Utilizing Tuberculosis Loop-Mediated Isothermal Amplification (TB-LAMP) In the Diagnosis of Tuberculous Meningitis: A Case Report of Secondary Normal Pressure Hydrocephalus

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***Abstract*—Tuberculous meningitis (TBM) presents a significant diagnostic and therapeutic challenge due to its nonspecific clinical manifestations and potential for rapid neurological deterioration. This report discusses the case of an 85-year-old Filipino woman with a history of treated pulmonary tuberculosis, asthma, and hypertension, who presented with increased sleep duration and impaired balance. A cranial CT scan revealed normal-pressure hydrocephalus, prompting further investigation. Despite negative cerebrospinal fluid (CSF) microscopy and culture, TB-LAMP testing yielded a positive result, confirming TBM. This case emphasizes the importance of considering TBM in patients from endemic regions who present with neurological symptoms and highlights the utility of TB-LAMP as a rapid and sensitive diagnostic tool. Early recognition and treatment of TBM are crucial to preventing severe complications and improving patient outcomes.**

Index Terms*—Tuberculous meningitis (TBM), normal pressure hydrocephalus (NPH), TB-LAMP, Cerebrospinal fluid, lumbar puncture Accepted and presented at the 29th Congress of the Asian Pacific Society of Respirology (APSR 2025), November 10–13, 2025, SMX Convention Center, Pasay City, Manila, Philippines.

I. INTRODUCTION

Tuberculosis (TB) remains a significant global health concern, with high mortality and morbidity rates worldwide. According to the World Health Organization (WHO, 2024), TB has likely reclaimed its position as the leading cause of death from a single infectious agent, surpassing coronavirus disease (COVID-19) after three years. In 2023, TB accounted for nearly twice as many deaths as HIV/AIDS. Over 10 million people develop TB annually, with incidence rising since 2021. [1]

In the Philippines, TB remains a major public health burden. As of December 31, 2023, the Department of Health (DOH) reported 612,534 TB cases nationwide (DOH, 2024). [2] Beyond its pulmonary manifestations, TB can affect multiple extrapulmonary sites, presenting diagnostic and therapeutic challenges. Among these, tuberculous meningitis (TBM) is the most severe and lethal form, often leading to substantial morbidity and mortality, particularly in high-prevalence regions such as the Philippines.[3,4] The nonspecific clinical presentation of TBM frequently results in delayed diagnosis and treatment initiation, exacerbating disease severity and increasing the likelihood of adverse outcomes.[5]

Normal pressure hydrocephalus (NPH), characterized by enlarged ventricular size and normal cerebrospinal fluid (CSF) pressure, presents an additional diagnostic challenge in patients with neurological symptoms.[6] While NPH has various underlying etiologies, including infectious processes such as TBM, determining the precise cause is crucial for appropriate management.

This case report presents a rare overlap of two complex conditions: normal pressure hydrocephalus secondary to TBM in an immunocompromised elderly patient. Traditional TBM diagnosis relies on acid-fast bacillus (AFB) staining and CSF culture, which are often time-consuming and lack sensitivity.[7] However, recent advancements in molecular diagnostics, particularly loop-mediated isothermal amplification (LAMP),

have demonstrated promising utility in rapidly and accurately detecting TB in CSF samples.[8]

In this report, we outline the diagnostic challenges in differentiating TBM-associated NPH, highlighting the role of TB-LAMP in facilitating early and accurate identification. Additionally, we discuss the implications of delayed diagnosis and the importance of prompt initiation of anti-TB therapy to mitigate the high mortality and morbidity associated with TBM. This case emphasizes the necessity of considering TB as a differential diagnosis in patients presenting with neurological symptoms, particularly in TB-endemic regions, and advocates for integrating innovative diagnostic tools such as TB-LAMP into routine clinical practice for improved patient outcomes.

II. CASE REPORT

This is a case of FLL an 85-year-old Filipino with a medical history of treated Pulmonary Tuberculosis, Bronchial Asthma, hypertension, and Left Hip Replacement Surgery due to a prior fracture, presented with progressive neurological symptoms. She had been experiencing increased sleeping time, imbalance, and episodes of confusion for several weeks. These symptoms were preceded by a five-week history of persistent cough, fever, and whitish sputum production. The patient was a passive smoker, chronically exposed to her husband's smoking habit.

