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A Woman with HIV, Brain Abscesses and Eosinophilia

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Keywords

HIV; brain abscess; trypanosomiasis; eosinophilia

Case description

A 38 year old woman originally from Honduras presented to a local hospital in Houston complaining of 10 days of progressive right sided hemiparesis and headache. She denied fever, visual disturbances, chills, or night sweats. The neurological exam revealed right sided hemiparesis with no sensory changes; cranial nerves and mental status testing were normal. There were no oral or ocular lesions, adenopathies, skin changes, hepatosplenomegaly or cardiac murmurs. Laboratory examination showed a white blood cell (WBC) cell count of 7.7 K/μl with 45% neutrophils and 30% eosinophils. Her renal and liver function tests were normal and magnetic resonance imaging of the brain (figure 1) showed multiple ring enhancing lesions. Subsequently, the patient was found to be HIV positive with a CD4 T cell count of 104 cells/mm^3 and a viral load of 216,952 copies /ml. She was started empirically on sulfadiazine (1500 mg every 6 hours) and pyrimethamine (75mg daily) for presumed toxoplasmosis, although her *Toxoplasma* serologies IgG and IgM were negative. A brain biopsy was performed (figure 2A and B).

What is your diagnosis?

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Trypanosoma cruzi reactivation in the central nervous system (CNS)

A biopsy of brain tissue showed the rod-shaped kinetoplasts that are a key diagnostic morphologic feature that separates the amastigotes of *T. cruzi* (and *Leishmania* spp) from *Toxoplasma* and *Histoplasma* (figure 2A and B). Polymerase chain reaction (PCR) was done on whole blood, buffy coat, red blood cells and unstained brain tissue, and all results were positive for *T.cruzi*. The patient was started on nifurtimox and remained stable for a few days. Subsequently antiretroviral therapy (ART) was started with lamivudine/zidovudine and lopinavir/ritonavir fixed combinations. After 4 days of receiving the ART therapy, the patient exhibited altered mental state which resulted in mechanical ventilation for airway protection. She next developed several other infectious complications in the intensive care unit, including coagulase negative *Staphylococcus* bacteremia, ventilator associated pneumonia, *Cytomegalovirus* reactivation, and finally worsening of her brain lesions and development of subdural abscess. She expired on day 54 of antitrypanosomal therapy.

The clinical presentation of Chagas disease in immunocompetent patients is very well described; however, the manifestations of American trypanosomiasis are quite diverse in immunosuppressed patients and usually represent reactivation of past infection [1,2,3]. The clinical picture in HIV-infected patients includes mainly CNS involvement with meningoencephalitis and brain abscesses, although myocarditis has been described in 25-44% of cases as well [2]. This is in contrast to reactivation in those patients who become immunosuppressed after solid organ or bone marrow transplantation, where subcutaneous nodules, panniculitis, and myocarditis are more common and CNS involvement is rarely reported [4]. Diagnosis of reactivation disease is facilitated by the fact that immunosuppressed patients display a high parasite burden, compared to immunocompetent patients with chronic Chagas disease, and the organisms can be readily identified by using standard microscopic techniques on fresh preparations of anticoagulated blood or buffy coat [2]; indeed, direct examination of the parasite in the cerebrospinal fluid (CSF) can also be performed in some cases of meningoencephalitis [2,3]. Additionally, the organisms have highly repetitive nuclear and kinetoplast DNA sequences that can be amplified by PCR in serum, whole blood, and tissue [1,4,5]. The sensitivity of PCR is amplified by the higher parasite burden seen in reactivation compared to chronic disease.

A recent review described 15 cases of patients co-infected with HIV and *T.cruzi* over a 15 year period in Argentina [3]. In this case series, the main clinical presentation included headache, seizures and focal neurological signs; concomitant cardiac involvement was present in 30% of the patients and mortality was 79%. The clinical presentation of CNS trypanosomiasis resembles toxoplasmosis, although the Chagas' brain lesions tend to be larger than those of *Toxoplasma* [6]. An interesting finding in this patient was the marked peripheral blood eosinophilia which is generally associated with other parasitic infections (eg., helminths) but has not been commonly associated with CNS Chagas. The etiology of the eosinophilia in this patient remains unclear, as an extensive work-up for helminthic infections was not possible due to the patient's condition, and it is unlikely that the patient's reactivation of Chagas disease contributed to the eosinophilia.

