Case Report

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Relevance and challenges of neuroimaging for childhood tuberculous meningitis diagnosis in a resource-constraint country: A case report and literature review

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Abstract

Objective: Tuberculous meningitis (TBM) may be an undiagnosed cause of childhood mortality or neurologic sequelae. Cranial computed tomography (CT) scan remains a relevant diagnostic and prognostic tool amidst negative cerebrospinal fluid or sputum findings for tuberculous meningitis (TBM) diagnosis. Delays in diagnosis and treatment increase morbidity in resource-constraint countries.

Case report: A seven-year-old boy was referred with three weeks history of fever, progressive body weakness, aphasia and unconsciousness (three days). He had right cranial nerve III palsy, generalized hypertonia, and hyperreflexia in right lower limbs. All tuberculosis tests were negative except the cranial CT findings of leptomeningeal enhancement with basilar involvement and evidence of obstructive hydrocephalus. He was managed with anti-tuberculous drugs, prednisolone, ventriculoperitoneal shunt, and physiotherapy, and made a significant recovery after a year of anti-tuberculosis treatment.

Conclusion: The cranial CT scan findings facilitate TBM diagnosis for which prompt treatment commencement is crucial for a good outcome.

Keywords: tuberculous meningitis; extrapulmonary tuberculosis; children; neuroimaging; Nigeria

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Pertinence et défis de la neuroimagerie pour le diagnostic de la méningite tuberculeuse de l'enfant dans un pays à ressources limitées : à propos d'un cas et revue de la littérature

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Résumé

Objectif de l'étude: La méningite tuberculeuse (MBM) peut être une cause non diagnostiquée de mortalité infantile ou de séquelles neurologiques. La tomodensitométrie (TDM) crânienne reste un outil diagnostique et pronostique pertinent parmi les résultats négatifs du liquide céphalo-rachidien ou des expectorations pour le diagnostic de la méningite tuberculeuse (MBM). Les retards de diagnostic et de traitement augmentent la morbidité dans les pays à ressources limitées.

Rapport de cas: Un garçon de sept ans a été référé avec trois semaines d'antécédents de fièvre, de faiblesse corporelle progressive, d'aphasie et d'inconscience (trois jours). Il avait une paralysie du nerf crânien droit III, une hypertonie généralisée et une hyperréflexie des membres inférieurs droits. Tous les tests de tuberculose étaient négatifs, à l'exception des résultats du scanner crânien d'un rehaussement leptoméningé avec atteinte basilaire et signes d'hydrocéphalie obstructive. Il a été pris en charge avec des médicaments antituberculeux, de la prednisolone, un shunt ventriculopéritonéal et de la physiothérapie, et a fait un rétablissement significatif après un an de traitement antituberculeux.

Conclusion : Les résultats de la tomodensitométrie crânienne facilitent le diagnostic de MBM pour lequel le début rapide du traitement est crucial pour un bon résultat.

Mots-clés: Méningite tuberculeuse, tuberculose extra pulmonaire, enfants, Neuroimagerie, Nigéria

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INTRODUCTION

Tuberculous meningitis (TBM) is often a fatal form of central nervous system (CNS) tuberculosis (1). Tuberculous meningitis causes extensive brain injury and, even with treatment, may result in permanent neuro-disability (1,2). Estimating global tuberculosis (TB) prevalence in children is difficult due to under diagnosis and inadequate data, especially in developing countries (3). Children below the age of 15 years constitute 12% of the total global TB cases of 10 million, with annual tuberculosis-related deaths of 40,000 (4). Nigeria ranked sixth among the eight high-burden TB countries according to the World Health Organization (WHO), with a current incidence rate of 219 per 100,000 population (3). The global burden of TBM is not well defined, but the incidence is estimated at one percent of all tuberculosis cases (5), reportedly in direct relation to the incidence of pulmonary tuberculosis (5,6). It is most common in children aged less than four years and may occur many years after the infection due to rupture of subependymal tubercles discharging the tubercle bacilli into the subarachnoid space (6,7).

The diagnosis of TBM requires a high index of suspicion, premised upon clinical presentation, progression of illness, and the local TB endemicity. Laboratory findings are usually inconsistent, which may delay treatment and worsen outcomes. The cerebrospinal fluid (CSF) examination and culture remain the primary diagnostic tool; however, results could be atypical and misleading (7). The CSF findings can also be normal in chemistry and cell count because the fluid is obtained proximal to the site of inflammation (6,7). Indeed, the culture of a small volume of CSF, as mostly done, may not demonstrate *Mycobacterium tuberculosis* (7). In 2013, the WHO recommended the use of GeneXpert MTB/RIF assay for extrapulmonary clinical specimens in children; however, its sensitivity for CSF in TBM cases is still relatively low, though higher than Bactec® culture (8,9).

