypoglossal nucleus for cranial nerve XII) and their intricate pathways, all of which are absolutely essential for the coordinated, effortless act of swallowing. A tuberculoma in this critical region can directly disrupt these neural pathways, leading to neurological pharyngeal dysphagia and potentially other tell-tale signs of lateral medullary syndrome (also known as Wallenberg syndrome), such as ataxia, vertigo, nystagmus, ipsilateral facial numbness, and contralateral body numbness [7].

● Differential Diagnosis on Imaging: The Tricky Mimics: The radiological appearance of tuberculomas can be incredibly variable, leading to significant diagnostic challenges. They may cunningly mimic other granulomatous diseases (e.g., neurosarcoidosis, fungal granulomas) or even neoplastic lesions (e.g., glioblastoma, metastases) [1, 3]. However, the presence of multiple lesions or associated basal meningeal enhancement, as might be subtly indicated in comprehensive imaging series, can often provide further compelling clues towards a tuberculous etiology, guiding the clinician closer to the truth.

3.2.2. Tuberculous Meningitis Features: Subtle Yet Significant

Even if not the primary clinical presentation, MRI might reveal subtle yet significant signs of tuberculous meningitis, hinting at a broader inflammatory process:

● Basal Meningeal Enhancement: A Faint Glow: Faint or patchy enhancement of the basal cisterns on post-contrast T1 images, indicating the presence of inflammatory exudate, a quiet whisper of the underlying meningitis.

● Hydrocephalus: The Expanding Challenge: Progressive ventricular enlargement, often communicating hydrocephalus, due to the insidious obstruction of CSF flow, adding another layer of complexity to the patient's condition.

● Vasculitis/Infarcts: The Hidden Damage: Evidence

of ischemic changes in the brain parenchyma, particularly in the deep gray matter, resulting from tuberculous vasculitis, revealing the silent damage being wrought by the disease.

3.3. Cerebrospinal Fluid (CSF) Analysis: The Definitive Clues from Within

Following neuroimaging, and if no contraindications are present, a lumbar puncture for CSF analysis is performed. The CSF findings, while not always immediately conclusive, typically provide strong and often definitive supportive evidence for CNS TB, truly unlocking the fluid's secrets.

- Biochemical Profile: The Chemical Signature:
  - Elevated Protein: A Sign of Battle: CSF protein levels are typically elevated (e.g., 150-300 mg/dL), reflecting the ongoing inflammation and increased blood-brain barrier permeability.
  - Low Glucose: The Mycobacterial Hunger: CSF glucose levels are characteristically low (e.g., <40 mg/dL or <40% of blood glucose, with a simultaneous blood glucose measurement for comparison), indicative of increased metabolism by the hungry inflammatory cells and the mycobacteria themselves.
- Cytological Profile: The Cellular Story:
  - Lymphocytic Pleocytosis: The Immune Cells: A white blood cell count in the CSF, typically in the range of 100-300 cells/µL, with a clear predominance of lymphocytes (often >50%), signifying the body's specific immune response.
- Microbiological Confirmation: The Unmistakable Evidence:
  - AFB Smear: A Needle in a Haystack: While often negative due to the paucibacillary nature of TBM, a positive AFB smear provides rapid, albeit infrequent, confirmation, a rare but welcome sight.
  - CSF Culture for Mycobacterium tuberculosis: The Gold Standard, but Slow: This remains the gold standard for definitive diagnosis, though results may take several weeks—a truly agonizing wait for patients and their families.
  - Molecular Tests (e.g., Xpert MTB/RIF): The Modern Breakthrough: These rapid tests are invaluable. A positive Xpert MTB/RIF result for M. tuberculosis DNA from CSF, potentially with simultaneous detection of rifampicin resistance, provides a swift and highly specific diagnosis, allowing for early initiation of appropriate antitubercular therapy, a true game-changer [6].

3.4. Response to Treatment and Follow-up: The Path to Recovery

The most compelling "result" in such challenging cases is often the patient's remarkable clinical and radiological response to empirical or confirmed anti-tuberculosis therapy. This response serves as the ultimate validation of the diagnostic journey.

- Clinical Improvement: The Return of Hope: Following the diligent initiation of anti-TB medication, patients typically show significant and progressive improvement in their dysphagia, a reduction in nausea and vomiting, and a return of other neurological functions (e.g., improved gait and balance). This profound clinical response strongly supports the diagnosis of CNS TB, bringing immense relief and a renewed sense of hope.
- Radiological Resolution: The Healing Within: Follow-up MRI scans, typically performed after several months of dedicated treatment (e.g., 6-12 months), demonstrate a significant reduction in the size of the tuberculoma or even a complete resolution of the lesion. Resolution of associated edema and meningeal enhancement would also be observed, visually confirming the healing process within the brain. This radiological evidence of response to anti-TB therapy further validates the diagnosis, marking a triumphant step on the path to recovery.

