*Case report*

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# Hemorrhagic brain lesions in a newly diagnosed HIV-1 infected patient

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## Abstract

We report the case of a previously healthy 29-year-old man who has sex with men who was admitted with sub-acute onset of headache, seizures and altered mental status. Physical examination revealed oral thrush, mental confusion and right hemiparesis. An unenhanced computed tomography of the brain revealed multiple rounded hemorrhages associated with perilesional edema and no enhancement was seen after contrast infusion. A rapid test for HIV-1 was positive and the CD4 T-lymphocyte count was 120 cells/mm$^3$. Pyrimethamine, sulfadiazine plus folinic acid and dexamethasome were started. After two weeks of treatment, the clinical condition and neuroimaging of the patient remained unaltered. A stereotactic brain biopsy was performed and the histopathologic examination confirmed the diagnosis of hemorrhagic toxoplasmosis. After a longer course of anti-Toxoplasma treatment due to an incomplete clinical and radiological response, the patient was discharged home. Hemorrhagic toxoplasmosis is a rare presentation of cerebral toxoplasmosis and should be considered in the differential diagnosis of hemorrhagic cerebral lesions in HIV-infected patients in order to initiate specific treatment promptly.

## Keywords

Cerebral toxoplasmosis, toxoplasmosis, diagnostic imaging, diagnosis, AIDS

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## Introduction

Incidence of acquired immune deficiency syndrome (AIDS)-related cerebral toxoplasmosis decreased markedly in the highly active antiretroviral therapy era. However, cerebral toxoplasmosis remains a condition with poor prognosis in the natural history of people living with human immunodeficiency virus (HIV)/AIDS[1] and continues to be a common cause of hospital admission in this population, particularly in resource-limited settings.[2] Definitive diagnosis of cerebral toxoplasmosis requires a compatible clinical syndrome; identification of one or more mass lesions by computed tomography (CT) or magnetic resonance imaging (MRI), and detection of the organism in a clinical sample.[3] In clinical practice, a presumptive diagnosis is made with a suggestive clinical syndrome and one or more expansive brain lesions on images. These lesions are usually ring-enhancing and have a predilection for the basal ganglia. However, the spectrum of radiological manifestations is broad and the diagnostic suspicion is vital for the timely introduction of antiparasitic treatment.[4–6] Here, we present a patient with hemorrhagic brain lesions due to *Toxoplasma gondii* in a newly diagnosed HIV-1 infected patient in São Paulo, Brazil.

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## Case report

A previously healthy 29-year-old man who has sex with men was admitted with sub-acute onset of headache, seizures and altered mental status. Physical examination revealed thrush, mental confusion and right hemiparesis. The patient was admitted to the Intensive Care Unit. An unenhanced CT of the brain performed on admission revealed findings compatible with hemorrhagic lesions and surrounding edema (Figure 1(a)) and no enhancing lesions were observed after contrast infusion. A brain CT angiography was normal. Carotid Doppler ultrasonography, electrocardiogram and lipid profile were normal. A rapid test for HIV-1 was positive and serology was negative for syphilis and hepatitis C virus. The CD4 T-lymphocyte count was 120 cells/mm$^3$ and the plasma HIV-1 RNA level was 78,776 copies/μL (4.9 log10); anti-*T. gondii* IgG was positive. Pyrimethamine 200 mg per os (PO) once followed by pyrimethamine 50 mg PO daily plus sulfadiazine 1500 mg PO q6h plus leucovorin 15 mg PO daily plus dexamethasone 4 mg intravenous (IV) q8h were started. After two weeks of treatment, the clinical condition and neuroimaging of the patient remained unaltered. A stereotactic brain biopsy was performed and histopathological study showed cerebral tissue with extensive areas of hemorrhagic necrosis and reactive gliosis and the immunohistochemical assay yielded antigens of *T. gondii* (Figure 2). Thus, the diagnosis of hemorrhagic cerebral toxoplasmosis was confirmed. Anti-*T. gondii* therapy was maintained and the dose of corticosteroids was progressively decreased until discontinuation.

After eight weeks of antiparasitic treatment and three weeks of corticosteroids, the patient presented consistent neurologic improvement and a new CT of the brain showed resolution of prior lesions (Figure 1 (b)). He was discharged home with residual hemiparesis and on maintenance antiparasitic therapy.

## Discussion

We present a very rare case of an HIV-infected patient with exclusively hemorrhagic brain lesions as a manifestation of cerebral toxoplasmosis.

Imaging studies, either CT or MRI, are key for the diagnosis of cerebral toxoplasmosis, with the latter being more sensitive than the former. The typical findings are multiple ring-enhancing lesions with surrounding vasogenic edema and mass effect in the basal ganglia, thalamus and corticomedullary junction.[4,5,7] On unenhanced CT images, cerebral toxoplasmosis usually appears as multiple hypoattenuating or isoattenuating lesions, although a single lesion may be seen.