Neuroimaging has a role in the diagnosis of TBM. Brain computed tomography (CT) or magnetic resonance imaging (MRI) reveals abnormal findings as the disease progresses such as basilar enhancement and hydrocephalus (7,10). Early neuroimaging study and treatment commencement may be life-saving. This investigation is often a hurdle in resource-poor settings where getting a CT scan or MRI may be problematic due to accessibility and affordability. We report a seven-year-old male child in whom a diagnosis of TBM was premised mainly on clinical presentation and brain CT findings and improved significantly on antituberculous treatment. This report highlights the relevance and challenges of accessing neuroimaging for the timely diagnosis of TBM in a resource-poor country.

CASE REPORT

A.O, a seven-year-old boy, presented in 2020 at the Emergency Paediatrics Unit of a tertiary centre in Ilorin, Nigeria, with three weeks history of high fever and progressive body weakness that was worse on the right side, and non-projectile, non-bilious vomiting. Five days before the presentation, he became aphasic and lapsed into unconsciousness two days later—no history of cough, significant weight loss, or drenching night sweats. There was history of contact with an adult tuberculosis case. He received the Bacille Calmette-Guérin (BCG) vaccine, and a BCG scar was present. Before presentation to the tertiary centre, he had artemether injections for malaria and antibiotics for sepsis in a private hospital.

At presentation, he was acutely ill-looking, unconscious (Glasgow Coma Score, GCS- 9/15), not pale, afebrile (axillary temperature 36.0^{0}C), not dehydrated, with no significant peripheral lymph node enlargement, and no pedal oedema. Anthropometry (weight-19kg, height-110cm) was normal for age and gender. Central nervous system examination revealed an unconscious child with reactive pupils, right cranial nerve III palsy, supple neck, negative meningeal irritation signs, generalised hypertonia, exaggerated reflexes on the right lower limbs and sustained ankle clonus on the same side. Power was 2/5 on the right limbs and 3/5 on the left limbs. The respiratory and cardiovascular findings were normal, except for tachypnoea (respiratory rate of 50 cycles/minute) and tachycardia (pulse rate of 144 beats/minute). The abdominal, ear, nose, and throat (ENT) examinations were normal.

The initial assessment was an intracranial space-occupying lesion, likely a cerebral abscess, for which we commenced antibiotics while awaiting investigations and results. However, by the third day of admission, he developed several episodes of generalised tonic convulsions, meningeal signs became positive, worsened GCS (5/15), global hypertonia, irregular respiration, and hypertension.

Table 1 shows the results of the various investigations conducted. Despite requesting a

cranial CT scan on the first day of admission, the cranial CT was not done till the fifth day of admission due to financial constraints. The brain CT showed leptomeningeal and basal enhancements with dilated ventricles [Figure 1]. On the sixth day post-admission, the neurosurgeons inserted a ventriculoperitoneal shunt for the hydrocephalus. He commenced antituberculous drugs (rifampicin, isoniazid, pyrazinamide and ethambutol) and prednisolone on the seventh-day post-admission.

By the second week after the commencement of antituberculous drugs, the GCS improved to 11/15, still hypertonic and aphasic. He regained full consciousness in the third week of admission and commenced physiotherapy. He was discharged home at the sixth week post-drug commencement, still aphasic, with cranial nerve III palsy and hypertonia. After a year of antituberculous treatment, he walks short distances without support, interacts well with people, enunciates clearly but slowly, and has resumed school. He undergoes medical follow-ups at the neurology clinic. The parents gave informed consent for the publication of the report.

DISCUSSION

The early clinical features of TBM are non-specific, including fever, malaise, headache, anorexia, and recent weight loss (5,11). A high index of suspicion is often needed to make the diagnosis at this stage. A history of contact with an adult with tuberculosis usually heightens the suspicion (11), similarly reported in the index case.

The duration of symptoms is usually greater than two weeks in about 50% of cases (7,11) The index case presented after three weeks of illness, having been managed for malaria and sepsis without any improvement. In a study among Nigerian patients, the mean duration of illness before the presentation was 3.7 weeks (12) The index child had no signs of meningeal irritation at presentation though there was a rapid rate of progression of signs and symptoms within one week of admission (fourth week of illness). The initial absence of evidence of meningeal irritation, with a subsequent rapid deterioration, has been reported in TBM (5,7,11).

The CSF obtained from the index case was xanthochromic, which is a probable CSF appearance previously reported (6,9) However, the normal glucose level and mildly elevated protein were not in keeping with expected levels in TBM (6,11). This CSF finding is comparable to a prior Nigerian report of normal CSF glucose, and normal CSF microscopy, culture, and sensitivity (12). However, it differs from an earlier report in Zaria, Nigeria, where 93.4% of the children with TBM had hypoglycorrhachia (13). The unusual clinical and laboratory features such as the absence of signs of meningeal irritation at presentation, normal CSF glucose, microscopy, culture and sensitivity, and the negative CSF GeneXpert result may lead to misdiagnosis or late diagnosis of TBM with an attendant high morbidity and mortality.

