8 Toxoplasmosis

Yun Sean Xie, Jason Handwerker

INTRODUCTION

Central nervous system (CNS) toxoplasmosis is an opportunistic infection caused by the intracellular protozoan parasite *Toxoplasma gondii*. This parasite may be acquired in utero or through the ingestion of infected meat or cat feces, as cats are its definitive host. While *T. gondii* infects a large portion of the population, it uncommonly causes significant disease in immunocompetent individuals. *T. gondii* typically causes disease in immunocompromised patients, such as in the setting of HIV/AIDS when the CD4 count has dropped below 100 cells per microliter.[1] With the advent of modern HAART therapy, the prevalence of toxoplasmosis in HIV/AIDS patients has dramatically decreased in developed countries. The clinical manifestations of CNS toxoplasmosis are nonspecific, with the most common presenting symptoms being headache, lethargy, fever, and focal neurologic signs. Chorioretinitis is the most common manifestation of congenital toxoplasmosis, which may also cause seizure, hydrocephalus, and psychomotor delay. Many individuals in the general population are seropositive for toxoplasma. Consequently, the clinical diagnosis of toxoplasmosis can be a dilemma. As a result, imaging is vital in establishing a presumptive diagnosis.

IMAGING FINDINGS

In congenital toxoplasmosis, calcifications are common, which may involve the subcortical and periventricular white matter, basal ganglia, and cortex (Fig. 8.1).[2] Subcortical cysts, volume loss, and hydrocephalus can also be seen. Cranial ultrasound is often the first imaging study obtained, although CT or MRI is helpful for further evaluation.

In immunocompromised patients, CNS toxoplasmosis typically presents as multiple lesions with a predilection for the deep gray nuclei and gray-white matter junctions but occasionally presents as a solitary lesion (Fig. 8.2). The imaging features are associated with necrotizing encephalitis on pathology (Fig. 8.3).[3] MRI of the brain including intravenous contrast is the imaging modality of choice for evaluating patients with suspected toxoplasmic encephalitis. Classically, the lesions have ring-like peripheral enhancement with an eccentric mural nodule, referred to as an "eccentric target sign" (Fig. 8.4).[4] However, the ring enhancement can be diminished or absent when a patient's CD4 count is very low. The lesions are usually centrally hypoattenuating on CT and T1 hypointense on MRI. The lesions may be T2 hyperintense to isointense internally depending on the level of organizing necrotic component. There may be mural hyperattenuation on CT or T1 hyperintensity on MRI secondary to subacute hemorrhage or increased protein content. The lesions demonstrate surrounding hypoattenuation on CT or T2 hyperintensity on MRI compatible with vasogenic edema. Toxoplasmosis lesions typically show decreased cerebral blood volume on perfusion imaging.

EVOLUTION OF DISEASE

In treated congenital toxoplasmosis, a reduction or resolution of intracranial calcifications may occur in the first year of life with concordant improvement in neurologic status.[5] However, severe cases may demonstrate marked persistent calcification, destruction of the cortex, and hydrocephalus. The prognosis of untreated infants is often poor, although treated infants remain at risk for developing sequelae later in life, especially retinal damage, which should be monitored.

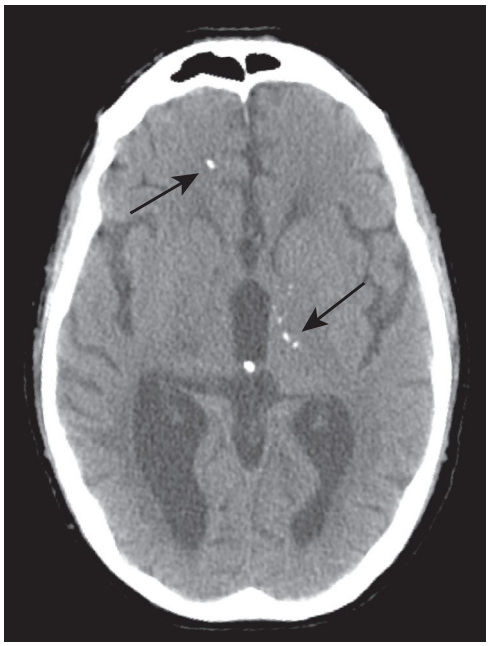

Figure 8.1. Congenital toxoplasmosis. Noncontrast CT demonstrating mild ventriculomegaly and calcifications in the right frontal subcortical white matter and left thalamus *(arrows)*.

