

# Concurrent Cerebral American Trypanosomiasis and Toxoplasmosis in a Patient with AIDS

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**We report a case of concurrent cerebral infection with *Trypanosoma cruzi* and *Toxoplasma gondii* in a patient with acquired immunodeficiency syndrome (AIDS). A 22-year-old El Salvadoran man initially improved during receipt of anti-toxoplasmosis therapy, but he had rapidly progressive hemiplegia. Magnetic resonance imaging showed an abnormal finding in the left internal capsule, and cytological analysis of cerebrospinal fluid revealed *T. cruzi* trypomastigotes. Despite prompt therapy with nifurtimox, the patient's mental status declined, and he died of nosocomial complications. Although infrequent, *T. cruzi* infection should be considered in the differential diagnosis of brain lesions in patients with AIDS from regions of endemicity.**

Opportunistic infections with parasites are common in patients who have AIDS. *Toxoplasma gondii* is the most common cause of focal brain lesions in patients with AIDS [1]. The clinical syndrome of encephalitis with deterioration in mental status, neurological dysfunction, fever, seizure, and headache in patients with antibodies to *T. gondii* with concomitant neuro-radiologic evidence (ring-enhancing lesions in the basal ganglia detected by CT and MRI) is highly suggestive of reactivated *T. gondii* infection. Short of demonstrating the presence of parasites in brain tissue, a rapid clinical response to empirical therapy bolsters evidence for the diagnosis of *T. gondii* infection [2].

Although less common than *T. gondii* infection, *Trypanosoma cruzi* infection (Chagas disease) also has the potential to cause fatal meningoencephalitis in patients with AIDS. *T. cruzi* most frequently affects the heart and the gastrointestinal tract in

patients without HIV infection, but in patients with AIDS, cerebral infection is the most common form of reactivation disease [3–8]. Single or multiple ring-enhancing lesions revealed by CT, which are similar to those seen in cases of toxoplasmosis, and hypodense tumor-like lesions have been reported [3, 5, 9–11].

In this report, we present the first case, to our knowledge, of cerebral coinfection with *T. cruzi* and *T. gondii* in a patient with newly diagnosed AIDS. This case illustrates the difficulty of diagnosing Chagas disease in a timely manner and the necessity for its consideration in the differential diagnosis of brain lesions in patients with AIDS from areas of endemicity.

**Case report.** A 22-year-old El Salvadoran man who arrived in the United States 2 years earlier presented to our hospital emergency department with a 2-day history of epistaxis. His medical history revealed occasional fevers, chills, sweats, sore throats, headaches, and a weight loss of ~4.54 kg (10 pounds) over the previous 2 months. The patient denied any rash, shortness of breath, contact with sick persons, or recent travel. Two months earlier, the patient had been in the emergency department for fatigue, headache, and feeling “spaced out.” A diagnostic work-up performed at that time, including a complete blood cell count, measurement of electrolyte levels, analysis of the CSF profile, chest radiography, and head CT, was normal. The patient's medical history was unremarkable. In El Salvador, the patient lived in a rural area where farm animals were abundant.