Cranial CT scan with contrast, or magnetic resonance imaging with gadolinium, is generally helpful in TBM. Findings include leptomeningeal and basilar enhancement consistent with meningeal inflammation and hydrocephalus (5,11,14), as similarly identified in the index case. Other possible findings include infarction, cerebritis, tuberculoma, or calcification (5,11,14) However, the cranial CT scan may be normal in the early stages in approximately 30% of cases (11). Brain MRI remains the most sensitive neuroimaging compared to the CT scan for detecting TBM. The MRI enhances features such as early infarcts, border zone encephalitis, cranial neuropathies, and leptomeningeal tubercles (5,11).

In resource-poor countries where most patients lack access to health insurance and health expenses are out-of-pocket, it is common for patients to experience delays in getting the required cranial CT scan. Moreover, the tertiary facilities either don't have the needed equipment, or it is nonfunctional, necessitating travel to a facility with the neuroimaging machine, causing transportation issues, further cost, and delay in diagnosis. All these serve as a barrier to timely TBM diagnosis and care. This challenge occurred in the index case whose CT scan was postponed for five days by financial constraints and at an outside facility due to non-functionality of the hospital's machine.

Multiple drug treatment is required to manage TBM, with drugs that adequately cross the blood-brain barrier to achieve a therapeutic concentration in the CSF (). According to the national tuberculosis treatment guidelines, TBM therapy involves using the first-line antituberculous drugs for twelve months (15). We managed the patient per guidelines.

CONCLUSION

A high index of suspicion is essential for diagnosing TBM in a resource-poor environment. The presence of non-specific

symptoms such as fever, and headaches, lasting more than two to three weeks, with altered consciousness and h poor response to antibiotics should raise suspicion of TBM. The CT scan findings of basal or leptomeningeal enhancement and the presence of obstructive hydrocephalus strengthen the possibility of TBM. Early treatment commencement is crucial for a good outcome.

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Conflict of Interest: The authors declare no conflict of interest.

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Table 1. Investigations done and their findings

Investigations	Findings
White blood count, WBC	Total: 19,000/µl, elevated. Neutrophils: 92%, neutrophilia Lymphocytes: 8%.
Malaria parasite	Not seen on film
Blood culture	Negative
HIV test	Negative
Electrolyte, urea and creatinine	Essentially normal findings.
CSF microscopy	Colour: xanthochromic WBC: < 5 cells per high power field No web/clot formation when allowed to stand for some minutes.
CSF biochemistry	Normal glucose level, mildly elevated protein (73mg/dl) The ratio of CSF glucose to serum glucose - 0.6
CSF GeneXpert	Negative for Mycobacterium *tuberculosis*
Mantoux test	Non-reactive
Brain CT scan	Leptomeningeal enhancement with basilar involvement and evidence of obstructive hydrocephalus.

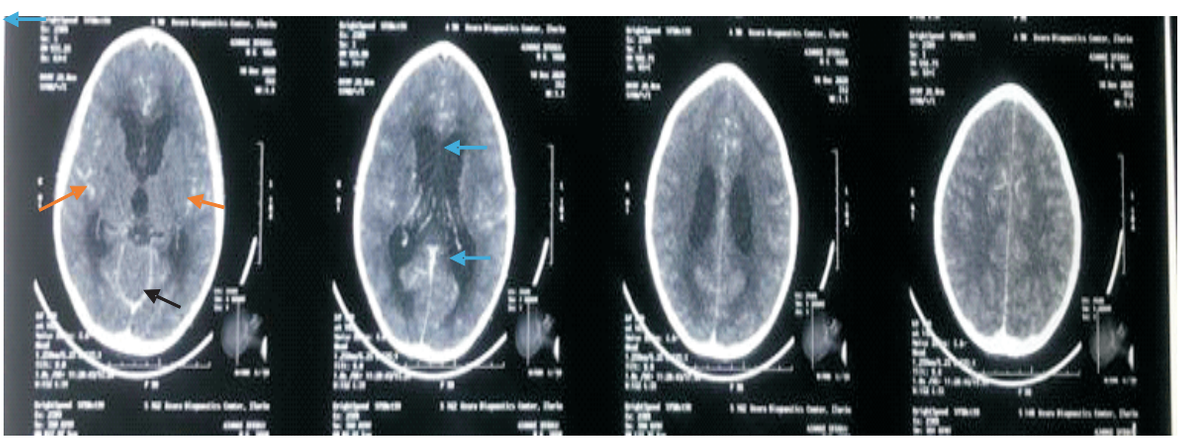

Figure 1. The Brain CT scan of the child with TBM. This contrast-enhanced axial image shows some distinct features of TBM, the orange and black arrows show leptomeningeal and basal enhancements, respectively and the blue arrows show dilated ventricles (hydrocephalus).