Since there are variable imaging appearances of CNS toxoplasmosis as well as imaging mimics that require different therapy, serial imaging is essential to assess response to therapy or to suggest an alternative diagnosis. When a presumptive diagnosis of toxoplasmosis in HIV/AIDs patients is established with serologic testing and lumbar puncture, it is typically treated with antiparasitic medications including sulfadiazine and pyrimethamine. Patients usually show clinical improvement 2 to 4 weeks after treatment initiation, which typically coincides with radiological improvement (Fig. 8.5). If there is lack of improvement clinically and radiologically at 2 to 4 weeks, an alternative diagnosis (especially CNS lymphoma) should be suspected. Imaging signs of improvement include decrease in size of the lesions and improvement of the surrounding vasogenic edema. Ultimately, healed or chronic lesions may show areas of encephalomalacia and calcification. The time to complete treatment response is variable, with lesions remaining evident for many weeks or months. As in other infections occurring in immunocompromised patients, a paradoxical worsening of symptoms and edema may occur following a rapid rise in CD4 count and an overwhelming inflammatory response to the infection; this is known as immune reconstitution inflammatory syndrome (IRIS).

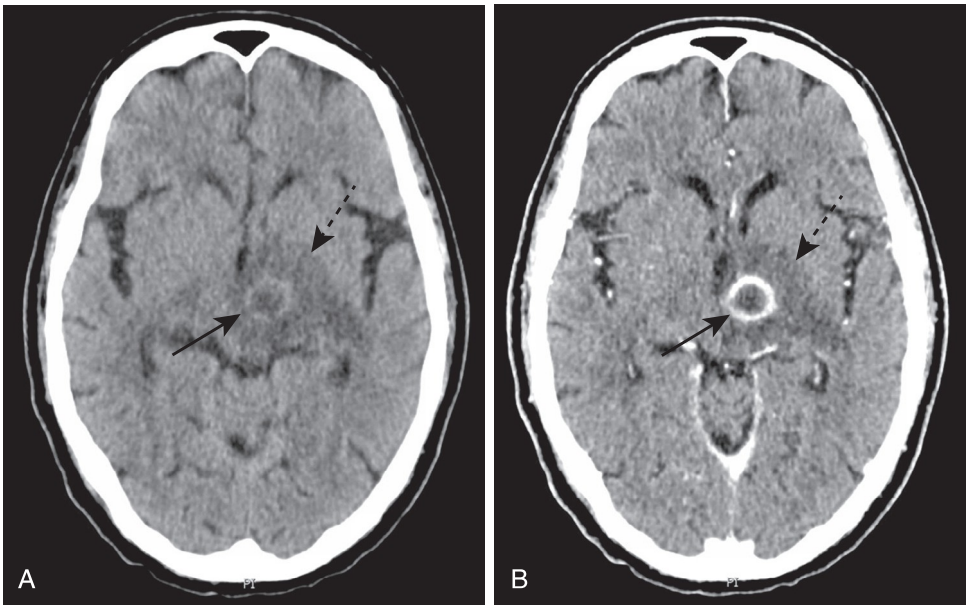

Figure 8.2. CNS toxoplasmosis in AIDS. (A) Precontrast CT and (B) postcontrast CT of the brain demonstrate a solitary mass in the left thalamus that is centrally hypoattenuating and peripherally enhancing *(arrows)* with surrounding vasogenic edema *(dashed arrows)*.