There is limited experience in the treatment of CNS Chagas reactivation in the setting of AIDS. There is often a delay of diagnosis due to the similarity of its presentation to CNS toxoplasmosis that may contribute to the high mortality. Despite this high mortality, small case series in patients co-infected with HIV and *T.cruzi* have shown decreased parasitemia and improved outcomes when patients were treated with benznidazole or nifurtimox [6,7], which are only available in the United States through the Centers for Disease Control and Prevention (CDC).

The duration of therapy with either of these agents has not been well studied for persons co-infected with HIV, and mortality during episodes of reactivation remains high, even in patients

who receive therapy [3,7]. It is currently recommended that all HIV-infected persons with epidemiologic risk factors for Chagas disease (such as living in an endemic country or having received blood, organs or tissue from someone from an endemic country) should be tested for antibody to *T. cruzi*, and antibody-positive patients may benefit from a single course of medication with benznidazole or nifurtimox [4,7]. Secondary prophylaxis with benznidazole (5mg/kg three times per week) has been described by some authors [3], especially when the CD4 count remains <200 cells/mm^3. However, given the paucity of data on efficacy and treatment regimen, CDC does not currently recommend secondary prophylaxis. Antiretroviral therapy (ART) should be initiated or optimized once a patient with acute disease is clinically stable, as the efficacy of benznidazole and nifurtimox are thought to require an intact immune system. Although no reports are available regarding *T. cruzi* infection and the development of immune reconstitution syndrome (IRIS), our patient deteriorated after initiation of ART which may suggest a component of IRIS.

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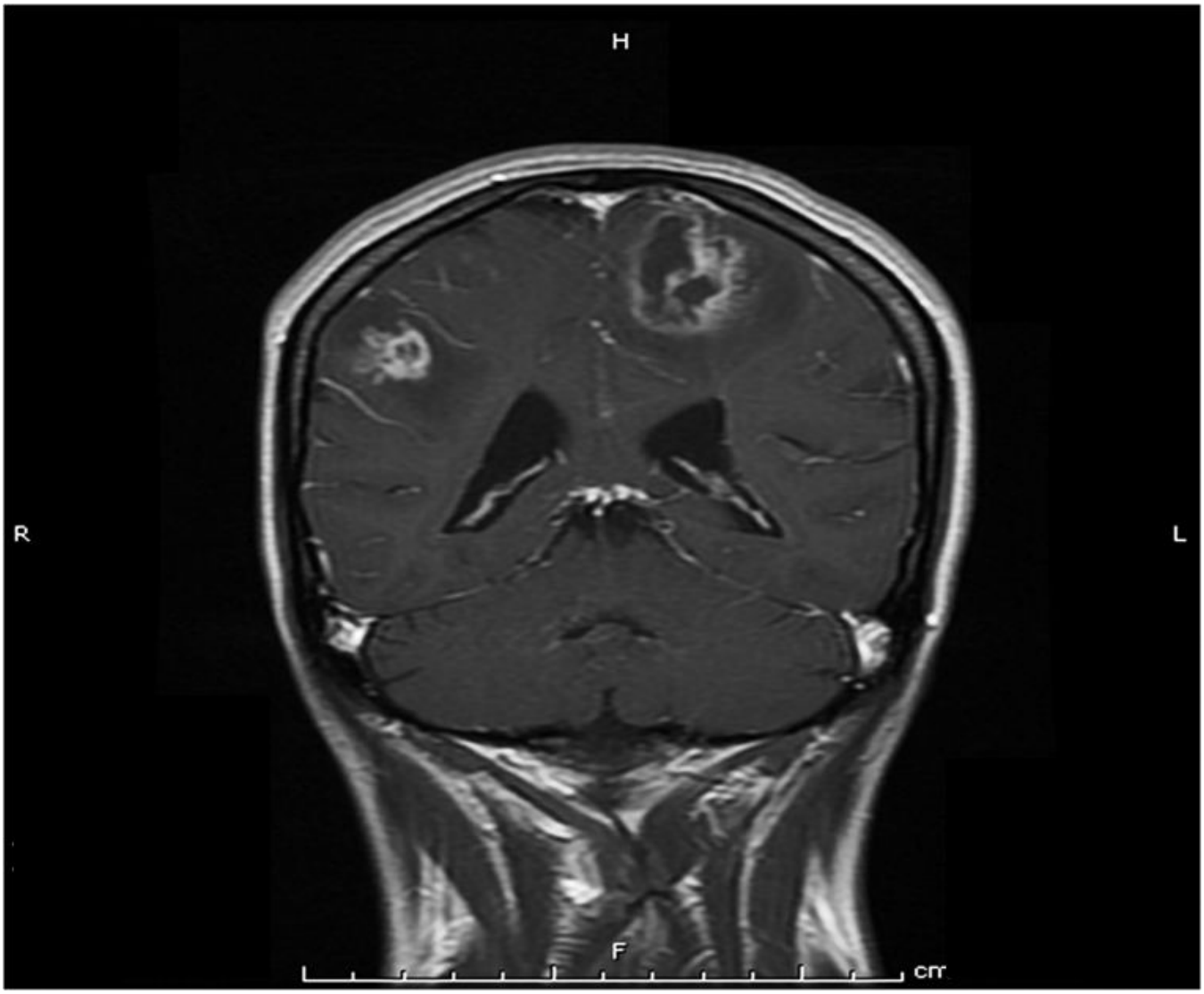