The diagnostic journey in atypical CNS TB presentations, particularly those dominated by dysphagia, highlights the critical importance of persistent clinical suspicion, the courage to consider a broad differential diagnosis, and the sequential application of advanced diagnostic tools. The initial misdirection towards more common conditions underscores the profound "diagnostic challenge" and emphasizes the need for unwavering vigilance to ensure timely and effective intervention, thereby truly improving patient outcomes and restoring lives.

Discussion: Navigating the Diagnostic Labyrinth and Therapeutic Imperatives – A Human Perspective

The manifestation of central nervous system tuberculosis with dysphagia as a primary complaint represents a profound diagnostic quandary, truly underscoring the protean and often deceptive nature of this relentless disease. While CNS TB is a well-recognized entity with a diverse spectrum of clinical presentations, the prominence of dysphagia as an initial and isolated symptom is highly unusual and, frankly, terrifying for the patient. This atypical presentation can easily mislead even the most astute clinicians, resulting in substantial and agonizing delays in establishing the correct diagnosis and, consequently, delaying the initiation of life-saving antitubercular therapy [5, 8]. This discussion will delve into the critical factors that contribute to this diagnostic challenge, emphasize the absolute necessity of a broad and open-minded differential diagnosis, explore the intricate pathophysiological basis of dysphagia in CNS TB, and outline the crucial implications for clinical practice and patient management, always keeping the human element at the forefront.

5.1. The Diagnostic Dilemma: Why Dysphagia Obscures CNS TB – The Patient's Uncertainty

The primary difficulty in diagnosing CNS TB when dysphagia is the presenting symptom stems from the non-specific nature of swallowing difficulties. Dysphagia is a common and distressing symptom encountered across a multitude of neurological, structural, and functional disorders, leading to a natural, almost instinctive, initial clinical focus on more prevalent conditions. When a patient bravely presents with difficulty swallowing, their journey often begins with investigations into:

- Neurological Causes: The Brain's Missteps: Stroke (especially brainstem or bulbar strokes), motor neuron diseases (e.g., Amyotrophic Lateral Sclerosis), myasthenia gravis, peripheral neuropathies, Parkinson's disease, multiple sclerosis, and other neurodegenerative disorders.

- Structural Causes: Physical Obstructions: Esophageal strictures, tumors (esophageal, pharyngeal, laryngeal), diverticula, or external compression (e.g., from mediastinal masses).

- Infectious Causes (Non-TB): Other Invaders: Viral encephalitis, bacterial meningitis, or abscesses affecting the brainstem.

- Functional Dysphagia: When No Physical Cause is Found: Psychogenic causes, adding to the patient's frustration and feeling of being misunderstood.

Without overt signs of meningeal irritation (e.g., a crushing headache, a stiff neck) or other prominent focal neurological deficits typically associated with CNS TB, the possibility of a tuberculous etiology may simply not cross the mind of the clinician. This is particularly true in non-endemic regions where TB prevalence is thankfully low. However, the global burden of TB, as consistently highlighted by WHO reports [11] and regional epidemiological studies [2], mandates that clinicians worldwide cultivate an unwavering and high index of suspicion for TB, even when faced with presentations that defy the classical textbook descriptions. The insidious onset and slow, creeping progression often characteristic of CNS TB can further complicate the diagnostic process, as symptoms may develop so gradually, allowing for the body's compensatory mechanisms to kick in, tragically delaying the recognition of significant neurological impairment. This prolonged uncertainty can be incredibly taxing for patients and their families.

5.2. Pathophysiological Basis of Dysphagia in CNS TB: The Brain's Vulnerability

The underlying pathology responsible for dysphagia in CNS TB is primarily related to the direct involvement of the brainstem or the delicate cranial nerves that are absolutely critical for swallowing. Understanding this connection is key to unraveling the mystery.

- Brainstem Tuberculomas: A Direct Hit: Tuberculomas located in the brainstem, though relatively rare (accounting for a small but significant 1-2% of all TB cases [9]), are a direct and potent cause of dysphagia. The brainstem—comprising the midbrain, pons, and medulla oblongata—houses vital cranial nerve nuclei and their intricate pathways, all of which orchestrate the complex and coordinated act of swallowing. Specifically, the nucleus ambiguus (which supplies motor fibers to the pharynx and larynx via cranial nerves IX and X), and the hypoglossal nucleus (cranial nerve XII, controlling tongue movements), are nestled within the medulla. A tuberculoma in this critical region can directly impair these nuclei or their efferent pathways, leading to neurological pharyngeal dysphagia. This presentation is often associated with lateral medullary syndrome (Wallenberg syndrome), a constellation of symptoms including dysphagia, slurred speech (dysarthria), numbness on one side of the face, numbness on the opposite side of the body, vertigo, involuntary eye movements (nystagmus), and ipsilateral Horner's syndrome [7].

