Neuroimaging Highlight

Editors: Mark Hudon, Richard Farb

An Infant with Central Nervous System Complications of Disseminated Tuberculosis

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A previously well, nine-month-old, Canadian-born, Caucasian infant presented with one month history of cough, irritability, and poor weight gain. Her past medical history was significant for open-heart surgery at age four months, with repair of a ventricular septal defect, closure of an atrial septal defect, and ligation of patent ductus arteriosus. There were no operative complications. Her development was normal for age. She had received her routine immunizations. There was no known infectious diseases contact or exposure to farm animals.

Initial examination revealed a lethargic infant with mild tachypnea and low-grade fever. Aside from decreased air entry at the right upper lobe (RUL), her general examination was normal. A chest x-ray confirmed complete RUL consolidation (Figure 1). Gram stain and routine bacteriologic culture from the bronchoalveolar lavage (BAL) were negative. On the third day of admission, she developed meningismus, bulging anterior fontanel, and new right-body focal and secondary generalized seizures. Brain computed tomography (CT) and magnetic

Figure 1: Chest X-ray showed right upper lobe consolidation and increased interstitial markings, with focal lucency (arrow) suggestive of cavitation. Sternotomy wires from prior surgery were seen.

Figure 2: Brain computed tomography (CT) with contrast showed multiple small enhancing lesions involving the cerebral hemispheres, brainstem, and cerebellum (arrows), with basal leptomeningeal enhancement (arrowhead).
resonance imaging (MRI) showed multiple small round enhancing lesions in her cerebral hemispheres, brainstem, and cerebellum, with basal leptomeningeal enhancement (Figure 2). Lumbar puncture was deferred because of increased intracranial pressure (ICP). Her seizures were managed with intravenous phenobarbital, and her antibiotics were changed from cefuroxime to vancomycin, cefotaxime, and metronidazole. Antituberculous therapy consisting of isoniazid, rifampin, ethambutol, and pyrazinamide was added on the fourth day, after a BAL specimen was reported positive for acid-fast bacillus. She also received pyridoxine and a six-week tapering course of dexamethasone. Thrombophilia studies, including antithrombin III, protein C, protein S, factor V Leiden, and prothrombin G20210A genotype were normal. Her immune workup and HIV antibodies were negative. Subsequent nucleic acid amplification and tuberculosis (TB) culture of BAL specimens confirmed the diagnosis of *Mycobacterium tuberculosis* infection.

Four days after starting anti-TB therapy, the patient developed left-sided focal seizures. Repeat brain CT and MRI showed hydrocephalus, with infarction involving the right temporoparietal and left corona radiata areas (Figure 3). Because of extensive brain injury, the patient was intubated, sedated, paralyzed, and then cooled to 34°C for 48 hours. An external ventricular drain showed elevated opening pressure of 20 cm water. Despite initial episodes of transient bradycardia and hypertension related to increased ICP, the patient was successfully extubated after one week. She made a remarkable recovery when reassessed two months later in the ambulatory clinic. Aside from truncal hypotonia and mild gross motor delay, there was no focal neurological deficit. She remained on supervised anti-TB therapy with isoniazid and rifampin. Her *M. tuberculosis* strain was subsequently found to be identical by molecular typing to an adult with pulmonary TB who had lived in the same apartment building.

Tuberculosis infection and disease in children usually represents recent transmission from symptomatic adults via airborne droplet particles. However, as shown by our case report, the absence of known infectious contact in a child at low epidemiologic risk does not exclude the possibility of TB disease. In 2001, the incidence of TB among children in Canada was 1.9 per 100,000. Nearly half of infected children were under five years of age. Children are more likely than adults to present with extra-pulmonary tuberculosis, and approximately 4% of children have central nervous system involvement. Central nervous system TB is associated with mortality rates of 13% to 76%, and permanent neurological deficit in half of children who survive.

The most common presentation of central nervous system TB is tuberculous meningitis (TBM). Tuberculous meningitis should be considered in the presence of basal leptomeningeal inflammation, persistent hydrocephalus, and cerebral infarction. The majority of infants involve the basal ganglia and, to a lesser degree, the anterior and middle cerebral artery distribution territories, due to vasculitis with secondary thrombosis and occlusion. Parenchymal granulomatous lesions called tuberculomas are commonly found in the brain and spinal cord of patients with miliary TB. They may be asymptomatic, or produce signs and symptoms similar to TBM. Noncaseating tuberculomas are usually small discrete lesions with uniform enhancement and surrounding edema on contrast enhanced brain CT, whereas caseating tuberculomas present as ring enhancing lesions, with either heterogeneous or hypointense core signal on T1-weighted MRI. Paradoxical enlargement of intracranial tuberculomas has been observed during initiation of antituberculous therapy and results from augmented host inflammatory responses rather than progressive infection.

Treatment of neurologic TB consists of initial administration of multiple anti-TB drugs, with subsequent modification in the regimen based on drug-susceptibility testing results. In North America, pediatric TBM is treated with isoniazid, rifampin, pyrazinamide, and aminglycoside or ethionamide for the first two months, followed by an additional seven to ten months of...
isoniazid and rifampin for susceptible strains. Supplementary pyridoxine is given to prevent isoniazid-related deficiency, which may cause neurologic complications such as peripheral neuropathy, seizures, or psychosis. Adjunctive therapy with corticosteroids has been shown in two randomized comparative trials to decrease mortality and morbidity in patients with TBM, particularly in those with depressed level of consciousness. Because duration of treatment is long, directly observed therapy is important to ensure medication compliance. Even though there may be no identifiable contact in up to 50% of pediatric neurotuberculosis cases, public health agencies should be notified to detect adults with infectious TB in the community.

REFERENCES