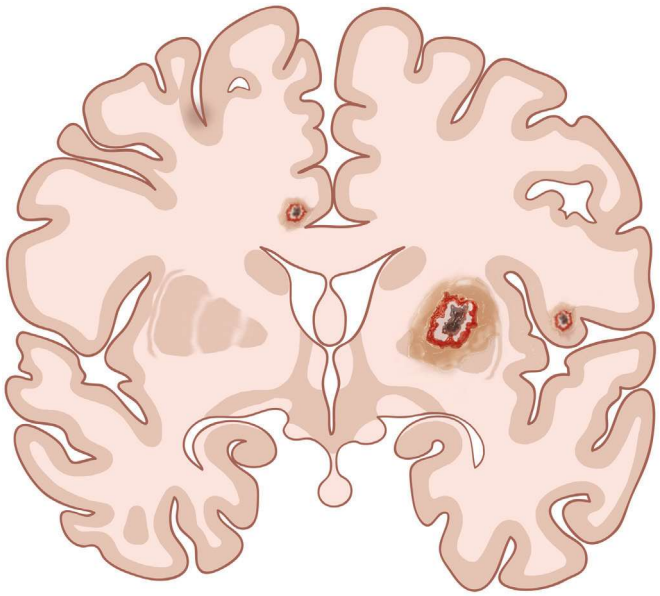

Figure 8.3. Illustration of a coronal section of the brain demonstrating toxoplasmosis necrotizing encephalitis involving the left basal ganglia and the gray-white junction.

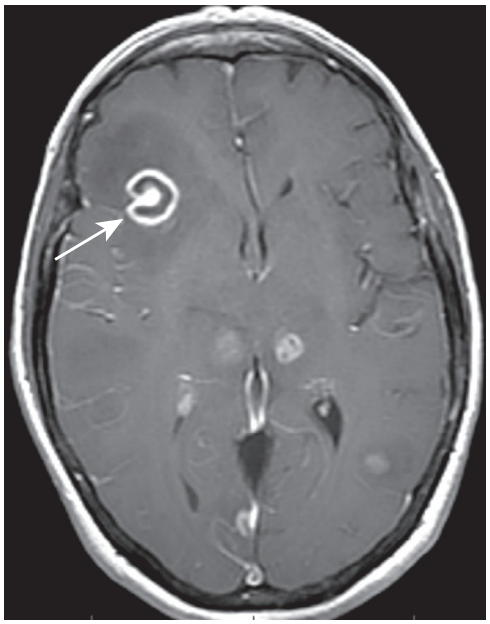

Figure 8.4. "Eccentric target sign." MRI of the brain with intravenous contrast demonstrates multiple enhancing lesions. The largest right frontal lobe lesion *(arrow)* illustrates the "eccentric target sign" characteristic of CNS toxoplasmosis.

MIMICS AND DIFFERENTIAL DIAGNOSIS

Congenital toxoplasmosis may closely resemble congenital cytomegalovirus (CMV), with ventriculomegaly and peripheral subcortical calcifications being more common in toxoplasmosis and polymicrogyria, cerebellar hypoplasia, and periventricular calcifications being more common in congenital CMV.[2]

The differential diagnosis of toxoplasmic encephalitis in immunocompromised patients almost always includes CNS lymphoma (Fig. 8.6). Single lesions with prominent mass effect but without a characteristic "eccentric target sign" or seronegative patients may particularly confound the diagnosis (Fig. 8.7). Hyperattenuating masses on CT and periventricular involvement favor lymphoma. However, in the setting of HIV/AIDS, there is a tendency for lymphoma to exhibit central necrosis prior to treatment, which may especially mimic toxoplasmosis. On MRI, diffusion-weighted images may be helpful differentiating lymphoma from toxoplasmosis given higher ADC values in toxoplasmosis lesions.[6] Perfusion imaging shows less cerebral blood volume and cerebral blood flow in toxoplasmosis than in lymphoma (Fig. 8.8). Positron-emission tomography shows decreased metabolism compared to lymphoma. Thallium-201 SPECT shows abnormal uptake in lymphoma but not in toxoplasmosis. Multiple other processes may mimic the appearance of toxoplasmosis lesions, including infections (e.g., tuberculosis, cryptococcosis and other fungal infections), metastatic disease, glioblastoma, subacute infarct or hemorrhage, radiation necrosis, and demyelination (Fig. 8.9).

