# Clinical Reasoning: A 35-year-old man with a right hemiplegia and a cerebral mass

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## SECTION 1

A 35-year-old man presented with progressive right face, arm, and leg weakness, and diffuse headache. He lived in rural northwest Argentina. He had a past medical history of sexually transmitted diseases. On examination, he was alert and fully oriented, and had a right hemiparesis with hyperreflexia and an extensor plantar reflex. Apart from low grade fever, the rest of the physical examination was unremarkable. The complete blood count revealed leukopenia (3,300 leukocytes/mL); renal function, liver tests, electrolytes, erythrocyte sedimentation rate, and glucose level were normal. He tested positive for HIV with a CD4 count of 18 cells/mm$^3$ and viral load of 133,400 copies/mm$^3$. Brain CT showed a nonenhancing left temporoparietal lesion with surrounding edema and midline shift.

**Questions for consideration:**

1. What are the possible etiologies of this intracerebral lesion?
2. What additional diagnostic testing would you consider at this point?

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See last page for Mystery Case responses

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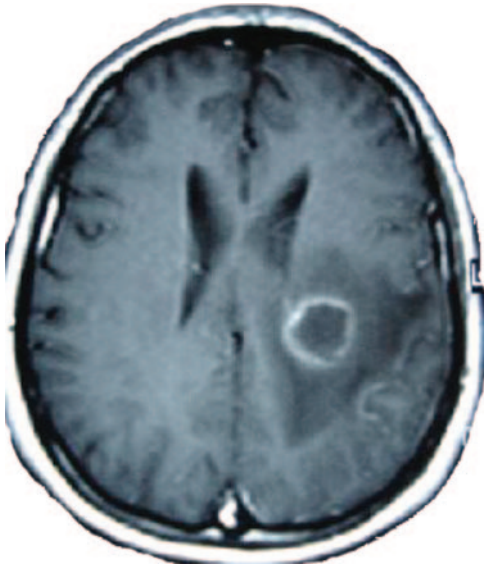
## SECTION 2

The patient was started on empirical treatment for toxoplasmosis without clinical improvement. A brain MRI with gadolinium performed days later showed a left temporoparietal mass with a ring-like enhancement pattern and marked perilesional edema (figure). Serologies for hepatitis B virus, hepatitis C virus, VDRL, and *Toxoplasma* (immunoglobulin G, immunoglobulin M, and immunoglobulin A subtypes) were negative. Blood cultures for bacteria, fungi, and mycobacteria were also negative. Since the patient lived in an endemic area, a search for Chagas disease was performed. The serology confirmed chronic Chagas disease (both indirect immunofluorescence and indirect hemagglutination tests were positive). Blood parasitological tests like microconcentration and Giemsa staining of thin and thick blood smears were also performed. Neither of these revealed the presence of the trypomastigote form of *Trypanosoma cruzi*.

**Questions for consideration:**

1. What is your differential diagnosis at this point?
2. What additional diagnostic tests would you consider at this point?

**Figure** Gadolinium-enhanced MRI displaying a ring-enhancing pattern and marked perilesional edema



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## SECTION 3

A lumbar puncture was performed. The CSF analysis showed 5 cells/mm$^3$, glucose 48 mg/dL (serum glucose: 97 mg/dL), $Cl^-$ 121 mEq/L, and protein 0.44 g/dL. PCR testing was negative for *Toxoplasma*, JC virus, and Epstein-Barr virus. A negative result for *Cryptococcus neoformans* was obtained with both India ink stain and antigen testing. A Giemsa-stained CSF smear revealed the presence of the trypomastigote form of *T cruzi.*

**Questions for consideration:**

1. How would you manage the treatment of an HIV-positive patient with cerebral tumor–like Chagas disease?
2. How long would you extend treatment?
3. What is the prognosis?

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## SECTION 4

As soon as the diagnosis of cerebral tumor–like Chagas disease was made (approximately 10 days after admission), the patient was started on benznidazole 5–7 mg/kg/d and he resumed highly active antiretroviral therapy. In the course of treatment, seizures appeared and were partially controlled with lamotrigine. The patient developed neutropenia later in the course of his treatment, which was attributed to benznidazole, which was then replaced by nifurtimox 8–10 mg/kg/d. After 3 months of treatment, the patient exhibited improvement in both his neurologic condition and his immune status.