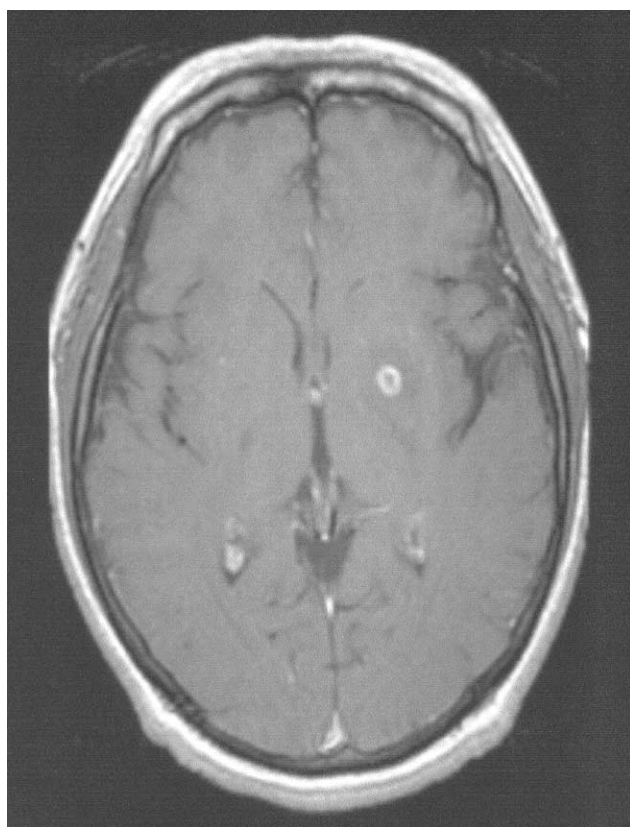
The initial physical examination revealed a temperature of 38.4°C (101.2°F), a pulse of 114 beats/min, a respiratory rate of 14 breaths/min, and a blood pressure of 109/66 mm Hg. The patient was alert, oriented, and thin. A head examination revealed thrush and left nostril epistaxis. He had tachycardia. Findings of neck, lung, abdomen, back, skin, and neurological examinations were unremarkable. The complete blood cell count, electrolyte levels, liver enzyme levels, coagulation panel findings, and chest radiograph findings were normal. The results of a rapid HIV test were positive, with a CD4<sup>+</sup> cell count of 77 cells/mm<sup>3</sup> (8%), and a CT scan of the head revealed ring-enhancing lesions in the left basal ganglia. An MRI of the brain further showed surrounding cerebral edema and an abnormal signal intensity in the corpus callosum (figures 1 and 2). The anti-toxoplasma IgG titer was positive, and results of blood cultures were negative.

Pyrimethamine, sulfadiazine, and leucovorin were administered, and sulfadiazine was later replaced with clindamycin because of a drug rash. The patient had a seizure during the

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**Figure 1.** Initial MRI revealing a ring-enhancing lesion in the left basal ganglia. There was near-complete resolution of this finding after 1 week of antitoxoplasmosis therapy.

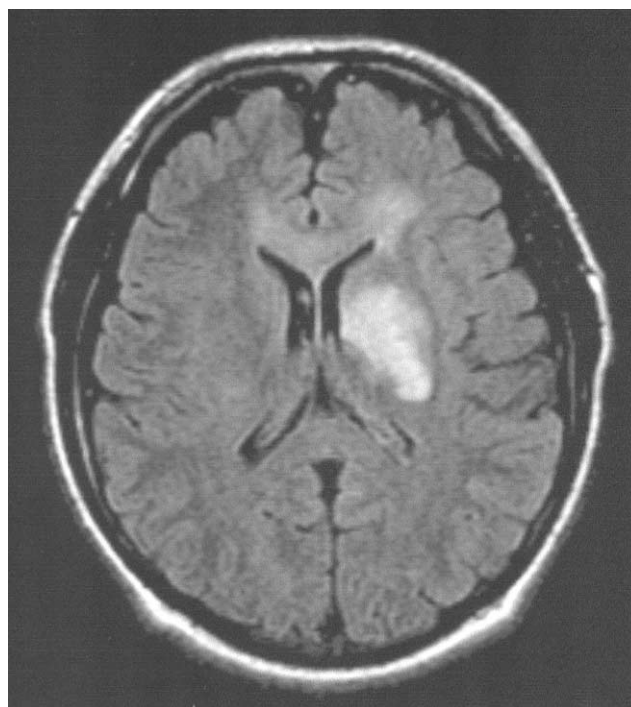
first week of therapy, and a second MRI of the brain revealed marked improvement in the appearance of lesions in the basal ganglia. He was also given nystatin for thrush, levetiracetam for seizure, and atovaquone for pneumocystis prophylaxis. He was discharged from the hospital in stable condition without corticosteroid therapy.

During the third week of therapy, the patient was brought to the emergency department with a 3-day history of ataxia and dysarthria. The patient had experienced a rapidly progressing right-side weakness. He did not have any fever, chills, nausea, vomiting, diarrhea, trauma, or recurrent seizure. According to his mother, he had consistently taken his medications while at home. A physical examination showed a temperature of 38.1°C (100.6°F), a pulse of 100 beats/min, a respiration rate of 20 breaths/min, and a blood pressure of 100/56 mm Hg. The patient was alert and oriented, but he was unable to speak or to move his right side. He had bilateral conjunctivitis, without uveitis, and moderate thrush. He had tachycardia, but results of neck, lung, abdomen, and skin examinations were normal. He had a shallow, 2-cm penile ulcer next to the glans penis. Although a neurological examination revealed that the patient's left side was completely normal, he