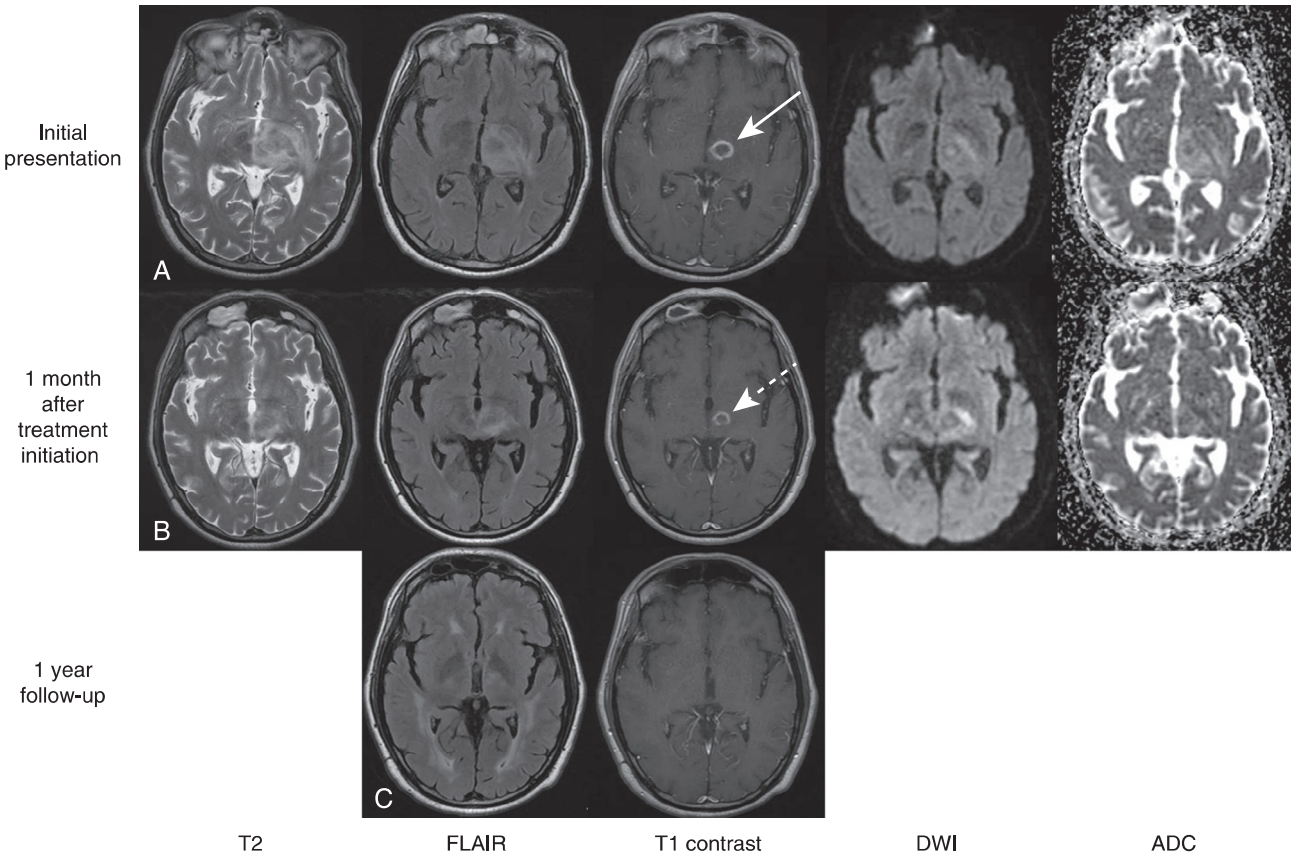

Figure 8.5. Evolution of CNS toxoplasmosis. Serial brain MRI images in a patient with AIDS presenting with progressive right-sided weakness and difficulty speaking. (Row A) Images at time of presentation demonstrate a left thalamic rim enhancing lesion *(arrow)* with surrounding T2/FLAIR hyperintense vasogenic edema and internal mild restricted diffusion. (Row B) Images 1 month after initiation of therapy demonstrate decreased size of the left thalamic rim enhancing lesion *(arrow)* with improvement of surrounding vasogenic edema and mild residual internal restricted diffusion. (Row C) Images 1 year after presentation demonstrate resolution of rim enhancing left thalamic lesion with a small focus of T2/FLAIR hyperintensity that likely represents gliosis. There is progression of periventricular white matter T2/FLAIR hyperintensity due to HIV encephalopathy.