Figure 1 question section.
T1 Magnetic resonance imaging of the brain shows bilateral ring enhancing lesions with extensive surrounding vasogenic edema and necrotic centers.

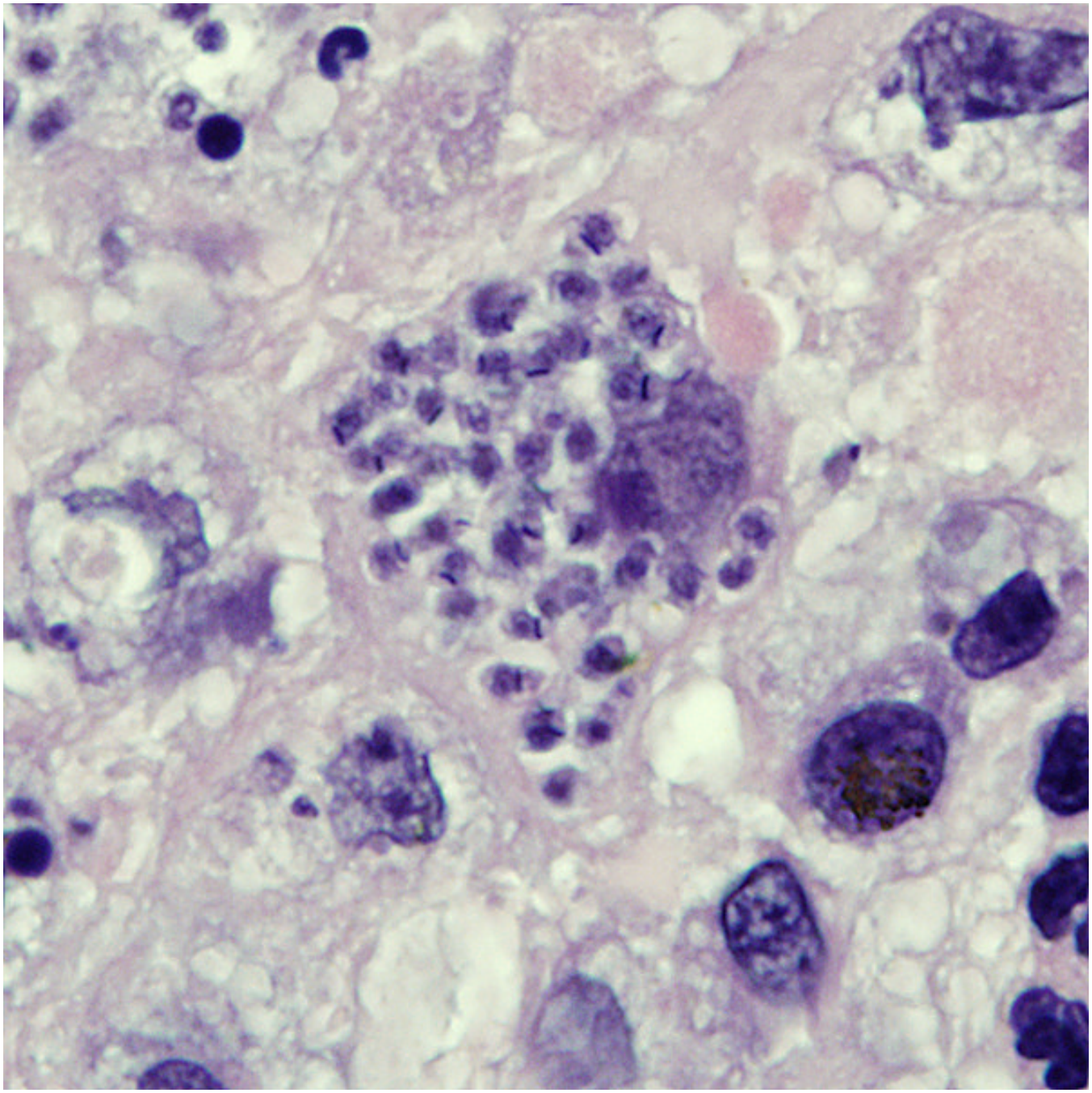

Figure 2A question section.
