

# Seronegative Central Nervous System Toxoplasmosis in HIV/AIDS

B Rao

## Citation

B Rao. *Seronegative Central Nervous System Toxoplasmosis in HIV/AIDS*. The Internet Journal of Internal Medicine. 2004 Volume 5 Number 2.

## Abstract

The Patient was a 38 year old white male who was diagnosed to have Human Immunodeficiency Virus (HIV) infection in 1989. He was apparently doing well on anti retro viral therapy until recently when he began to experience symptoms of ataxia and weakness. Magnetic Resonance Imaging (MRI) of the brain revealed several ring enhancing lesions. A broad differential diagnoses including Tuberculosis, Lymphoma, Cryptococcosis, Toxoplasmosis, and possible metastasis were considered. The patient was empirically treated for Toxoplasmosis even though the serology was negative for the same. Further invasive diagnostic testing was withheld awaiting results of a repeat MRI two weeks into the treatment. There was near complete resolution of these lesions within a fortnight of institution of anti microbial therapy. This article likes to emphasize on the fact that a trial of anti Toxoplasma therapy is warranted prior to further invasive diagnostic testing even in the immediate absence of IgM antibodies to Toxoplasma gondii.

## INTRODUCTION

The causes for multiple ring enhancing cerebral lesions (MRECL) in patients with Human Immunodeficiency Virus (HIV) infection/ Acquired Immune Deficiency Syndrome (AIDS) range from resolving hematomas and infarcts to infections and malignancies [5, 6]. A clinical approach to the diagnosis and management of these patients emphasizes on a trial of antimicrobials based on serological evidence of infection prior to further invasive diagnostic testing to avoid potential complications and discomfort related to brain biopsy[1, 2]. However, IgM antibodies to Toxoplasma are often absent in patients with HIV/AIDS[3, 7]. In the Seronegative cases the dilemma facing the physician is whether to biopsy the lesion for an accurate diagnosis or empirically treat the patient for Toxoplasmosis. We discuss the management of a patient with HIV/AIDS with MRECL who was Seronegative for Toxoplasmosis that resolved with treatment with Pyrimethamine and Sulfadiazine.

## CASE REPORT

Our patient was a 38 year old white male who was known to have HIV since 1989. He had been doing reasonably well on anti retro viral therapy given the duration of his illness. His last Cluster of Differentiation 4<sup>+</sup> (CD4<sup>+</sup>) count done about a month ago was 225/L and his viral load was 51,000 copies/mL. He initially presented to his primary care doctor

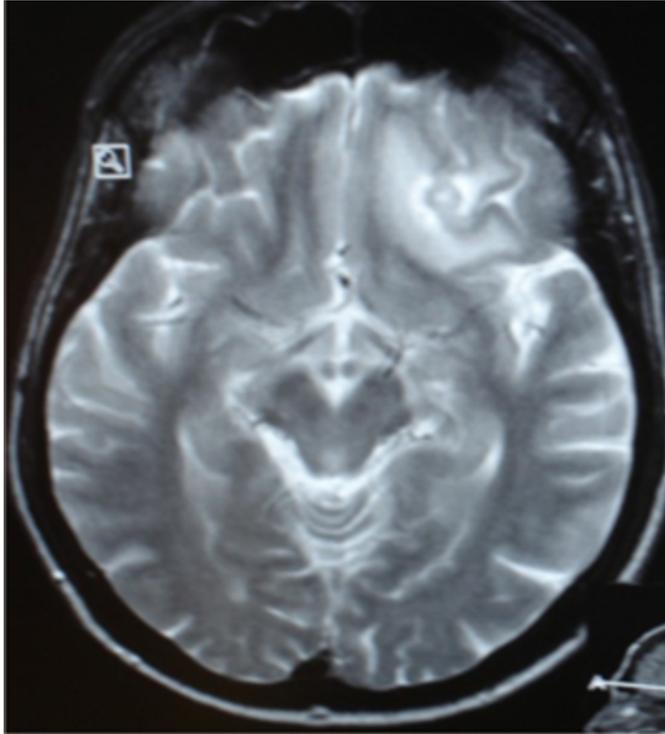
with complaints of blurry vision, unsteady gait and frequent falls in the recent past. Computerized Tomography (CT) scan of his head done by his doctor revealed diffuse white matter disease which dictated the need for further diagnostic testing. Serum IgG for Toxoplasma was found to be negative a few years ago.