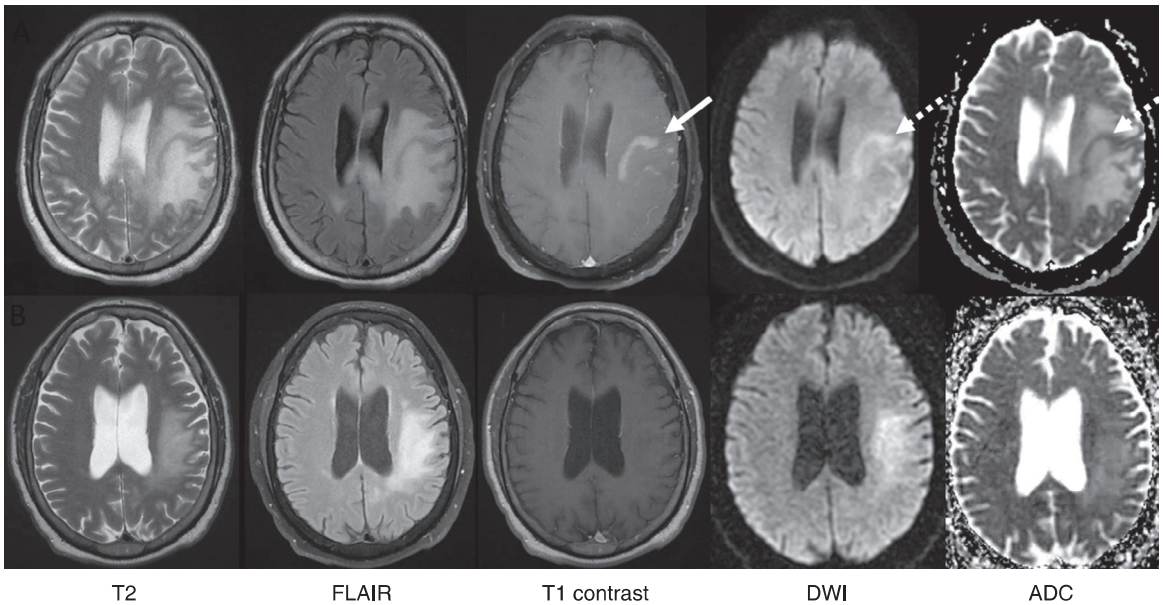

Figure 8.6. CNS lymphoma. Serial brain MRI images in a patient with CNS lymphoma. *Top row:* At the time of presentation, images demonstrate a curvilinear enhancing left corona radiata lesion *(arrow)* with associated restricted diffusion *(dashed arrow)* and surrounding T2/FLAIR hyperintense edema. *Bottom row:* At 1-month follow-up, images demonstrate a dramatic response to treatment with steroids. There is resolution of the previously seen enhancement and restricted diffusion as well as marked decrease in the associated edema.