Image was taken at 1000x magnification from a brain biopsy section stained with hemotoxylin and eosin (H & E).

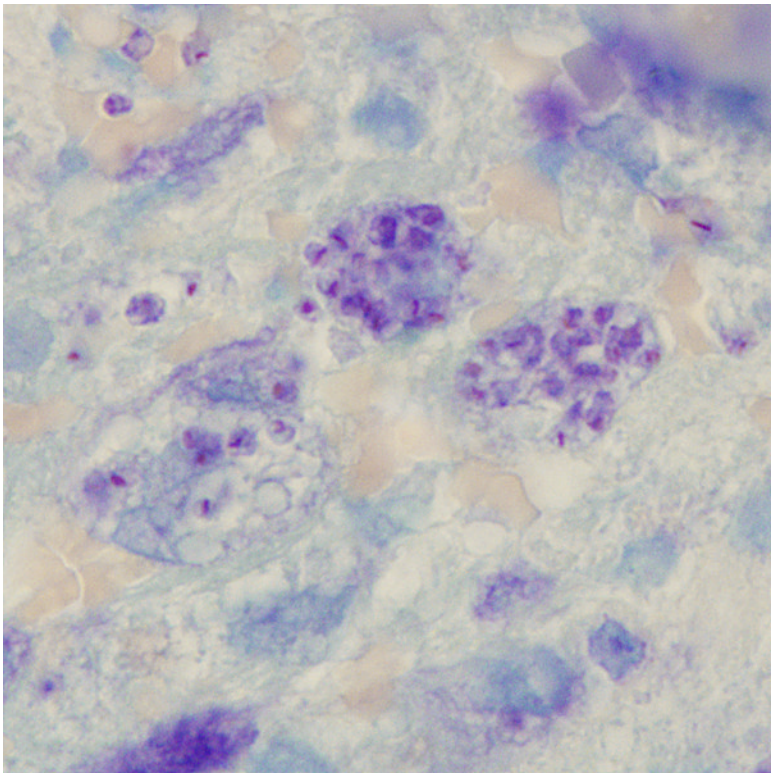

Figure 2B question section.
Image was taken at 1000x magnification from a brain biopsy specimen section stained with Giemsa.