Upon admission, she was drowsy but arousable, producing incomprehensible sounds. Her Glasgow Coma Scale (GCS) score was 12/15 (E4V2M6). There was no evidence of meningeal irritation (negative Kernig's and Brudzinski's signs), and motor and sensory examinations were unremarkable. Notable physical examination findings included tachycardia (132bpm), tachypnea (28cpm), bibasal rales, wheezing in all lung fields, and pale conjunctivae, indicative of respiratory and neurological involvement. Other aspects of the physical examination were normal.

III. DIAGNOSTIC WORKUP

A cranial computed tomography (CT) scan done showed normal pressure hydrocephalus (NPH). Additional findings included a lacunar infarct in the left basal ganglia and bifront parietal periventricular ischemic changes.

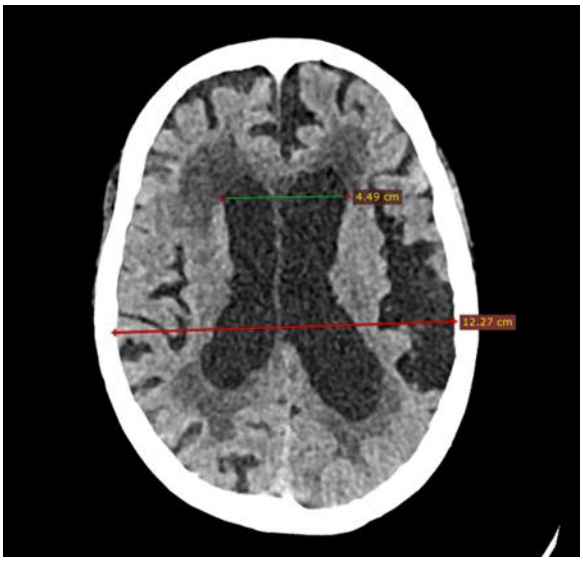
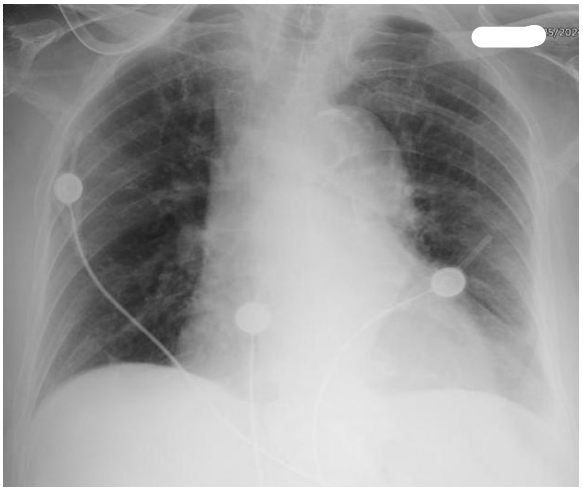


Figure 1: Cranial CT scan (plain)

The frontal, occipital, and temporal horns of the lateral ventricles are dilated. The maximum width of the frontal horns measures 4.49 cm while the maximum internal diameter of the skull measures 12.27 cm with an Evans index of 0.365 (NV: <0.30).

The patient was then subjected to lumbar puncture, which was able to extract a clear, colorless CSF fluid with an opening pressure of 19cms H20. The CSF analysis showed a total WBC of 40 cells/cu.mm, 98% of lymphocyte predominance, and 2% PMNS. There is only a total RBC count of 8 cells/cu.mm. Cerebrospinal fluid (CSF) examination showed elevated CSF protein (78.9 mg/dl) and low CSF glucose. The CSF microscopy, culture, and sensitivity were negative, negative for Cryptococcal agglutination, and no acid-fast bacilli were isolated from the CSF. However, the CSF TB LAMP (TB Loop-Mediated Isothermal Amplification) revealed a POSITIVE result. Based on well-established case definition criteria of tuberculous meningitis research, the patient was diagnosed with definite tuberculous meningitis confirmed with the presence of M. tuberculosis in the CSF using the TB-LAMP, along with a total score of 13, which includes clinical criteria (symptom duration of more than five days (4), cough >2 weeks (2), cerebrospinal fluid criteria (clear appearance (1), lymphocytic predominance (1), protein concentration greater than one g/L (1), absolute cerebrospinal fluid glucose concentration less than 2.2 mmol/L (1)), cerebral imaging criteria

(hydrocephalus (1), basal meningeal enhancement (2).[7] Other labs are hypokalemia of 2.3, elevated FBS (8.02mmol/L), normal C-reactive protein, CBC, sodium, creatine, and liver enzymes. Chest X-ray PA view showed Basal pneumonia, left. (Figure 2A). Sputum CS revealed Moderately heavy growth of Staphylococcus aureus and moderately heavy growth of Klebsiella pneumoniae.