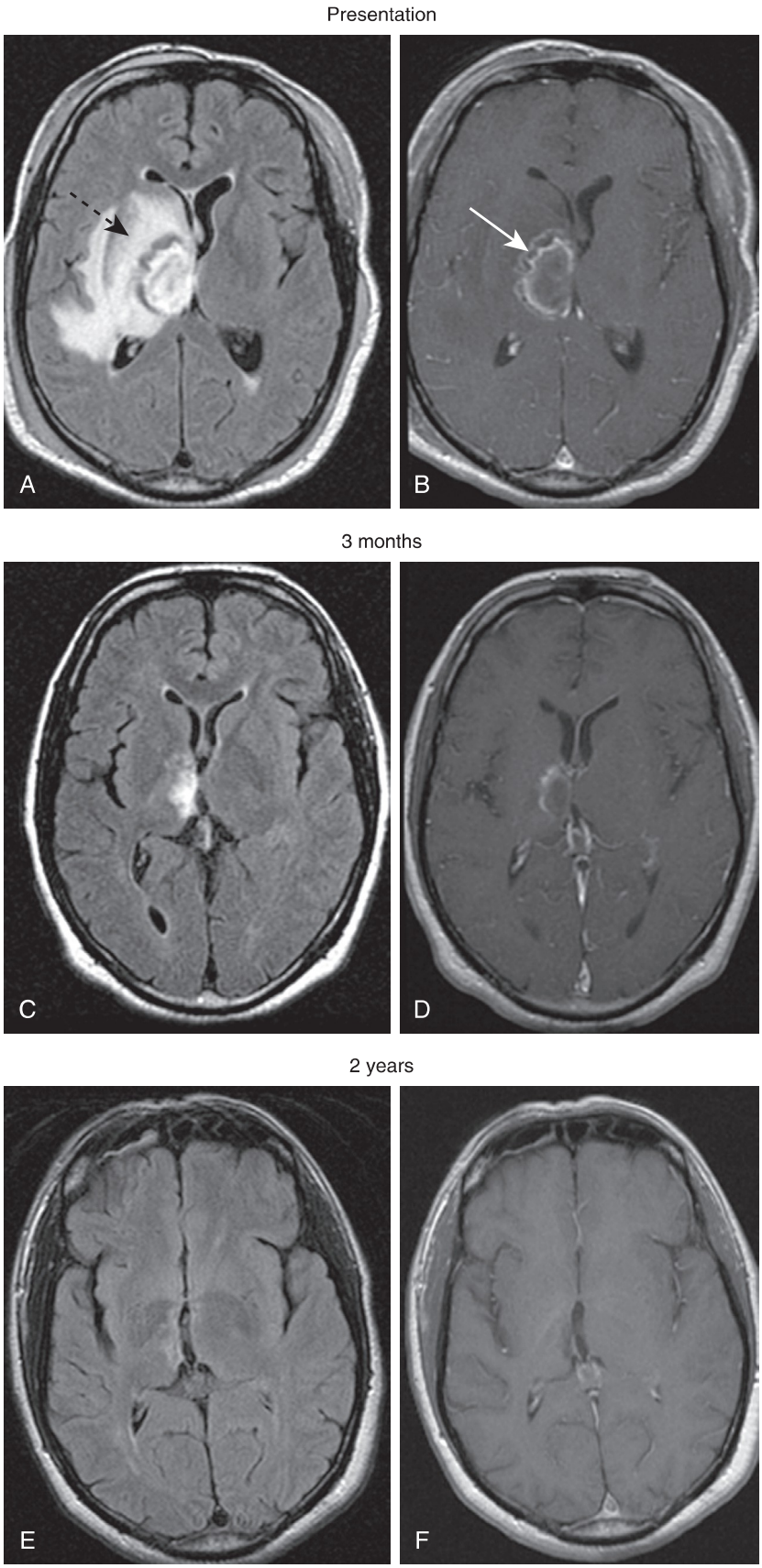

Figure 8.7. CNS toxoplasmosis mimicking tumor. Serial brain MRI images in a patient with CNS toxoplasmosis. *Top row:* Axial T2 FLAIR (A) and postcontrast T1 (B) images at time of presentation demonstrate a large rim enhancing right thalamic lesion *(arrow)* with extensive surrounding T2 hyperintensity *(dashed arrow)*. *Middle row:* At 3 months after initiation of therapy, axial T2 FLAIR (C) and postcontrast T1 (D) images demonstrate marked decrease in size of the right thalamic enhancing lesion with improvement of surrounding vasogenic edema. *Bottom row:* At 2-year follow-up axial T2 FLAIR (E) and postcontrast T1 (F) images demonstrate resolution of enhancement with residual encephalomalacia at the site of the prior lesion. *(Images courtesy Divya Bolar, MD, PhD, Massachusetts General Hospital, Boston.)*