The patient was admitted to the hospital for further work up and management of his problem. On examination, the patient was afebrile and had essentially stable vital signs. There were no cardiac murmurs and his chest was clear to auscultation. He had an unsteady gait, a positive Romberg's sign, decreased plantar reflex on the right and decreased visual acuity in both eyes. MRI of his head demonstrated MRECL scattered in the white matter of the left frontal lobe, right occipital lobe and left cerebellar hemisphere [Figures 1 & 2]. Serum IgM for Toxoplasma was found to be negative. After contemplation, the patient was started on presumptive treatment for cerebral Toxoplasmosis with Pyrimethamine 100 mg Per Oral (PO) q daily and Sulfadiazine 1000 mg POq 6 hrs. Serum tests for Cryptococcal and Histoplasma antigens; blood cultures and Rapid Plasma Reagin (RPR) were negative.

Figures 1 & 2: MRI of the Brain demonstrating ring enhancing lesions visible in the left Frontal lobe, left Cerebellar hemisphere and right Occipital lobe.

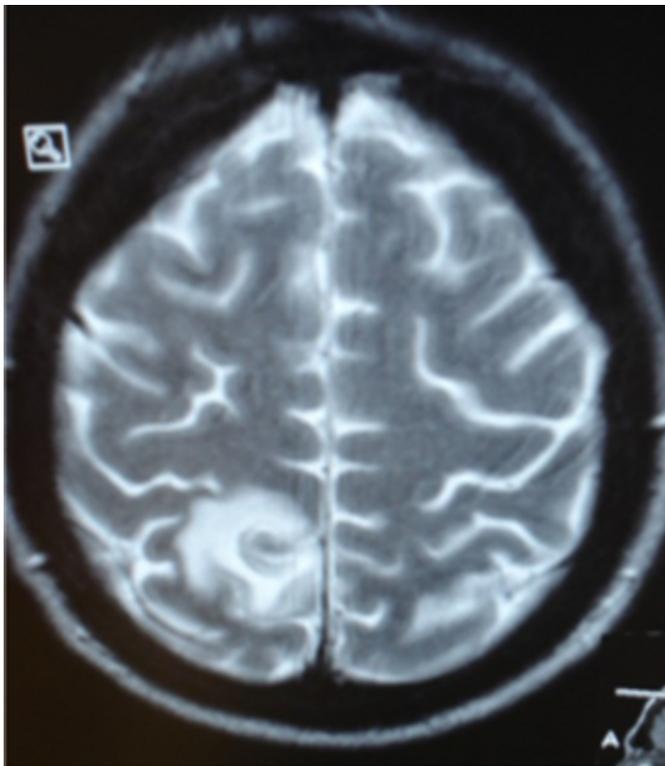
**Figure 1**

Figure 1



**Figure 2**

Figure 2



The patient was also started on Abacavir, Atazanavir and Lamivudine for his HIV infection and was given Folinic

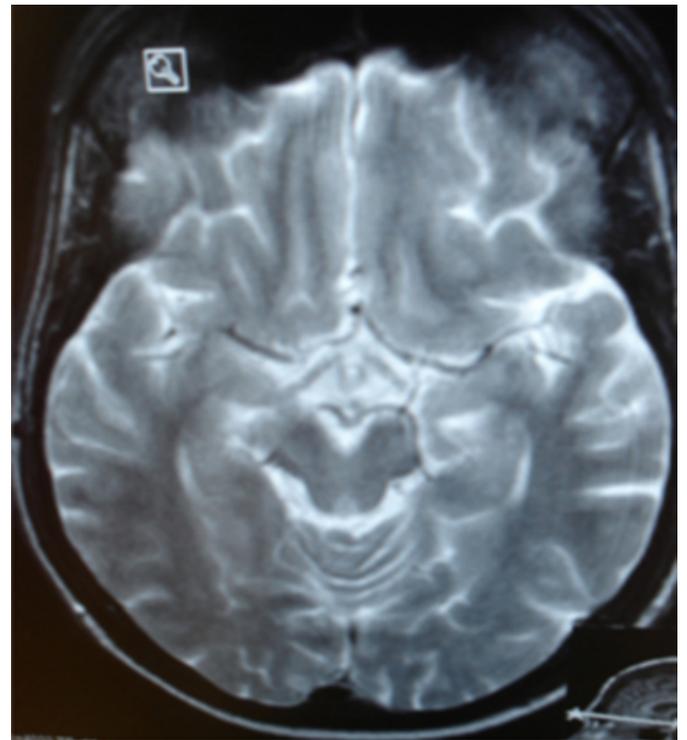
Acid as a 'rescue' medication. He was also started on Levetiracetam after an Electro Encephalogram (EEG) was obtained. The option of Invasive diagnostic testing such as stereotactic biopsy was reserved for failure of resolution of these lesions after a trial of two weeks of therapy with the above named drugs.