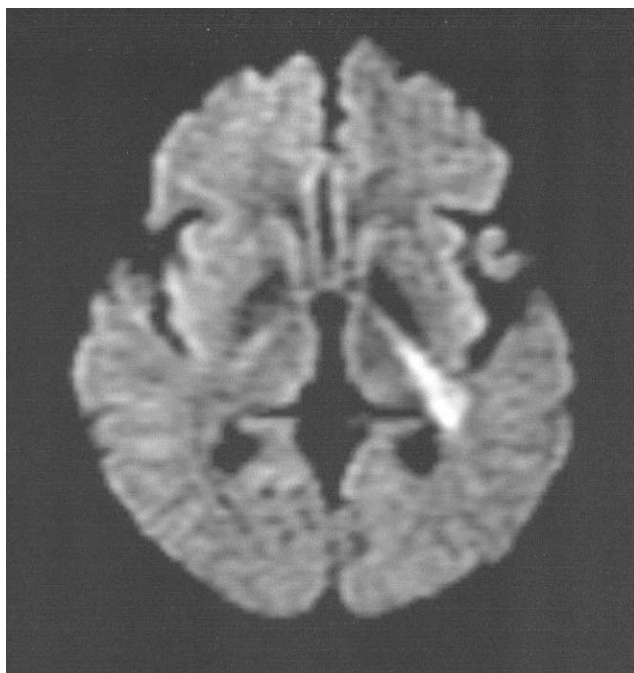
had right-side facial droop, decreased gaze to the right, and moderate right arm and leg weakness, with increased deep-tendon reflexes and down-going toes. Results of a sensory examination were normal.

The complete blood cell count, electrolyte levels, liver enzyme levels, coagulation panel findings, and chest radiograph findings were again normal. CT and MRI of the brain showed complete resolution of the left basal ganglia lesion, the surrounding edema, and the abnormal signal in the corpus callosum. On a diffusion-weighted MRI, however, there was a new, abnormally increased signal intensity in the posterior limb of the left internal capsule (figures 3 and 4). The CSF profile was also completely normal, with <1 leukocyte, and results of bacterial and fungal cultures were negative. PCR for JC virus, tests for detection of coccidioidomycosis antibody and cryptococcal antigen, and results of a viral encephalitis panel (including tests for Epstein-Barr virus, cytomegalovirus, varicella-zoster virus, and herpes simplex virus) and a Venereal Disease Research Laboratory test were all negative. Findings of electroencephalography, electrocardiography, and echocardiography were unrevealing.

Given the conjunctivitis, the penile ulcer, an elevated erythrocyte sedimentation rate of 98 mm/h, and the unusual MRI finding, vasculitis or neuro-Beçet syndrome was considered. Primary CNS lymphoma and progressive multifocal leukoencephalopathy were thought to be less likely etiologies. Empirical dexamethasone was initiated, but the patient's neurological func-



**Figure 2.** Fluid-attenuated inverse recovery image demonstrating abnormal signal intensity in the region of the ring-enhancing lesion, as well as in the anterior corpus callosum.



**Figure 3.** Diffusion-weighted MRI revealing a new area of abnormal high-signal intensity in the posterior limb of the left internal capsule, suggesting restricted diffusion.

tion continued to decline over the next week. A lumbar tap yielded bloody CSF, and empirical acyclovir was given, until a subsequent cytological examination of a CSF specimen detected *T. cruzi* (figure 5). A buffy-coat smear also revealed parasites. Nifurtimox obtained from the Centers for Disease Control and Prevention (CDC; Atlanta) was given at 10 mg/kg per day in 4 divided doses. Unfortunately, the patient's mental status further declined, which resulted in aspiration pneumonia and sepsis requiring mechanical ventilation. During the following days, the patient did not show any sign of recovery, despite aggressive medical management, and his family elected to withdraw care.

