MR Imaging in Toxoplasmosis Encephalitis after Bone Marrow Transplantation: Paucity of Enhancement despite Fulminant Disease

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Summary: We present a patient who underwent bone marrow transplantation (BMT) after developing chronic myelocytic leukemia. Four months after BMT, he became comatose and died. MR imaging revealed multifocal brain lesions that were progressive but produced no edema. Postcontrast studies revealed that most of the lesions were nonenhancing. There was only discrete, irregular leptomeningeal enhancement with possible minimal enhancement of the cortex and subcortical white matter. Autopsy showed overwhelming toxoplasmosis encephalitis. This case illustrates that toxoplasmosis lesions may lack obvious contrast enhancement in the brain of the immunocompromised patients, despite severe involvement. Recognition of this unusual MR imaging manifestation of toxoplasmosis should lead to earlier diagnosis and treatment.

Toxoplasmosis encephalitis is an opportunistic infection most commonly seen in AIDS patients. At MR imaging, lesions are multiple, commonly located in the deep central nuclei, posterior fossa or lobar at the gray-white matter junction, with prominent associated mass effect and edema. After gadolinium administration, the lesions typically show intense parenchymal enhancement (1). After bone marrow transplantation (BMT), brain infections occur with a frequency of 2–4%. The spectrum of infections is variable, favoring bacteria, fungi, or viruses (2). Cerebral toxoplasmosis is a rare complication after BMT, with a prevalence of less than 1% in the United States (3). We report the case of a patient who developed fatal cerebral toxoplasmosis characterized by multiple progressive MR imaging lesions that showed a surprising paucity of enhancement and lack of edema on serial studies.

Case Report

Six months after receiving the diagnosis of advanced-stage chronic myelocytic leukemia (CML), a 39 year-old-man received cyclophosphamide 60 mg/kg, antithymocyte globulin and underwent total-body irradiation and allogeneic BMT. Immediately after BMT, he began to receive IV steroids and cyclosporine to prevent graft-versus-host disease. One week after BMT, he developed a neutropenic fever that was treated with broad-spectrum antibiotics, including cephalosporine, acyclovir, and amphotericin-B. IV steroids were discontinued and were not used again. Although he remained neutropenic, the fever subsided and his general condition improved. Approximately 3 months after BMT, he developed headaches. Brain MR imaging was performed (Fig 1). Tacrolimus (FK-506) replaced cyclosporine. The patient developed recurrence of fever, despite continuous antibiotic coverage, and the diagnosis of pneumo- tosis intestinalis was made. He underwent a right cholecystectomy with ileostomy. Anaerobic coverage was added. Twenty-four hours after surgery, he developed confusion, lethargy, and inability to follow commands. Neurologic examination was significant for myoclonic jerks involving the right upper and both lower extremities. Laboratory investigations showed a peripheral white blood cell count of 790/L, hemoglobin of 7.1 g/dL, and platelets of 44,000/L. Lumbar puncture revealed CSF protein to be at 137 mg/dL, glucose at 80 mg/dL, and white cell count at 77/L (100% lymphocytes), and Gram, acid fast bacilli, and India ink stains. Polymerase chain reaction (PCR) results for herpes simplex and toxoplasmosis and cytology findings for malignant cells were negative. Pre- and post-transplant serology findings for toxoplasmosis were previously negative and testing was not repeated during the neurologic illness. Because of the continuous deterioration in the patient’s condition, brain MR imaging was repeated 2 days later, 6 days after the initial MR imaging (Fig 1). During the following week, he became progressively obtunded and comatose. Two additional repeated spinal taps showed increasing protein content in the CSF, but otherwise similar results in comparison to the first spinal tap. PCR for toxoplasma was not repeated in the CSF or serum because of previously negative results. A third MR imaging study, 18 days after the initial one, was performed (Fig 1). Single-voxel MR spectroscopy was performed (Fig 2). Intrathecal chemotherapy was initiated for presumptive metastatic disease, but the patient died 10 days after the onset of neurologic symptoms. Brain autopsy revealed widespread necrotizing toxoplasmosis encephalitis of the cerebrum, cerebellum, basal ganglia, midbrain, and pons, with abundant toxoplasma cysts and trophozoites (Fig 3). No other opportunistic infection, leukemic infiltrate, or lymphoproliferative disorder was identified. The lungs showed toxoplasmosis pneumonitis, confirmed by specific antibodies.

Discussion

Our case is an example of a non-AIDS immunocompromised patient with severe multiorgan toxoplasmosis and a fulminant course, rapid deterioration, and death. Despite significant cerebral involvement, the diagnosis was not made during life. The paucity of enhancement and lack of edema were
**Fig 1.** Three serial MR imaging studies obtained during a period of 18 days. Images were obtained by the fluid-attenuated inversion recovery (FLAIR) sequences, with the exception of columns 4 and 6, which were obtained by the postgadolinium T1-weighted sequence. The initial study (top row) revealed a few nonspecific white matter lesions that were thought to be related to cyclosporine toxicity. The lesions were not seen on noncontrast T1-weighted images or diffusion-weighted images (not shown). After gadolinium administration, lesions were nonenhancing, except for the left parietal-occipital lesion, which shows faint, questionable enhancement. Because of neurologic deterioration, brain MR imaging was repeated (middle row) 6 days after the initial study, revealing worsening lesions in the subcortical white matter, cerebellum, bilateral thalamus, and basal ganglia, with no mass effect or abnormal parenchymal enhancement; there was possibly some increased leptomeningeal enhancement. During the following week, the patient became progressively obtunded and comatose. A third MR imaging study obtained 18 days after the initial study (bottom row) showed continuous progression of lesions in size and distribution, which at this time involved much of the brain. There was a remarkable lack of mass effect and lack of parenchymal enhancement of most lesions; irregular meningeal enhancement with secondary involvement (perhaps by meningeal spread) of the cortex and subcortical areas was suggested. A few lesions were hyperintense on diffusion-weighted images. Apparent diffusion coefficient maps were not obtained to distinguish restricted diffusion versus T2 shine-through (not shown). MR imaging was performed at 1.5 T with the following parameters on each day. Fast spin-echo FLAIR: 5-mm axial sequences with 1-mm section gaps, TR/TE/TI of 10,002/145/2200, matrix of 192×256, one signal averaged, and 22-cm field of view. T1-weighted images: 5-mm axial sequences with 1-mm section gaps, TR/TE of 500/20, matrix of 192×256, one signal averaged, 22-cm field of view.

**Fig 2.** Single-voxel MR spectroscopy (right panel) by using a stimulated-echo acquisition mode with a TR of 1500 ms and TE of 30 ms. The spectral pattern is technically limited and suboptimal (note the poor baseline). A 2.5×2.5 cm voxel of the right putamen lesion was localized based on the FLAIR axial image on day 18 (left panel) at the level of the frontal horns of the lateral ventricle. The spectral pattern shows, from left to right, a moderate increase in choline (solid arrow), a moderate reduction in n-acetyl-aspartate (solid arrow), and a marked lactate peak (solid arrow). There is also a mild prominence of (amino acid) peak (dashed arrow).
Cerebral toxoplasmosis should be considered in BMT patients with an unexplained neurologic deterioration despite a lack of enhancement or mass effect at MR imaging.

**References**

3. Slavin MA, Meyers JD, Remington JS, Hackman RC. *Toxoplasma


