

**Title:**

**Butterfly Lesion on MRI: Cryptococcus Meningoencephalitis with Unusual Imaging in a Patient with AIDS**

**Authors:**

Mary Henary (1), Jennifer Oster, DO, MPH (2), Antonio Liu, MD (2)

(1) Ross School of Medicine

(2) Department of Neurology, Adventist Health White Memorial

**Author details:**

Mary Henary

Ross School of Medicine

Mailing Address: Ross University School of Medicine, Miramar, FL, 33027-4150, USA

Email address: maryhenary050@gmail.com

Jennifer Oster, DO, MPH

Department of Internal Medicine, Adventist Health White Memorial, Los Angeles

Mailing address: 1720 E. Cesar E Chavez Ave., Los Angeles CA 90033

Antonio Liu, MD Department of Neurology, Adventist Health White Memorial, Los Angeles

Department of Neurology, Adventist Health White Memorial, Los Angeles

Mailing address: 1720 E. Cesar E Chavez Ave., Los Angeles CA 90033

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#### Key Clinical Message

In immunocompromised patients, including patients with AIDS, with neurologic complaints we propose including Cryptococcus meningoencephalitis in the differential diagnoses when the butterfly pattern is encountered on MRI.

**Abstract:**

On magnetic resonance imaging (MRI), a butterfly lesion is most commonly described in Glioblastoma Multiforme (GBM), however we report an unusual case of Cryptococcus Meningoencephalitis with the butterfly lesion on MRI. This infection is generally diagnosed via lumbar puncture, however MRI may reveal perivascular space involvement, dilation and leptomeningeal enhancement.

**Introduction:**

*Cryptococcus neoformans* is a saprophytic fungus that is isolated from soil contaminated with pigeon extracts and is the third most common cause of central nervous system (CNS) infections in immunocompromised patients including Cryptococcus Meningoencephalitis. As the fungal infection enters the human body by way of inhalation, the respiratory tract is the primary site of infection. The fungi spread hematogenously from the respiratory tract to the CNS. Once in the CNS, the fungus travels to the Virchow-Robin spaces, known as the perivascular space, which subsequently become dilated due to the activation of inflammatory markers. Once in the Virchow-Robin space, the fungus can cross the blood-brain-barrier, where it multiplies and causes neurological symptoms. Classical symptoms noted with Cryptococcus Meningoencephalitis include headache, fever, encephalitis, seizures, and focal neurological deficits, stroke, increased intracranial pressure, coma and death. This infection is generally diagnosed via lumbar puncture, however if MRI is obtained it may reveal perivascular space involvement and dilation in addition to leptomeningeal enhancement. The butterfly pattern is more commonly associated with primary CNS lymphoma, GBM, inflammatory diseases and infectious etiologies such as toxoplasmosis (2). However, we present a case of a 37-year-old Hispanic male with AIDS and MRI demonstrating this pattern. His only symptoms at presentation included a moderate 5/10 headache and increased seizure activities. Upon further evaluation, spinal fluid analysis revealed Cryptococcus, with the MRI findings as shown below. As noted in worldwide literature, Cryptococcus meningoencephalitis usually causes dilated Virchow-Robin space (3), lesions in basal ganglia and/or hydrocephalus (4). The case discussed here demonstrates a “butterfly” lesion originating from the bilateral medial temporal areas, crossing the midline via the corpus callosum, which has rarely been previously reported.

**Case:**

A 37-year-old right-handed male presented to our emergency room with new onset progressively worsening seizures. His past medical history included congestive heart failure, hypertension, AIDS (untreated) and end stage kidney disease (ESKD) on hemodialysis three days weekly for the past 10 years. The patient had 2 episodes of seizures within one week in the days leading up to admission into the hospital. He also complained of acute on chronic 4/10 generalized headache. The patient had not been taking medication and had inconsistent follow-up. CD4 count was unknown on admission.

Vital signs revealed a temperature 38 degrees Celsius, heart rate of 119 beats per minute, respiratory rate of 18 breaths per minute and blood pressure of 126/82. Physical examination revealed a thin male with normal mentation. He was alert and oriented x 4, coherent and free of psychosis. His neck was supple, cranial nerves II-XII were intact bilaterally. Motor exam revealed 5/5 strength in bilateral upper and lower extremities without tremor, myoclonus, asterixis, abnormal tone nor dystonia. Sensation to light touch was intact and deep tendon reflexes were 2/4 throughout. Finger-nose-finger was intact with no dysmetria nor dysdiadochokinesia. While observed frequently pacing in hallways, the patient had normal gait.