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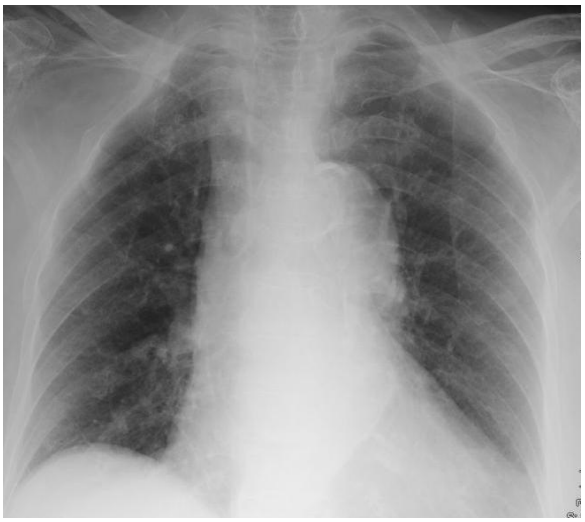

B

Figure 2A/2B: Chest radiographs on admission and upon discharge. Pneumonic infiltrates at the left basal area and hazy densities on left upper lobe were noted during admission (A). There was regression of findings in the discharge chest X-ray (B).

IV. TREATMENT AND CLINICAL COURSE

The patient was diagnosed with definite tuberculous meningitis with non-obstructing hydrocephalus, based on positive TB-LAMP results and a TBM research case definition score of 13.[7] She was initiated on a standard anti-tuberculous regimen (rifampicin, isoniazid, ethambutol, pyrazinamide) and intravenous steroids. Acetazolamide was administered to manage hydrocephalus. Targeted antibiotic therapy addressed pneumonia, and potassium replacement and glucose control were implemented.

By the fourth week of admission, the patient demonstrated marked clinical improvement. She was more alert, coherent, and hemodynamically stable. Follow-up chest radiography showed regression of pneumonic infiltrates. (Figure 2B)

V. DISCUSSION

This case report highlights a rare and complex overlap of two neurological conditions: normal pressure hydrocephalus (NPH) secondary to tuberculous meningitis (TBM) in an immunocompromised elderly patient. It emphasizes the critical role of loop-mediated isothermal amplification (TB-LAMP) in the timely and accurate diagnosis of TBM, addressing key diagnostic challenges and emphasizing the need for early therapeutic intervention.

Diagnosing TBM remains a significant challenge, particularly in differentiating it from other causes of NPH. Traditional diagnostic methods, such as acid-fast bacillus (AFB) staining and cerebrospinal fluid (CSF) culture, suffer from low sensitivity and prolonged turnaround times, often delaying definitive diagnosis and treatment.[3,7] Although culture remains the gold standard, its low yield—attributed to the paucibacillary nature of TBM—limits its clinical utility.[9] Polymerase chain reaction (PCR)-based methods offer improved sensitivity but are costly and require stringent quality control, restricting their widespread use, especially in resource-limited settings.[10]

To address these limitations, molecular diagnostics such as TB-LAMP have emerged as a promising alternative. TB-LAMP offers a rapid, highly sensitive, and cost-effective method for detecting *Mycobacterium tuberculosis* in CSF samples, facilitating early diagnosis and timely initiation of anti-TB therapy. Studies have shown that TB-LAMP can detect *M. tuberculosis* in up to 88.23% of culture-negative cases, outperforming conventional microbiological techniques.[10] Unlike PCR, TB-LAMP

requires minimal infrastructure and provides results within 60 minutes, making it an ideal tool for use in endemic regions and tertiary healthcare centers.[8]

Given the insidious onset and nonspecific symptoms of TBM, delayed diagnosis often leads to poor outcomes. In this case, the patient's Glasgow Coma Scale (GCS) score classified them as stage II TBM, highlighting the importance of early recognition and intervention.[9] The classic CSF findings of low glucose, elevated protein, and lymphocytic pleocytosis, though suggestive of TBM, lack specificity, necessitating more advanced diagnostic tools. TB-LAMP provided a crucial diagnostic advantage in this case, confirming TBM despite negative AFB smears and cultures, thereby enabling the early initiation of anti-TB therapy and potentially mitigating further neurological decline.