A new MRI showed a remarkable reduction in both the size of the lesion and its corresponding edema.

**DISCUSSION** Chagas disease, also known as American trypanosomiasis, is an endemic parasitosis of Central and South America caused by the flagellated protozoan *T cruzi*. Although uncommon in the United States, its prevalence is expected to increase due to immigration from endemic areas.[1] It is transmitted to humans by hematophagous Triatominae insects, and occasionally by other routes (blood transfusions, IV drug use, and congenitally[2]).

The disease course can be divided into 3 phases: acute, indeterminate, and chronic. The chronic phase is characterized by prominent cardiac and gastrointestinal involvement (10%–30%), but often it can remain asymptomatic.[3] In AIDS and other severe immunodeficient states, there is an increased risk of disease reactivation, with a particular predilection for the CNS (75% of cases) both in the form of meningoencephalitis and intracranial mass lesions.[4] This is especially true for patients with AIDS with CD4 counts $<200$ cells/mm$^3$. Cerebral Chagas disease presenting as a tumor-like lesion is often clinically and radiologically indistinguishable from other more prevalent opportunistic diseases, like toxoplasmosis and lymphoma, and should be included in the differential diagnosis of patients with AIDS from endemic areas.[5]

Diagnostic tests like CSF direct examination (Giemsa stain) and PCR techniques[6,7] could provide a prompt diagnosis, avoiding the need for a brain biopsy.

The antiparasitic drugs benznidazole and nifurtimox are considered standard treatment.[8,9] Even though there is a lack of agreement regarding treatment duration, it would be wise to maintain antiparasitic therapy until a CD4 count $>200$ cells/mm$^3$ has been reached.[9]

Cerebral Chagas disease has a poor prognosis, often leading to death within weeks of diagnosis.[10] A high level of suspicion, coupled with early diagnosis and treatment, is the only way to achieve a better prognosis.

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## MYSTERY CASE RESPONSES

We invited residency programs, medical student preceptors, and individuals to utilize this Mystery Case as an educational tool to develop trainees' clinical reasoning skills. Groups or individuals read the case presentation, developed their own differential diagnoses, and determined what would be their next step in either diagnosing or treating the patient. Here are the responses to our first Mystery Case.

We had 23 responses to this first Mystery Case. All were from individual residents rather than groups. All responses were thoughtful and many were quite de-

tailed, including several alternative diagnoses and extensive descriptions of the respondent's approach to the diagnosis and management of this patient.

All respondents considered the fact that the patient had HIV and was immunocompromised in their differential diagnosis. All respondents included toxoplasmosis and CNS lymphoma at the top of their differential. All described many of the other most common considerations, and most outlined appropriate courses of diagnosis and management. Six respondents considered the patient's area of residence in South America as relevant to the diagnosis, most discussing the possibility of neurocysticercosis. Only 2 respondents, however, included the diagnosis of trypanosomiasis—infection with *T cruzi*, or Chagas disease—in the differential: Kate Ahmad, The Canberra Hospital, Canberra, Australia, and Peter Armanas, Walter Reed Army Medical Center, Washington, DC. Additional considerations, in descending order of the number of times which they were cited, included bacterial abscess, cryptococcus and other fungal infections, viral infections, neurocysticercosis, glioma, metastases, tuberculoma, syphilis, progressive multifocal leukoencephalopathy, infarction, and tumefactive multiple sclerosis.

Half of the respondents recommended starting empiric therapy for toxoplasmosis, followed by brain biopsy if there were no response after several weeks. All suggested measuring serologies against many infectious organisms, though several expressed concerns about performing lumbar puncture due to the presence of the mass lesion. Seven suggested magnetic resonance spectroscopy as a way to distinguish tumor, infection, and vascular lesions.

This first Resident & Fellow Section Mystery Case points to the importance of considering diagnoses of infections uncommonly seen in the United States when evaluating immunocompromised patients from other countries. It is likely that with the increase in international travel we will all see more patients like this one.

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*Resident & Fellow Section Editor*

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