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Case Report

Tuberculosis Meningitis in a Immunocompetent Host

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Received: July 02, 2019; **Published:** September 09, 2019

Abstract

Tuberculous meningitis in the pediatric population leads to high rates of mortality and morbidity. Because of this, it is pertinent to establish early diagnosis and prompt treatment. The diagnosis can be challenging, but there are key findings both clinically and radiographically that help to establish a high suspicion for the disease. In this report, we present an immunocompetent 2-year-old female with *Mycobacterium tuberculosis* meningitis. This case of TB meningitis in an immunocompetent patient is remarkable in its uncharacteristic presentation with no obvious initial source of TB infected contacts or travel history.

Keywords: *Tuberculous Meningitis; Mycobacterium tuberculosis*

Introduction

In 2015, an estimated 10.4 million people were living with tuberculosis (TB) across the globe [1]. TB has now surpassed HIV in global disease-specific mortality, causing 700,000 more deaths than HIV since the HIV pandemic started. More than 1.8 million people worldwide died from TB in 2015, most of which have been due to pulmonary TB and TB/HIV co-infections [2]. Nearly 10% of all adult TB-related infections and 20% of pediatric TB cases are extrapulmonary in nature [3,4]. Tuberculous meningitis (TBM) represents roughly 1% of all cases of tuberculosis (TB), but, leads to the highest mortality and morbidity rates in children of all forms of extrapulmonary TB despite adequate treatment. It is the most common form in children younger than six years of age and usually appears 3 to 6 months after initial infection. Outcomes of infection include death in up to 50% of cases. Even those who survive may face devastating neurological deficits including developmental delay, seizures, hydrocephalus, and cranial nerve palsies [5]. Clinical outcomes rely on timely diagnosis and initiation of treatment. We present the case of a 2-year-old previously healthy female, who presented with unsteady gait and vomiting. The patient was initially mis-diagnosed which led to delay in treatment and poor neurological outcomes.

Case Report

The patient was a 2-year-old previously healthy girl who presented to the emergency department with unsteady gait for 1 day and vomiting for one month. The patient also had intermittent fevers with a T max of 101 and a complaint of headaches. She was seen at the primary care office twice prior to arrival and initially was diagnosed with a viral illness but upon return one week later, was diagnosed with Streptococcal pharyngitis via a positive rapid strep test and given a 7-day course of Amoxicillin. She continued to have fever, vomiting, and headaches. Subsequently, a family member whom is also a physician then gave a course of Cefdinir for 14 days. The child completed

4 days of this treatment without improvement. Her immunizations were up to date and she had no history of sick contacts. Her family denied any travel history.

On physical exam, the child was afebrile and vital signs were normal. She was lethargic and ill appearing. Her mucous membranes were dry, and pupils were appropriately responsive to light. The was no neck stiffness. The remainder of her exam was without significant findings.

Her white blood cell count was 14.5 x 10^3/mcL with 70% neutrophils and 21% lymphocytes; hemoglobin level was 13.8 g/dL; platelet count was 510 x 10^3/mcL; sodium 125 mmol/L. Urinalysis and toxicology were negative. CT brain w/o contrast showed a moderate to severe communicating hydrocephalus in addition to associated diffuse cerebral sulcal effacement and partial effacement of basal cisterns and transependymal flow of CSF. MRI showed diffuse basilar leptomeningeal enhancement and associated communicating hydrocephalus, small infarcts of perforating vessels and edema or infection in the midbrain and upper pons. In light of her clinical history, meningitis was suspected.

