

A Diagnostic Conundrum in a Case of Severe CNS Infection: PCR May Not Always be the Key to Diagnosis

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Introduction

On presentation alone, it is difficult to differentiate between the many etiologies of CNS infection. While there is variability in laboratory and imaging results, the clinical presentations overlap. Molecular techniques have been increasingly utilized in problematic cases wherein etiology may not be obvious in terms of history and epidemiologic exposure. However, as shown in the following case, PCR additionally has limitations.

Case Presentation

A 25-year-old Caucasian woman with no medical history presented with worsening headache, hearing loss, double vision, and photophobia for three weeks. While reportedly afebrile at home, she was found to have a temperature of 103F. She was born and raised locally with no history of travel, intravenous drug use, or obvious sick contacts. She was a stay-at-home mother who rarely left the house.

Brain MRI was significant for multiple tiny abscesses throughout the white matter and infratentorial cerebellum, with pulmonary CT imaging showing miliary nodules throughout her lungs. Cerebrospinal fluid (CSF) sampling showed red cell count of 54, white cell count of 655 with 82% neutrophils, glucose of 8 and protein of 134; therefore initiated on empiric antibiotic coverage for bacterial meningitis. Her HIV test was negative. Her CSF gram stain, fungal smear and AFB smear were negative, so they were sent for DNA sequencing.

Presentation (Continued)

The patient's clinical and mental status deteriorated despite broad-spectrum antibiotic coverage, so empiric Toxoplasma treatment was added due to a positive Toxoplasma IgG result. Repeat brain imaging showed development of acute obstructive hydrocephalus prompting placement of a ventriculostomy drain. Repeat CSF sampling showed improved pleocytosis and chemistries, but CSF sent for sequencing had no bacterial, fungal, Toxoplasma gondii, no non-tuberculous Mycobacteria and Mycobacterium tuberculosis DNA detected. Bronchoalveolar lavage did not yield any pathogens. Empiric antifungal therapy was added due to still worsening clinical status.

Repeat brain MRI imaging showed progression of leptomeningeal enhancement, marked progression of hydrocephalus and multiple new acute infarcts within the basal ganglia and periventricular white matter as well as diffuse cerebral edema causing significant mass effect and downward cerebellar tonsillar herniation. A third sampling of CSF finally showed numerous acid-fast bacilli on smear which was then rapidly identified as Mycobacterium tuberculosis by DNA probe. Patient was started on quadruple TB regimen but due to irreversible neurological damage, the family decided on comfort care.

Imaging

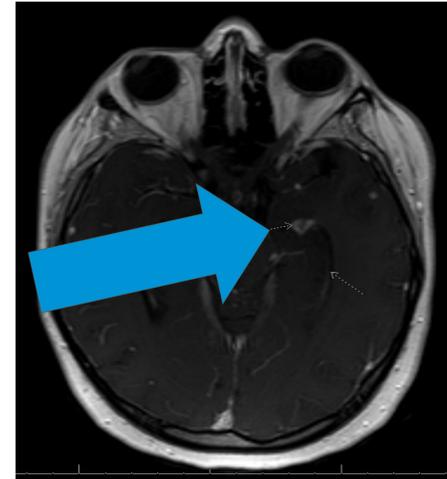


Figure 1a. MRI Head: coronal view of ring enhancing lesion

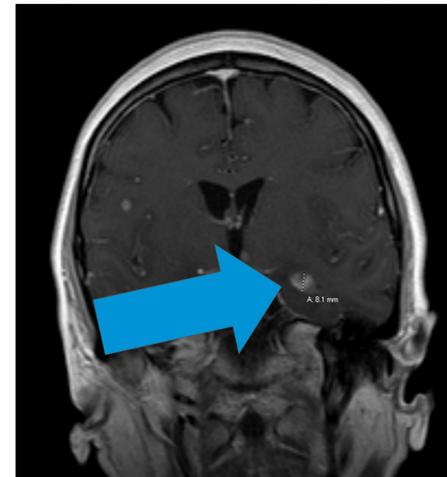


Figure 1b. MRI Head: sagittal view of ring enhancing lesion

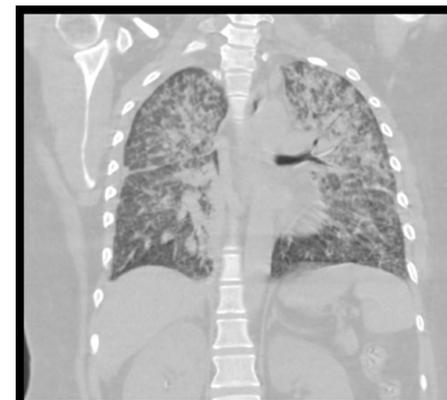


Figure 2: CT Chest: Coronal view showing scattered miliary nodules

Discussion

Tuberculous meningitis is one of the most severe forms of extrapulmonary tuberculosis and is unfortunately associated with mortalities that can be as high as 74%. Early diagnosis is paramount as clinical outcomes depend on early initiation of therapy, making it very difficult in patients with whom epidemiologic history may be lacking or inadequate. In contrast to more common bacteria with generational times of minutes, MTB can have generational time of 20 hours. Therefore, while AFB cultures continue to be the gold standard for diagnosis, incubation time remains a limiting factor for diagnosing TB¹.

Broadly, AFB smears are used in conjunction with rapid PCR testing and the combination of these two can guide clinical decision making as sensitivities vary regarding the coexistence of cultures².

When AFB smears are positive, PCR sensitivity rates are 94%; but when negative, sensitivities drop to 54%³. The initial AFB smears in this case were negative, hence the delay in anti-TB therapy. Why her AFB smears were negative is the foundational question of this case, and answers can only be speculated. One possible explanation is that the patient's bacterial burden was initially not high enough for detection in our 3 samples.

These AFB smears remained undetected until the patient's bacterial burden was elevated to the point of detection. While that burden finally allowed for diagnosis, by time the burden was high enough, the patient had regressed too far to have successful anti-MTB treatment.

References

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