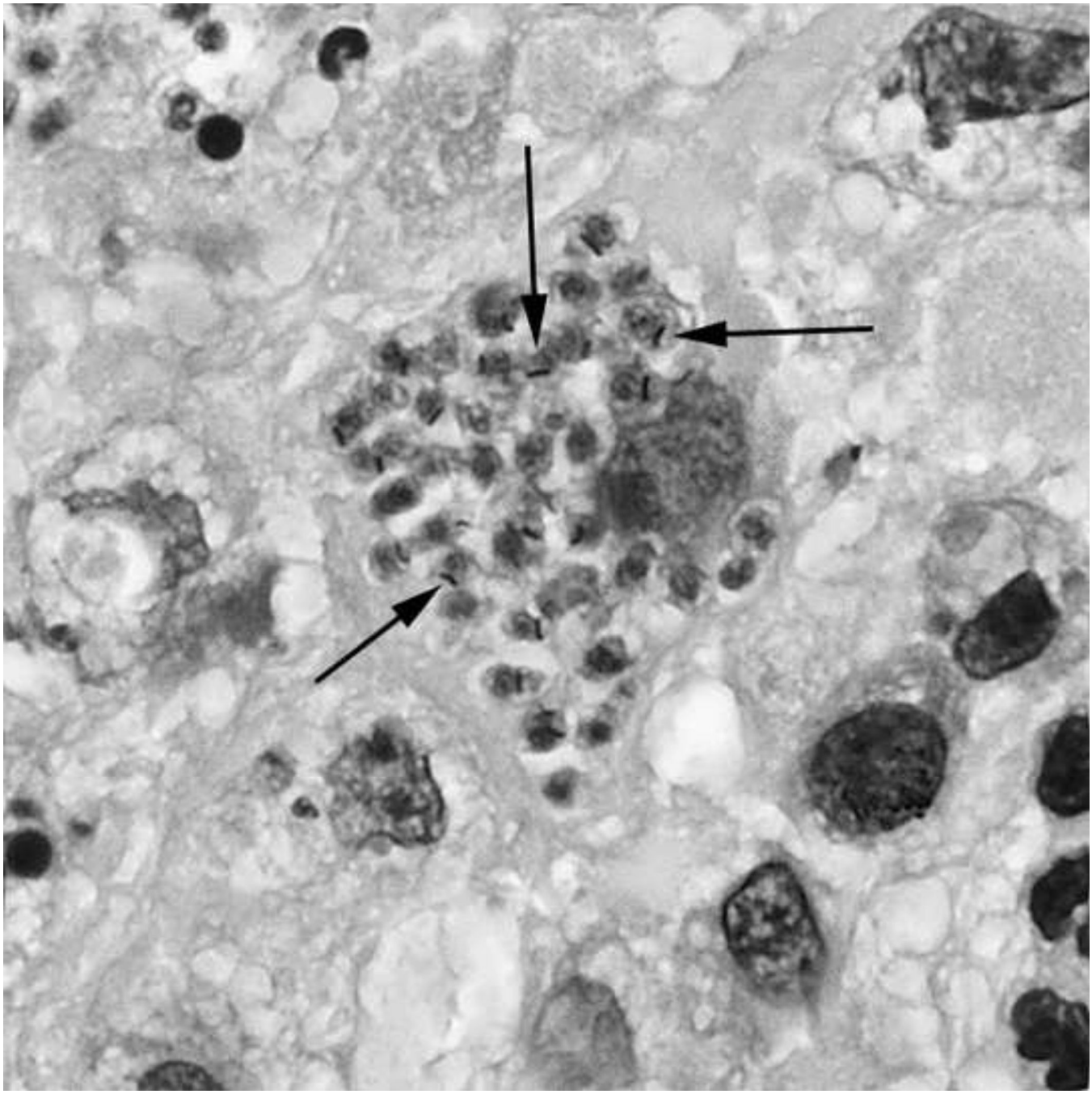

Figure 2A answer section.
Nests of *T. cruzi* amastigotes with several darkly stained, rod-shaped kinetoplasts are seen in glial cells (arrows). Kinetoplasts are a key diagnostic morphologic feature that separates the amastigotes of *T. cruzi* (and *Leishmania* spp) from *Toxoplasma* and *Histoplasma*.