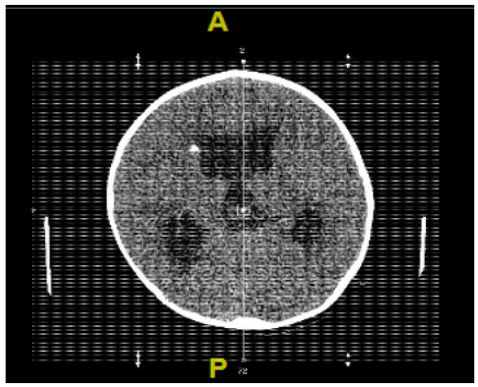


Figure A: *Head CT demonstrating hydrocephalus.*

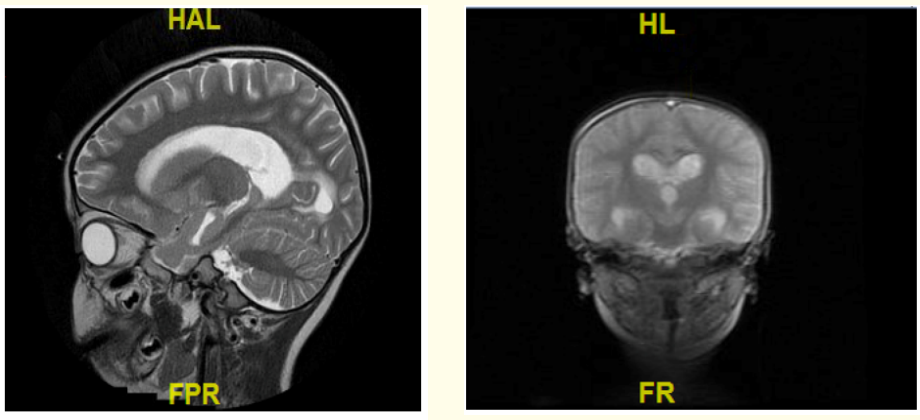


Figure B and C: *Depicting diffuse basilar leptomeningeal enhancement and associated communicating hydrocephalus.*

It was decided to proceed with a lumbar puncture followed by intubation of the child as there were concerns for protecting the airway. The child was started on Vancomycin and Ceftriaxone. The neurosurgeon was consulted, and the child went to the OR for evacuation and an external ventricular drain was placed. Results from the lumbar puncture showed elevated protein, low glucose, and lymphocytosis. The family was asked about travel again including anyone living in the home. They remembered that the child's grandmother, who lives with them, had in fact traveled to Indonesia six months prior for a funeral. A PPD was immediately placed on the patient's forearm and it later showed induration 8 x 10 mm therefore treatment was initiated. The treatment included Isoniazid, Rifampin, Pyrazinamide, and Ethionamide. Coccidiomycosis titers were sent and Fluconazole was initiated in addition. The results were negative for Coccidomycosis so Fluconazole was stopped after 15 days of treatment. Within this time, the child's grandmother was confirmed to have active pulmonary tuberculosis.

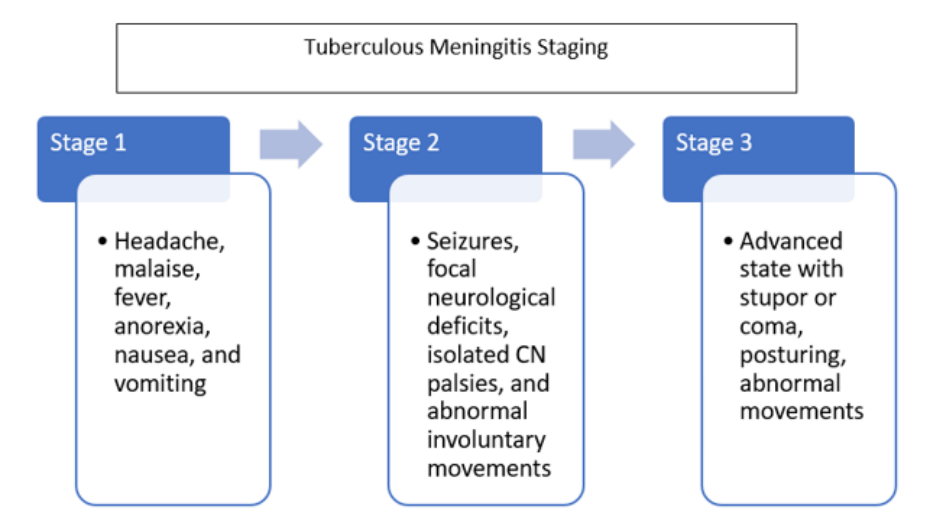
The patient was extubated once she could secure her own airway but she continued to be non-responsive with devastating neurological findings including diffuse rigidity and persistent upward gaze. Given the severity of the meningitis, the child also experienced hyponatremia which was corrected.

