“Too Numerous to Count” Lesions on Magnetic Resonance Images of the Brain
(See pages 1545–6 for Photo Quiz)

Figure 1. A, T1-weighted MRI with gadolinium enhancement shows multiple lesions in the cortex and periventricular area. The prominent lesions are indicated by arrows. B, Fluid-attenuated inverse recovery (FLAIR) image shows areas of increased signal intensity in the cortex and periventricular area, which are indicated by arrows. C, T1-weighted MRI with gadolinium enhancement shows multiple lesions in the cerebellum. The prominent lesions are indicated by arrows. D, FLAIR image shows areas of increased signal intensity in the cerebellum, which are indicated by arrows.

Diagnosis: Tuberculomas in the brain with meningitis (figure 1).

Empirical therapy with isoniazid, rifampin, ethambutol, and pyrazinamide was initiated within 24 h after the patient’s second admission to the hospital. A nucleic acid amplification test (MTD; Gen-Probe) was performed on the CSF specimen obtained from the patient on readmission, and the result was now positive. Subsequently, there was growth of Mycobacterium tu-
Tuberculosis can involve the CNS and can cause intracranial tuberculomas, meningitis, and/or vasculitis. Intracranial tuberculoma affects people of all ages, but the incidence is higher among pediatric patients [1]. There is an increased incidence of CNS tuberculosis among patients with HIV infection [2]. Intracranial tuberculomas are thought to be secondary to hematogenous spread from elsewhere in the body; they can be single or multiple and can be located anywhere in the cerebrum, brainstem, and posterior fossa [3]. Tuberculomas in the brain give rise to corresponding focal symptoms. Tuberculous meningitis typically occurs as a result of rupture of a subependymal tubercle, rather than as a result of hematogenous spread [4]. Clinical manifestations include severe headache, altered mental status, stroke, hydrocephalus, and cranial neuropathies [5].

The CSF WBC count of patients with tuberculosis meningitis generally ranges from 0 to 1500 cells/mm³. The protein levels are usually elevated and the glucose levels may be low, especially in patients with advanced disease [6, 7]. Direct examination of CSF for M. tuberculosis by acid-fast smear has a low sensitivity (<20%), and large volumes of CSF from several lumbar punctures are often needed to detect M. tuberculosis organisms [8]. Timely diagnosis is hampered by the limitations of standard microbiological techniques. Acid-fast smears of CSF lack sensitivity for M. tuberculosis, and cultivation of the organism can take weeks. Findings of CT scans with contrast and MRI scans have been reported as equally sensitive for visualizing intracranial tuberculomas. However, MRI findings are superior for demonstrating the extent of lesions, especially for brainstem tuberculomas [9]. MRI or CT scan findings may also show basilar meningeal enhancement and/or signs of intracranial hypertension, such as hydrocephalus [10]. Nevertheless, the potential role of MRI and CT scan findings in the diagnosis of intracranial tuberculomas is limited by the fact that other infectious or neoplastic diseases may present with similar radiologic findings. If a biopsy is required, stereotactic biopsy provides a higher yield and has a lower risk of procedure-associated complications than does a biopsy performed after direct visualization of the lesion [11].

Nucleic acid amplification by various methods has been extensively used in the diagnosis of pulmonary tuberculosis. Nucleic acid amplification–based tests for detection of M. tuberculosis complex in non–respiratory-tract specimens are still considered investigational. As in the case of our patient, for whom both CSF nucleic acid amplification tests were performed at the same laboratory (the Microbiology Service at the National Institutes of Health, Bethesda, MD), false negative results may occur [12, 13]. Lang and colleagues [14] assessed how use of different positive cutoff values affected the sensitivity of the MTD test for analysis of CSF to diagnose tuberculous meningitis. They found a sensitivity of 33% using a cutoff of >30,000 relative light units (RLUs), and a sensitivity of 83% using a cutoff of >11,000 RLUs; the specificity was 100% at both cutoff values but decreased at positive cutoff values of <11,000 RLUs. Our result of 2978 RLUs for the first CSF specimen was well below even the lower threshold used in the study by Lang and colleagues [14]. It is interesting that this first specimen, which would have to be considered unambiguously negative for M. tuberculosis according to the MTD result, also had culture results that were negative for M. tuberculosis, whereas the second specimen, obtained only 2 weeks later, had a very high MTD result (2,141,151 RLUs), and also had culture results that were positive for M. tuberculosis. A possible explanation for the different results for the 2 specimens might be that a tuberculoma ruptured into the meningeal space during the 2-week interval.

References

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