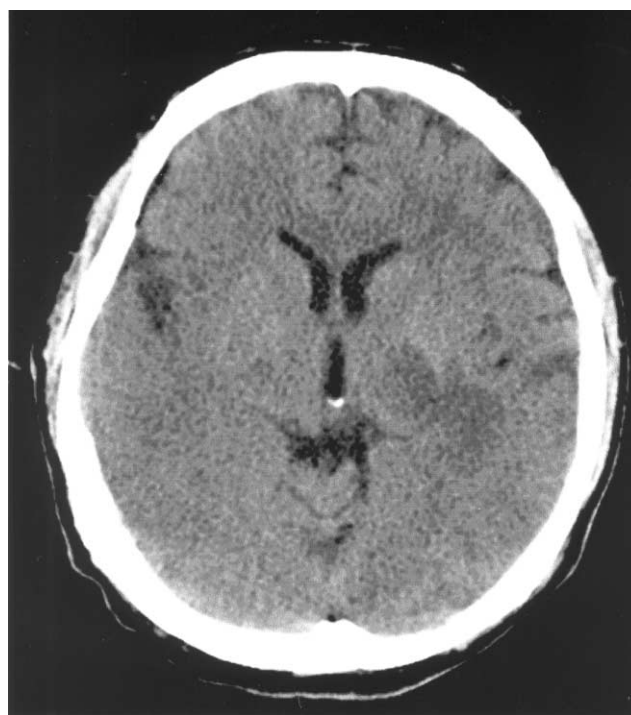
**Discussion.** The patient's initial presentation was typical of CNS toxoplasmosis, one of the indicator conditions in the 1993 CDC case definition of AIDS [2, 12]. He received a diagnosis of AIDS, with a CD4<sup>+</sup> cell count of 77 cells/mm<sup>3</sup> (8%), he had anti-toxoplasma IgG, and he had typical ring-enhancing lesions in the left basal ganglia revealed by CT and MRI. After initiating the antitoxoplasmosis therapy, the patient's brain lesions resolved, which is expected in cases of CNS toxoplasmosis.

The progressive hemiparesis, however, was not typical of CNS toxoplasmosis, and we sought an alternate etiology. The presence of conjunctivitis, a penile ulcer, and an elevated ESR, coupled with the unusual MRI finding, suggested possible vasculitis or neuro-Behçet syndrome. The CSF profile remained normal, and results of various serological tests for infectious causes were also negative. Fortunately, the discovery of the parasite in the CSF led to the diagnosis of cerebral Chagas disease.

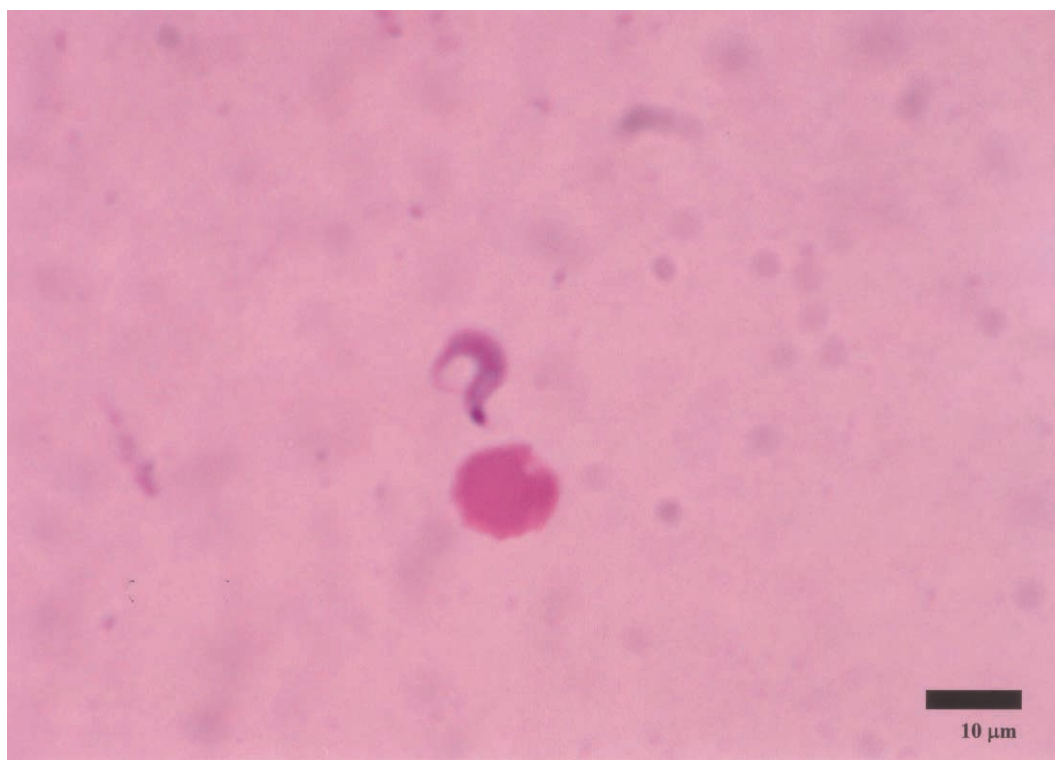
A review of the literature shows that the seroprevalence of chronic Chagas disease is high among immigrants from regions in which AIDS is endemic, including El Salvador, the homeland of our patient. Among 205 Nicaraguan and El Salvadoran immigrants living in the Washington, D.C., area in 1984 and 1985, 4.9% were infected with *T. cruzi*, and parasites were recovered in 50% of attempted xenodiagnostic analyses [13]. Among 988 blood donors at Los Angeles County hospital in mid-1987, 380 were born in countries of endemicity, and the overall seroprevalences of *T. cruzi* was 1.1% [14]. In a recent study of 1.1 million blood donations in Los Angeles area in 1998, 7.4% of donors were born and had resided in regions of endemicity, and 0.018% were confirmed to be seropositive, up from 0.010% in 1996 [15].