The patient returned to the hospital in two weeks. His gait and visual disturbances had begun to resolve. A repeat MRI of the head showed 50%-80% resolution of the Occipital and Cerebellar lesions and near complete resolution of the Frontal lobe lesions [Figures 3 & 4].

Figures 3 & 4: A repeat MRI done two weeks after institution of antimicrobial therapy demonstrates near complete resolution of these lesions.

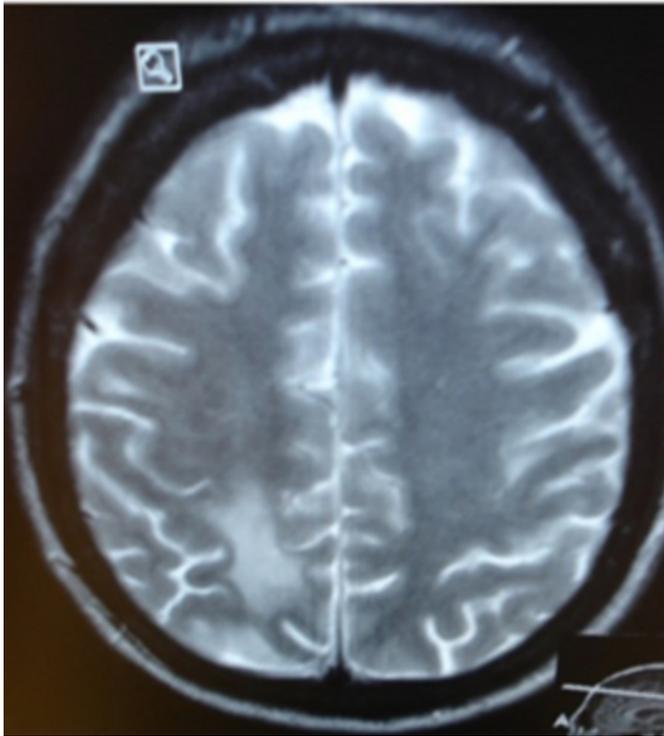
**Figure 3**

Figure 3



**Figure 4**

Figure 4



## DISCUSSION

Cerebral Toxoplasmosis is a common cause of MRECL in a patient with HIV/AIDS. Serological tests for Toxoplasma include detection of IgG and IgM antibodies but serum tests for IgM antibodies are generally negative in patients with AIDS [ 3, 7, 9] and had been as low as 0 – 9 % in various studies; amongst patients who showed a response to anti Toxoplasma therapy.[9, 10] Several commercial kits for Toxoplasma serologic testing are available. However, the sensitivity and specificity of these kits may vary widely from one commercial brand to another.[3, 11] The kit used in our patient was a commercial ELISA kit with a sensitivity of 90% and specificity of 100 % to detect anti Toxoplasma IgM but these numbers have no bearing in patients with HIV/AIDS as their immune response is blunted and they fail to produce the required IgM.

A negative IgM test essentially excludes recent infection, but a positive IgM test is difficult to interpret because Toxoplasma-specific IgM antibodies may be detected by EIA for as long as 18 months after acute acquired infection. [3, 8] Toxoplasma-specific IgG antibody levels in AIDS patients often are low to moderate, but occasionally no specific IgG antibodies can be detected .[3, 7]

Some authors recommend an aggressive diagnostic approach

to MRECL in a patient with HIV/AIDS with negative antitoxoplasma blood serology in order to pursue urgent treatment for a suspected malignancy. [1]

Other authors recommend a conservative line of management which includes a trial of antimicrobials prior to invasive testing and leave the option of the aggressive line with the care giver. [2]

We would favor the conservative strategy to approach these lesions as demonstrated by this case report. There was a near complete resolution of these lesions in our patient which was evidently Toxoplasmosis. Brain biopsy is indicated if patients fail to respond or worsen after seven days of institution of antimicrobial therapy. [2]

Polymerase Chain Reaction of the cerebrospinal fluid for Toxoplasma DNA has been suggested as an additional diagnostic approach by some [12] but a lumbar puncture is often not feasible in a patient with intracerebral space occupying lesions.