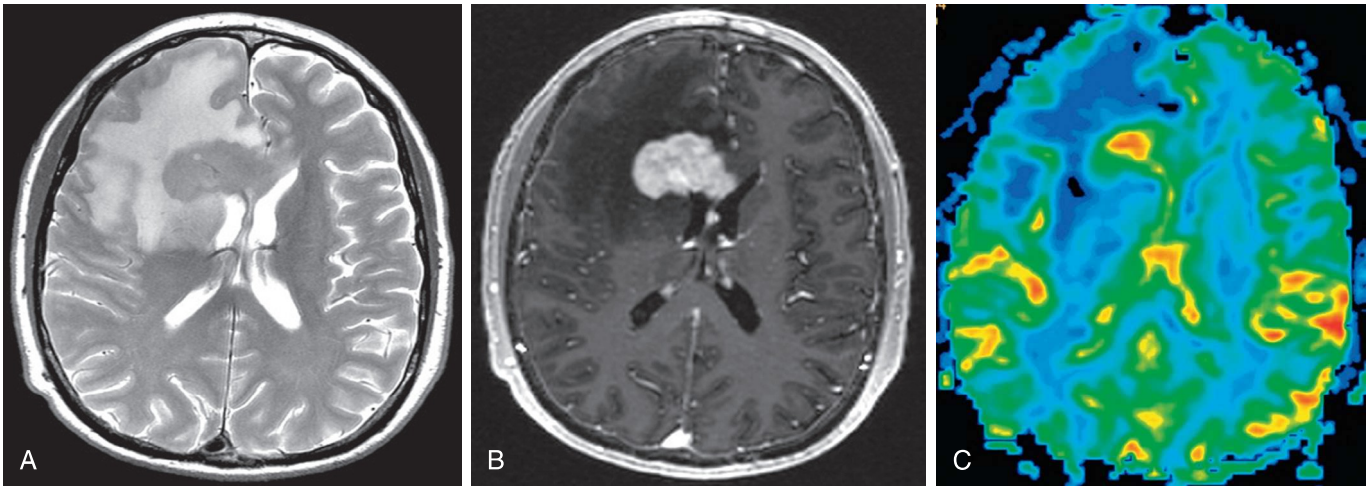

Figure 8.8. Perfusion imaging for CNS lymphoma. Brain MRI images demonstrate extensive vasogenic edema associated with a T2 hypointense (A), homogeneously enhancing callosal mass (B) with associated elevated relative cerebral blood volume (C).

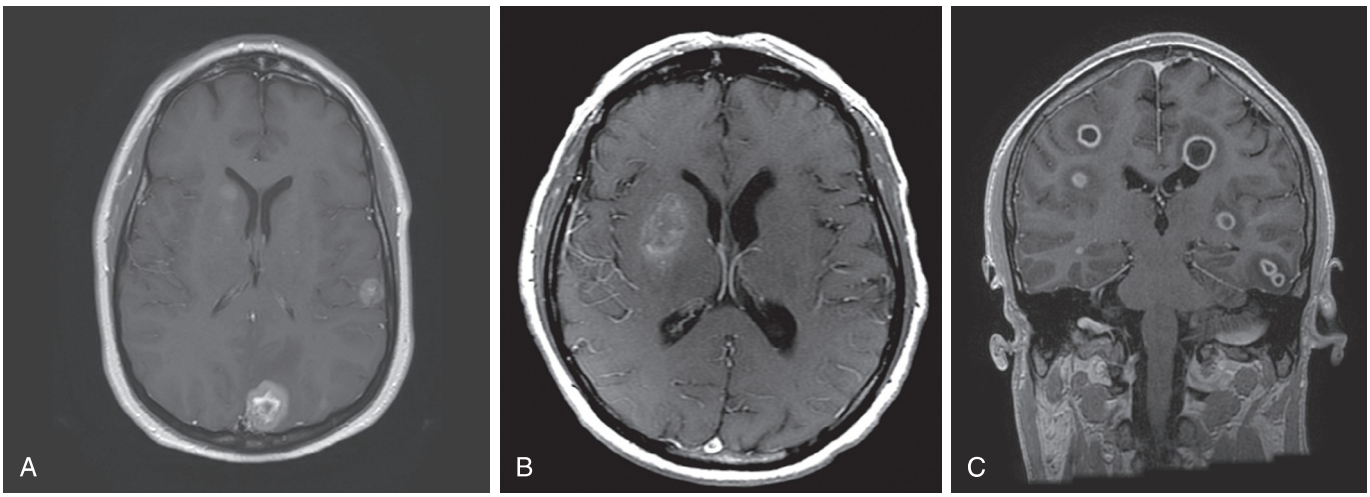

Figure 8.9. CNS toxoplasmosis mimics. Brain MRI studies with intravenous contrast. Axial postcontrast T1 images demonstrate (A) multiple densely enhancing renal cell metastases involving the right basal ganglia and cortex, and (B) large right basal ganglia heterogeneously enhancing lesion due to a subacute infarct. A coronal postcontrast T1 image (C) demonstrates numerous scattered smooth ring enhancing abscesses due to *Streptococcus mitis* septicemia.

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