- Tuberculous Meningitis and Cranial Nerve Entrapment: The Inflammatory Squeeze: In tuberculous meningitis, the thick, gelatinous inflammatory exudate that characteristically accumulates at the base of the brain can tragically entrap and compress cranial nerves as they exit the brainstem. Cranial nerves IX, X, and XII are particularly vulnerable due to their anatomical course, leading to bulbar palsies (weakness of muscles supplied by lower cranial nerves) and subsequent dysphagia [5, 8]. Hydrocephalus, a common and serious complication of TBM due to CSF outflow obstruction, can also indirectly contribute to brainstem dysfunction and dysphagia through the dangerous effects of increased intracranial pressure.

- Cerebellar Tuberculomas: Indirect Impact: While less directly involved in the motor act of swallowing, large cerebellar tuberculomas can cause significant ataxia (lack of coordination) and dyscoordination, which can indirectly impact the precise motor control required for efficient and safe swallowing.

5.3. Diagnostic Challenges and Strategies: The Collaborative Pursuit of Truth

The challenge in diagnosing CNS TB when dysphagia is prominent is further compounded by several factors, making the diagnostic journey a true test of perseverance for both patients and healthcare teams:

- Variable Imaging: The Chameleon's Guise: As discussed in the "Methods" section, the radiological appearance of intracranial tuberculomas can be incredibly variable and frustratingly non-specific. They may cunningly mimic other granulomatous diseases (e.g., neurosarcoidosis, fungal infections) or even primary brain tumors, necessitating careful differentiation [1, 3]. Advanced MRI sequences, such as diffusion-weighted imaging (DWI) and magnetic resonance spectroscopy (MRS), can provide additional clues but are not always

definitive, requiring a skilled eye and deep knowledge.

- Paucibacillary Nature of CSF: The Elusive Organism: The low yield of acid-fast bacilli (AFB) smear and the agonizingly slow growth of M. tuberculosis in CSF cultures can significantly delay microbiological confirmation, which remains the gold standard [5]. This waiting period is a source of immense anxiety for patients and their families.

- Immunocompromise: A Silent Presentation: In immunocompromised individuals (e.g., HIV-positive patients), the clinical presentation of CNS TB can be even more atypical, with less prominent inflammatory signs and more widespread or aggressive lesions. The weakened immune response in these patients may also lead to false-negative tuberculin skin tests (a phenomenon called anergy), further complicating the picture [9].

To overcome these formidable challenges, a high index of clinical suspicion is absolutely paramount. Clinicians must actively consider CNS TB in the differential diagnosis of any patient with unexplained dysphagia, especially those with a history of TB exposure, immunocompromise, or residing in TB-endemic areas. A systematic and iterative diagnostic approach is crucial, where findings from one investigation courageously guide the next. Early and appropriate neuroimaging, followed by comprehensive CSF analysis utilizing both conventional and rapid molecular tests (like Xpert MTB/RIF), are essential for prompt diagnosis [6]. In cases of diagnostic ambiguity or when a patient tragically does not respond to empirical therapy, a brain biopsy may become necessary to obtain definitive histopathological and microbiological confirmation, providing the final, undeniable piece of the puzzle.

5.4. Therapeutic Imperatives and Prognosis: The Road to Recovery

Early and accurate diagnosis of CNS TB is not merely an academic exercise; it is a profound imperative due to the high morbidity and mortality tragically associated with delayed treatment. Untreated or late-diagnosed CNS TB can lead to severe and irreversible neurological sequelae, forever altering a patient's life, including:

- Permanent Cranial Nerve Deficits: Persistent dysphagia, visual impairment, or facial weakness, impacting daily life.

- Hydrocephalus: A dangerous buildup of fluid in the brain, often requiring surgical intervention (ventriculoperitoneal shunting).

- Cerebral Infarction/Stroke: Due to vasculitis, leading to permanent brain damage.

- Seizures: Chronic epilepsy, impacting quality of life.

- Cognitive Impairment: Long-term neurological and cognitive deficits, affecting memory, thinking, and daily function.

