

Episode 49

Problem Representation

A 38-year-old woman from El Salvador presented with subacute headaches, fevers, and vomiting, found to have an upper lobe opacity with randomly distributed pulmonary nodules as well as a lymphocytic pleocytosis on CSF analysis.

Diagnosis

Based on her imaging findings of miliary pulmonary nodules, the suspicion for TB was very high. A repeat LP was performed that was positive for MTB PCR. CSF culture eventually returned positive for MTb complex that was resistant to pyrazinamide, suggestive of *M. bovis*. Patient was eventually treated with RIPE + Levofloxacin and Prednisone for disseminated TB including TB meningitis.

Teaching Points

- Active infections with *Mycobacterium tuberculosis* can be broadly divided into “pulmonary” and “extrapulmonary”, with extrapulmonary infections typically representing the sequelae of hematogenous dissemination of the Tb bacillus. Interestingly, tuberculous meningitis is thought to occur when a subcortical or meningeal focus of bacilli and granulomatous material are released into the subarachnoid space, rather than by hematogenous spread directly to the CNS¹. The resulting inflammation can lead to cranial nerve deficits, vasculitis, and possible blockage in the flow of the cerebrospinal fluid, resulting in hydrocephalus. The most serious consequence is the development of vasculitis in the vessels of the circle of Willis resulting in catastrophic infarctions.
- The cerebrospinal fluid in tuberculous meningitis will typically show a low cell count (<300/mm³) with a predominance of lymphocytes, a low glucose concentration (<2.2mmol/L), and an elevated protein concentration (>0.8g/L); however, the glucose and protein concentrations may be normal².
- *Mycobacterium bovis* accounts for 1.3-1.6 percent of tuberculosis cases in the United States³. Tuberculosis due to *M. bovis* is clinically and radiographically indistinguishable from tuberculosis due to *M. tuberculosis*. Identification of Pyrazinamide resistance in an MTB complex strain should prompt consideration of *M. bovis*. Treatment of *M. bovis* usually consists of two months of isoniazid, rifampin, and ethambutol, followed by seven months of isoniazid and rifampin⁴.

Clinical Reasoning Pearl

Epidemiological and contextual factors are incredibly powerful in shaping our differential diagnoses for various syndromes, especially when infectious diseases are under consideration.

For example:

The most common causes of miliary pulmonary nodules include tuberculosis, histoplasmosis, and coccidioidomycosis. The patient from this episode was originally from El Salvador, making tuberculosis the most likely etiology here. However, if the past was from Central Valley California or Ohio River Valleys, then coccidioidomycosis or histoplasma, respectively, could have been more likely.

References

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2. Donald PR, Schoeman JF. Meningitis. Tuberculous meningitis. *N Engl J Med*. 2004;351:1719-1720.
3. Scott C, Cavanaugh JS, Pratt R, Silk BJ, LoBue P, Moonan PK. Human Tuberculosis Caused by *Mycobacterium bovis* in the United States, 2006-2013. *Clin Infect Dis*. 2016;63(5):594-601. doi:10.1093/cid/ciw371
4. Nahid P, Dorman SE, Alipanah N, et al. Executive Summary: Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. *Clin Infect Dis*. 2016;63(7):853-867. doi:10.1093/cid/ciw566