Serum studies revealed a WBC count of  $7.4 \times 10^9$  cells/L and lactic acid of 0.7 mmol/L while liver and kidney function tests were within normal ranges. The initial non-contrast head CT demonstrated increased white matter in the bilateral temporal lobes. Cerebrospinal fluid (CSF) examination was intended to further delineate findings on CT. Lumbar puncture was therefore performed with an opening pressure of 42 cm CSF. Fluid color was pale-yellow, and clarity was slightly hazy. There was an RBC count of 330 per  $\text{mm}^3$ , WBC count was 60 per  $\text{mm}^3$  (with cell differential count showing 30 segmented neutrophils per  $\text{mm}^3$  and 70 lymphocytes per  $\text{mm}^3$ ), glucose was found to be 3 mg/dl, and protein was 406 g/dl. Microscopic examination revealed 3+ yeast/high powered field. CSF Cryptococcus titer resulted as 1:2560. CSF was negative for Coccidioidomycosis, HSV, and West Nile. MRI brain on hospital day 2 (Fig.1) revealed no DWI abnormality. However, on FLAIR sequence, there were symmetric confluent signal densities involving the medial temporal lobes, hippocampal bodies, para hippocampal gyri extending upward and joining at the splenium of the corpus callosum and crossing the midline.

An Infectious Disease specialist was consulted who restarted Highly active antiretroviral therapy (HAART), and immediately placed the patient on Amphotericin B and flucytosine. The patient was also started on Levetiracetam 500 mg per oral twice daily. Patient did not have witnessed seizures while inpatient. Unfortunately, the patient signed out against medical advice and left the hospital on hospital day 3. Per Patient's nephrologist, Patient presented sporadically for dialysis with intermittent ED visits in a neighboring hospital in the months to follow. Eventually, the Patient was unfortunately lost to follow-up.

**Discussion:**

We report a case of a 37-year-old Hispanic male with a significant past medical history of ESKD, CHF, and AIDS who presents with new onset, worsening seizure activity and a moderate headache. Initially our leading etiology was infectious including toxoplasmosis and cryptococcus, however we also considered malignancies such as primary central nervous system (CNS) lymphoma and GBM. Upon testing, CSF fluid analysis demonstrated findings that correlated with Cryptococcus Meningoencephalitis and cytology was negative for lymphoma or other malignancy. Interestingly, the MRI of this patient formed the so-called butterfly pattern. Based on prior published literature, Cryptococcus Meningoencephalitis on imaging may demonstrate dilation of Virchow-Robin space while others have described bilateral Basal Ganglia lesions (4) and only few reports demonstrate the type of FLAIR sequence abnormality we see in this untreated patient who has AIDS (5). As it is well-described in the literature that the butterfly lesion may have a broad differential, the patient's MRI pattern may lead to initial consideration for lesions such as glioma or lymphoma (2). However, in immunocompromised patients, including patients with AIDS, with neurologic complaints we propose including cryptococcus meningoencephalitis in the differential diagnoses when the butterfly pattern is encountered on MRI.

**Conclusion:**

Based on prior published literature, Cryptococcus Meningoencephalitis demonstrates dilation of Virchow-Robin space (2) or bilateral Basal Ganglia lesions (3). Few reports demonstrate the type of FLAIR sequence abnormality we see in this patient who has AIDS. Our patient's MRI demonstrated hyperintensity in FLAIR sequence in the form of the butterfly pattern. This case shows an unusual appearance of Cryptococcus meningoencephalitis as a butterfly lesion on MRI.

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(2) Department of Neurology, Adventist Health White Memorial, Los Angeles

### **Author contributions:**

Author 1: Mary Henary – Performed background research on condition and began drafting manuscript

Author 2: Jennifer Oster, DO, MPH – Performed additional background and revised critically for content

Author 3: Antonio Liu, MD – Primary neurologist and attending providing care for patient, prepared manuscript and provided images

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### **Figure Legend:**

**Figure 1.** Fluid-attenuated inversion recovery (FLAIR) sequence of MRI showing “butterfly lesion” crossing over via Corpus Callosum