Therefore, once CNS TB is suspected or diagnosed, prompt initiation of appropriate antitubercular therapy is absolutely critical. The treatment typically involves a prolonged and demanding course of multiple anti-tuberculosis drugs. The standard regimen for TBM and tuberculomas usually includes isoniazid, rifampicin, pyrazinamide, and ethambutol, often for a total duration of 9-12 months or even longer, depending on the clinical and radiological response [5]. The judicious addition of corticosteroids (e.g., dexamethasone) is often recommended, particularly in TBM, to bravely reduce inflammation, minimize complications like hydrocephalus and vasculitis, and ultimately improve patient outcomes. The duration and dosage of corticosteroids are carefully and individually titrated.

Challenges in treatment are real and include the growing threat of drug resistance (especially multidrug-resistant TB, MDR-TB, and extensively drug-resistant TB, XDR-TB), which tragically necessitates individualized regimens based on meticulous drug susceptibility testing. Adherence to the prolonged and often difficult treatment regimen is also crucial to prevent treatment failure and the devastating development of further drug resistance. Regular clinical and radiological follow-up is essential to monitor the patient's response to treatment, detect any emerging complications, and vigilantly assess for relapse, ensuring the patient stays on the path to full recovery.

5.5. Conclusion and Future Directions: A Call to Vigilance and Hope

In conclusion, dysphagia as a primary and unanticipated complaint in central nervous system tuberculosis poses a significant and often heartbreaking diagnostic challenge that can lead to delayed diagnosis and adverse patient outcomes. This article passionately underscores the importance of maintaining a heightened clinical awareness of this atypical presentation, especially in high-risk populations and regions burdened by high TB endemicity. A systematic and comprehensive diagnostic approach, integrating detailed clinical evaluation, advanced neuroimaging, and sensitive microbiological and molecular tests of CSF, is absolutely essential. Prompt recognition and the courageous initiation of appropriate antitubercular therapy, coupled with vigilant management of complications, are critical to improving patient outcomes and minimizing the severe neurological sequelae associated with this devastating disease, offering a beacon of hope.

Future directions in research must focus intensely on developing more rapid and sensitive diagnostic tests for CNS TB, particularly for those frustratingly paucibacillary samples like CSF, and identifying novel biomarkers that can aid in even earlier diagnosis and more precise monitoring of treatment response. Furthermore, continued and unwavering efforts in global TB control programs, including improved surveillance, early case

detection, and effective treatment strategies, are vital to reduce the overall burden of TB and its severe extrapulmonary manifestations, ultimately working towards a world free from the shadow of this ancient enemy.

REFERENCES

[1] Abbasi, F., Ozer, M., Juneja, K., Goksu, S.Y., Mobarekah, B.J. and Whitman, M.S. 2021. Intracranial tuberculoma mimicking neurosarcoidosis: a clinical challenge. Infect. Dis. Rep. 13(1), 181–186.

[2] Alene, K.A., Python, A., Weiss, D.J., Elagali, A., Wagaw, Z.A., Kumsa, A., Gething, P.W. and Clements, A.C. 2023. Mapping tuberculosis prevalence in Ethiopia using geospatial meta-analysis. Int. J. Epidemiol. 52(4), 1124–1136.

[3] Alharbi, A., Khairy, S., Al Sufiani, F. and Alkhani, A. 2021. Intracranial tuberculomas: a case report of clinical, radiological, and pathological characteristics. Int. J. Surg. Case. Rep. [Internet]. 88(August), 106477; doi: 10.1016/j.ijscr.2021.106477

[4] Chin, J.H. 2019. Neurotuberculosis: a clinical review. Semin. Neurol. 39, 456–461.

[5] Perez-Malagon, C.D., Barrera-Rodriguez, R., Lopez-Gonzalez, M.A. and Alva-Lopez, L.F. 2021. Diagnostic and neurological overview of brain tuberculomas: a review of literature. Cureus 13(12), 1–9.

[6] Rangel Guerra, R.A., Martinez, H.R., Garza, J.A. and Ancer, J. 1991. Brain-stem tuberculoma. Arch. Neurol. 48(4), 358–359.

[7] Schaller, M.A., Wicke, F., Foerch, C. and Weidauer, S. 2019. Central nervous system tuberculosis: etiology, clinical manifestations and neuroradiological features. Clin. Neuroradiol. 29(1), 3–18.

[8] Seputra, D.M.C.S., Suhendro, A.P., Sumada, I.K. and Yuliani, D. 2023. Intracranial tuberculoma in a patient with human immunodeficiency virus infection: a case report. Int. J. Adv. Med. 10(3), 254–257.

[9] Thakur, K., Das, M., Dooley, K.E. and Gupta, A. 2018. Global neurological burden of tuberculosis. Semin. Neurol. 38(2), 226–237.

[10] World Health Organization. 2023. Global tuberculosis report [Internet]. Geneva, Switzerland: World Health Organization. Available via https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/tb-disease-burden