Although cardiac and gastrointestinal manifestations of Chagas disease are common in the general population in areas where AIDS is endemic, a CNS disease due to reactivated chronic *T. cruzi* infection is more common in patients infected with HIV in such areas [7, 8]. Clinical features of cerebral *T. cruzi* infections reported in literature share some similarities with those of CNS toxoplasmosis. Encephalitis syndromes of both parasitic infections include focal neurological dysfunction, fever, seizure, and headache, which are indicative of intracranial hypertension and meningitis [4, 8, 10].

There are, however, distinguishing aspects of the 2 parasitic infections. A history of exposure or travel to regions where



**Figure 4.** Nonenhanced CT scan performed 3 weeks after the initial presentation showing a new, mass-like area of low attenuation at the posterior limb of the left internal capsule.



**Figure 5.** A *Trypanosoma cruzi* trypomastigote is seen next to an RBC in a CSF specimen. Bar, 10  $\mu$ m.

AIDS is endemic raises the suspicion of Chagas disease. In addition, concomitant cardiac or gastrointestinal disease suggests the possibility of Chagas disease [8]. A CSF profile may be normal, as in our case, or may be associated with a high opening pressure, mild lymphocytic pleocytosis, hypoglycorrhachia, and a high protein level, but none of these parameters is specific. Serological testing, though not standardized, may be helpful in cases with a high index of suspicion. On occasion, motile *T. cruzi* trypomastigote is identified in CSF or blood smears [8, 10].

Neuroimaging findings may be different for these 2 parasitic infections. In *T. cruzi* infections, single or multiple hypodense lesions, with or without ring-enhancement, on CT scans have been reported [9]. A nodular-shaped chagoma that enhances on CT imaging may also be seen. It can appear as a hypointense lesion on a T1-weighted MRI sequence that enhances with gadolinium contrast or as a hyperintense mass on a T2-weighted MRI [16]. Lazo et al. [16] suggest that *T. gondii* infections generally involve the cerebral cortex and the basal ganglia, whereas *T. cruzi* infections primarily affect the white matter [17]. Findings of initial CT and MRI for our patient were consistent with *T. gondii* infection. The MRI from the second admission showed abnormally increased signal intensity in the posterior limb of the left internal capsule that was atypical for either disease. However, the last nonenhanced CT scan dem-

onstrated a mass-like hypodense structure in this region, which may represent a chagoma (figure 4).

Our patient's fatal outcome is typical of reported cases of cerebral *T. cruzi* infections. In one review, the number of case-fatalities was high, with a 10-day median duration of survival [8]. Nifurtimox and benznidazole are considered to be equally efficacious in treating cerebral *T. cruzi* infections, but treatments with either medication have had only anecdotal success [8, 10, 17]. At this time, the most optimal therapeutic protocol has not been defined.

In summary, we reported a case of concurrent *T. gondii* and *T. cruzi* cerebral infections in a patient with AIDS. Although cerebral *T. cruzi* infection is not common, it should be a part of the differential diagnosis for HIV-infected patients from regions where AIDS is endemic, especially if such patients are not improving as rapidly as expected during antitoxoplasmosis therapy.

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**Conflict of interest.** C.K.B.: Speakers' bureau of Roche, Abbott, and Wyeth Pharmaceuticals and consultant for Roche and Abbott. All other authors: No conflict.

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