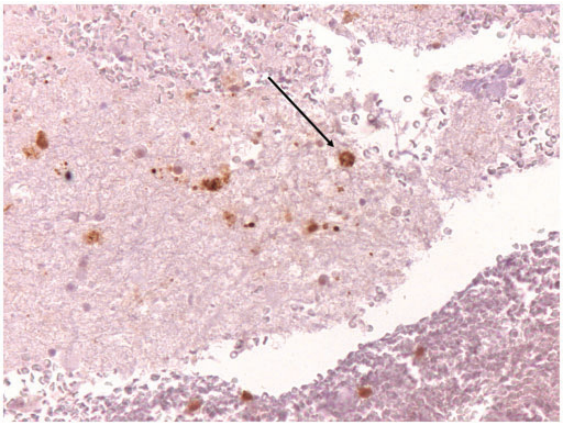

**Figure 2.** Immunohistochemical assay for *Toxoplasma gondii* shows some cysts (arrow) (magnification 400×).

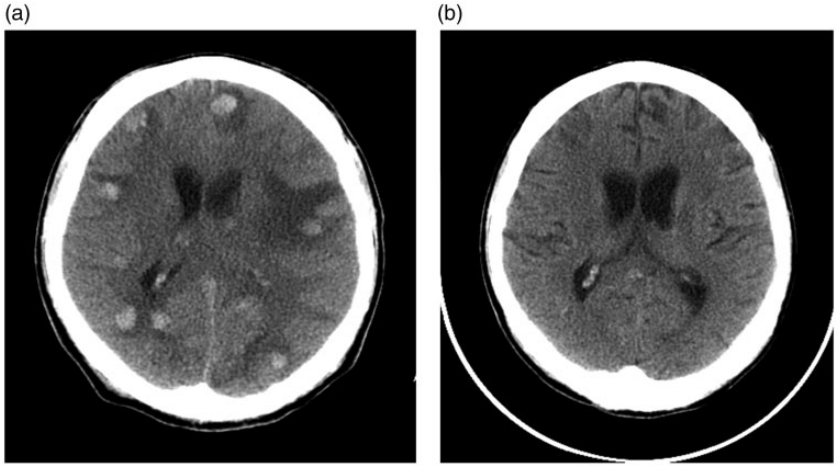


**Figure 1.** (a) Non-contrast-enhanced computed tomography (CT) revealing multiple intraparenchymal hyperdense rounded areas compatible with hemorrhagic lesions and surrounding edema. (b) Two months after anti-Toxplasma treatment, a contrast-enhanced CT showed resolution of prior lesions.

On contrast-enhanced CT images, these lesions may have a thin, smooth or poorly-defined rim of enhancement, solid eccentric nodular enhancement or less often no enhancement.[4,5,7] Hemorrhagic changes have been reported rarely in clinical series of cerebral toxoplasmosis[4,7,8] and there are few case reports.[9–17] Hemorrhagic cerebral toxoplasmosis may involve the cortical gray, basal ganglia, brainstem or cerebellum and can occur before or after the onset of antiparasitic treatment.[9–14] In most reports, hemorrhagic cerebral toxoplasmosis showed: (i) small isolated areas of hemorrhagic foci or within the lesions; or (ii) cerebral ring hemorrhagic lesions.[16–18] However, exclusively multiple rounded hemorrhages associated with perilesional edema can be the unique radiological finding,[11] as was observed in the present case. CT was used in all reports of hemorrhagic cerebral toxoplasmosis but some studies performed MRI.[12,13,16,17] Interestingly, a single study reported a high proportion of hemorrhagic lesions: 7 (64%) of 11 patients with cerebral toxoplasmosis showed compatible findings on precontrast axial T1 weighted MRI scans. Six of these cases had hemorrhagic lesions on initial clinical presentation and one developed hemorrhagic lesions during the treatment.[18] Only three (43%) of these seven cases had shown any evidence of hemorrhage on CT scans, demonstrating the higher sensitivity of MRI in hemorrhagic toxoplasmosis.[18]

Of the patients with cerebral toxoplasmosis who eventually improve, 86% will show clinical improvement by day 7 of treatment and 95% will show radiographic improvement by day 14 of treatment.[8,19]

Patients presumptively treated for cerebral toxoplasmosis should be monitored clinically and radiographically within the next 10 to 14 days. Lack of response to therapy, indicated by the persistence or worsening of clinical symptoms and expansive brain lesion(s) observed in CT or MRI, indicates the need for a diagnostic stereotactic biopsy.[20] This classical recommendation was followed in the present case. However, it is important to note that this algorithm was devised as a means to determine the need for biopsy in the patient most likely to have primary central nervous system lymphoma,[21] the most common differential diagnosis of cerebral toxoplasmosis in high-income countries, but not in low- and middle-income countries, where other infectious diseases can be observed (for example, tuberculosis or Chagas' disease). Nowadays, earlier biopsy should be strongly considered if results from imaging, serology and/or cerebrospinal fluid (CSF) polymerase chain reaction (PCR) studies are negative and suggest an etiology other than cerebral toxoplasmosis.[3] Longer courses may be necessary if disease is extensive or response is incomplete at six weeks.[3] It is possible that in some cases of hemorrhagic cerebral toxoplasmosis, particularly those multiple, extensive and/or localized lesions in the posterior fossa, the response may be slower too. Some of these features were observed in the present case.

In the present case, lumbar puncture was not performed due to lack of molecular diagnosis at the time of admission to the hospital. Currently, the PCR test for *T. gondii* in CSF could have confirmed the diagnosis of cerebral toxoplasmosis and avoided brain biopsy.

HIV-related cerebral toxoplasmosis should be considered in the differential diagnosis of exclusively hemorrhagic cerebral lesions. Empiric treatment should be initiated timely and a slow clinical and radiological response might be expected.

## Declaration of conflicting interests

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