Discussion

Typical clinical findings

Although TBM is seen in miliary tuberculous cases, the central nervous system (CNS) can be the sole site for active infection. The initial CNS lesion is often a small submeningeal focus that develops during lymphohematogenous spread of primary tuberculosis infections. The granuloma which forms into the subarachnoid space or ventricular system then ruptures causing diffuse inflammatory meningitis. Thick gelatinous exudates develop across the base of the brain and impair the flow of the cerebrospinal fluid. This results in hydrocephalus [6]. This can be seen in greater than 50% of patients at presentation. The hydrocephalus itself increases the risk of cerebral ischemia leading to infarcts. The infarcts are associated with a poor prognosis [7].

Early recognition of TBM is vital but can be difficult. Signs and symptoms include fever, headache, irritability/behavioral changes, and vomiting without diarrhea. Neck stiffness is typically absent early on in the disease [8]. The TBM course is divided into three stages.



Figure

Diagnosis

One must have a high suspicion for TBM as it is very difficult to diagnose. The diagnosis relies on isolation of the organism or indirect confirmation such as the PPD skin test. AFB smear and culture are needed for definitive diagnosis. The workup should include a lumbar puncture which may show hypoglycorrhachia, protein elevation and CSF mononuclear pleocytosis. Chest radiograph may show pulmonary disease while neuroimaging may show hydrocephalus, tuberculomas, basilar meningitis, or infarcts. Basal enhancement, due to inflammation of the meninges and presence of exudate is considered one of the most sensitive imaging findings for TBM. Infarcts are rarely visible on the admission CT because they typically take about two weeks to develop [9,10].

Coccidiomycosis may also present in the same manner. Therefore, it is important to differentiate between TBM and Coccidomycosis because the treatment is quite different. Fluconazole is the appropriate treatment for Coccidomycosis infection. In order to diagnose this, anti-Coccidioides antibodies in the serum or CSF should be detected [11].

Treatment

Treatment for TBM should be initiated immediately for any child who develops meningitis and hydrocephalus for no other apparent reason. Treatment includes two months of isoniazid, rifampin, pyrazinamide and an aminoglycoside or ethionamide, once a day, followed by 7 to 10 months of isoniazid and rifampin, once a day or twice a week for nine to twelve months total. Children who have TBM should also be screened for HIV. Adjunctive corticosteroids can also decrease mortality and are recommended [12].

Conclusions

1. Tuberculous meningitis (TBM) represents roughly 1% of all cases of tuberculosis (TB), but, leads to the highest mortality and morbidity rates in children of all forms of extrapulmonary TB despite adequate treatment.
2. One must have a high suspicion for TBM as it is very difficult to diagnose. The diagnosis relies on isolation of the organism or indirect confirmation such as the PPD skin test.
3. Treatment for TVM includes two months of isoniazid, rifampin, pyrazinamide and an aminoglycoside or ethionamide, once a day, followed by 7 to 10 months of isoniazid and rifampin, once a day or twice a week for nine to twelve months total.

Conflict of Interest

All authors have no conflict of interest to disclose.

Informed Consent

Written informed consent was obtained from the patient's family for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Acknowledgement

We would like to thank Department of Pediatrics at UNLV for their support.

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Volume 15 Issue 10 October 2019