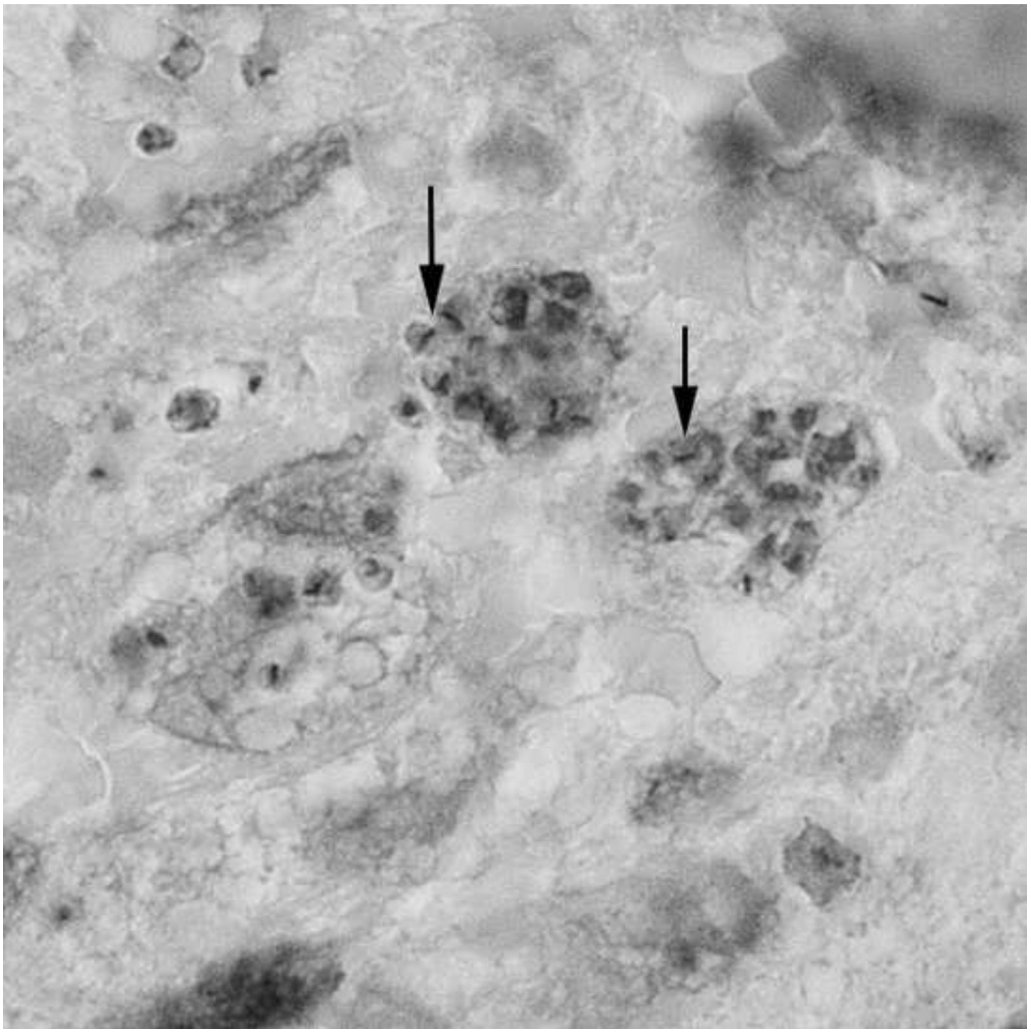

Figure 2B answer section.
The kinetoplasts of the amastigotes appear as prominent dense reddish staining rods (arrows).