## CONCLUSION

Toxoplasmosis should be one of the top differentials kept in mind for a MRECL in the immunocompromised host. The decision to initiate or withhold a therapeutic trial of antimicrobials should not be based on the results of antibody testing alone.

Patients with CD4<sup>+</sup> T cell counts < 100/L and IgG antibody to Toxoplasma should receive prophylaxis for toxoplasmosis with a daily regimen of a single double-strength tablet of Trimethoprim/Sulfamethoxazole. Secondary prophylaxis for toxoplasmosis may be discontinued in the setting of effective antiretroviral therapy and increases in CD4<sup>+</sup> counts to greater than 200/L. [4]

Those who are seronegative should be counseled about ways to minimize the risk of primary infection including avoiding the consumption of undercooked meat and careful hand washing after contact with soil or changing the cat litter box. [4]

## ACKNOWLEDGEMENTS

I thank Dr.Pratap Chand for helping me prepare this article and Dr.Jeremy Jones in guiding me through the process.

## CORRESPONDENCE TO

Bhaskar Rao MD 537 S Third Street, Apt 511 Louisville KY 40202 Tel:502-295-5427 Email: bhaskarrao009@yahoo.com

**References**

1. Antinori A, Ammassari A, De Luca A, et al: Diagnosis of AIDS-related focal brain lesions: A decision-making analysis based on clinical and neuroradiologic characteristics combined with polymerase chain reaction assays in CSF. *Neurology* 48:687, 1997
2. Harrison's Textbook of Internal Medicine- Chapter 173. Human Immunodeficiency Virus Disease: AIDS and Related Disorders
3. CDC Document. Laboratory Identification of Parasites of Public Health Concern-Toxoplasmosis. [http://www.dpd.cdc.gov/DPDx/HTML/Toxoplasmosis.asp?body=Frames/S-Z/Toxoplasmosis/body\\_Toxoplasmosis\\_serol1.htm](http://www.dpd.cdc.gov/DPDx/HTML/Toxoplasmosis.asp?body=Frames/S-Z/Toxoplasmosis/body_Toxoplasmosis_serol1.htm)
4. CDC Document. Masur H et al: Guidelines for preventing opportunistic infections among HIV-infected persons-2002. *Ann Intern Med* 137:435, 2002 -infected persons-2002. *Ann Intern Med* 137:435, 2002
5. Neuroimaging of central nervous system infections. Hunter JV - *Semin Pediatr Infect Dis* - 01-APR-2003; 14(2): 140-64
6. S Ray, B Kundu, S Kundu, S Roy, S K Sharma Distinguishing Neoplastic and Non-Neoplastic Ring Enhancing Lesions of the Brain Detected in CT and/or MRI With the Help of Correlative Nuclear Imaging -The Indian Journal of Radiology and Imaging-May 2002
7. Treating Opportunistic Infections Among HIV-Infected Adults and Adolescents Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America
8. Singh S. Mother-to-child transmission and diagnosis of toxoplasma gondii infection during pregnancy. *Indian J Med Microbiol* 2003;21:69-76
9. Singh S; Singh N; Maniar JKAIDS associated toxoplasmosis in India and its correlation with serum tumour necrosis factor-alpha, *Journal of Parasitic Diseases*. 1996 June; 20(1): 49-52
10. Meisheri YV, Mehta S, Patel U. A prospective study of seroprevalence of Toxoplasmosis in general population, and in HIV/AIDS patients in Bombay, India. *J Postgrad Med* 1997;43:93-7
11. Decoster A, Lambert N, Germaneau C, Masson C. Toxoplasmosis serodiagnosis: comparison of Access Toxo IgM II assay compared to AxSYM Toxo IgM and Vidas Toxo IgM assays. *Ann Biol Clin (Paris)*. 2000 Nov-Dec;58(6):721-7.
12. José E. Vidal, Fabio Antonio Colombo ,et al PCR Assay Using Cerebrospinal Fluid for Diagnosis of Cerebral Toxoplasmosis in Brazilian AIDS patients *J Clin Microbiol*. 2004 October; 42(10): 4765-4768

**Author Information**

**Bhaskar Rao, M.D.**

Department of Internal Medicine, University of Louisville