The management of TBM requires a multidisciplinary approach, integrating antimicrobial therapy, adjunctive corticosteroids, and, in select cases, neurosurgical interventions. First-line anti-TB medications—isoniazid, rifampicin, pyrazinamide, and ethambutol—must be used in combination for 9 to 12 months, with extended treatment duration in cases of poor response.[3] Adjunctive corticosteroid therapy, particularly with dexamethasone or prednisolone, has been shown to improve survival by reducing inflammation and intracranial pressure.[7]

In cases where TBM leads to NPH, neuroimaging and CSF analysis play a crucial role in early detection and management. Ventriculoperitoneal (VP) shunting is a well-established intervention for hydrocephalus secondary to TBM, alleviating symptoms and preventing further neurological deterioration.[8] However, in our patient, the neurological deficits were not severe enough to warrant surgical intervention, emphasizing the need for individualized treatment strategies based on disease severity and progression.

This case highlights the necessity of considering TBM as a differential diagnosis in patients presenting with neurological symptoms, particularly in TB-endemic regions. It also advocates for the integration of innovative diagnostic tools such as TB-LAMP into routine clinical practice to enhance early detection, facilitate timely treatment, and ultimately improve patient outcomes. By addressing the limitations of conventional diagnostic methods, TB-LAMP represents a valuable advancement in the fight against TBM, reducing diagnostic delays and associated morbidity and mortality.

VI. CONCLUSION

This case highlights the urgent need for improved recognition and management of tuberculous meningitis (TBM) to prevent severe complications and fatal outcomes. The rapid progression of hydrocephalus in our patient underscores the critical importance of early diagnosis and timely initiation of anti-TB therapy to mitigate neurological deterioration.[3,7]

Given the diagnostic challenges associated with TBM, enhancing the training and knowledge of healthcare professionals in identifying early clinical and radiological signs is essential. Bacteriological confirmation remains difficult due to the low yield of conventional methods; therefore, empirical treatment based on clinical suspicion and cerebrospinal fluid (CSF) findings should not be delayed.[9]

The incorporation of loop-mediated isothermal amplification (LAMP) into routine diagnostic workflows represents a major advancement in TBM detection, particularly in cases with low mycobacterial loads where traditional tests fail to provide rapid confirmation. Studies have demonstrated that LAMP offers superior sensitivity, specificity, and a rapid turnaround time of just 60 minutes, making it a valuable tool for facilitating early diagnosis and treatment initiation.[10] Its ease of use and affordability make it particularly advantageous in resource-limited settings, where timely intervention is critical for reducing morbidity and mortality.

Hence, continued research and implementation of innovative diagnostic techniques such as LAMP, combined with increased awareness and education among healthcare providers, will be crucial in addressing the global burden of TBM. Strengthening diagnostic capacity and ensuring early treatment initiation can significantly improve patient outcomes and reduce TBM-related mortality, particularly in endemic regions.

CONFLICT OF INTEREST
None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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INFORMED CONSENT FOR CASE REPORT PUBLICATION

I, _____ (Patient's full name), hereby consent to the publication of my medical case details, including clinical history, diagnostic findings, treatment outcomes, and relevant medical images, in a medical case report. I understand that the purpose of this publication is to contribute to medical knowledge, education, and research and that my identity will be kept confidential.

1. Nature of the Case Report: I understand that the case report will provide a detailed description of my medical condition, including its presentation, diagnosis, management, and clinical outcomes. This may include information such as laboratory test results, imaging studies, and medical interventions.
2. Purpose of the Publication: I acknowledge that the purpose of publishing this case report is to share medical insights and experiences with healthcare professionals, researchers, and the broader medical community. The publication may appear in medical journals, textbooks, conferences, or online platforms dedicated to medical education and research.
3. Confidentiality: I understand that my personal information, including my name, address, and other identifying details, will not be included in the case report. Any information that could potentially identify me will be anonymized or omitted to protect my privacy.
4. Potential Risks: I acknowledge that there may be potential risks associated with the publication of my case report, including loss of privacy and confidentiality. However, I understand that all reasonable efforts will be made to ensure that my identity remains confidential and that my medical information is presented accurately and ethically.

5. Voluntary Consent: I confirm that my consent to publish this case report is voluntary, and I have not been coerced or unduly influenced to provide this consent. I understand that I have the right to withdraw my consent at any time before the publication process is completed.
6. Questions and Clarifications: I have had the opportunity to ask questions and seek clarification regarding the publication of my case report. All my questions have been answered to my satisfaction.

By signing below, I indicate that I have read and understood the information provided in this informed consent form, and I consent to the publication of my case report as described.

Patient's Signature: _____ Date: _____

Witness's Signature (if applicable): _____ Date: _____