

# Acute Disseminated Encephalomyelitis (ADEM) as a Radiologic Finding of a HIV- infection with Cerebral Toxoplasmosis Infection

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## Acute Disseminated Encephalomyelitis (ADEM) as a Radiologic Finding of a HIV-infection with Cerebral Toxoplasmosis Infection

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### ABSTRACT

*Toxoplasma gondii* is a pathogenic opportunistic parasite that infect a range of hosts, including human of up to approximately one third of the human population. After the acute infection phase has passed, the parasite will remain in the host body as an intramuscular or intraneuronal cyst and it will be entirely controlled by the host immune system. Reactivation of cerebral toxoplasmosis in patients with immunodeficiency can result in severe immunopathologic response. We reported a case of a 40-year old male who had human immunodeficiency virus (HIV) with cerebral toxoplasmosis, the patient came with complaint of headache accompanied by multifocal neurologic deficits, with positive result on serologic test for *Toxoplasma gondii*, however the radiologic finding was acute disseminated encephalomyelitis (ADEM), which was not characteristic for cerebral toxoplasmosis. After administration of combination therapy regimen with pyrimethamine and clindamycin for six weeks, the patient showed clinical improvement of improved dysmetria, dysidiadokinesia and ataxia symptoms.

**Keywords:** Cerebral toxoplasmosis, acute disseminated encephalomyelitis, HIV, AIDS, ADEM

### Introduction

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*Toxoplasma gondii* is still one of the global health burden, and it is the most common opportunistic infection affecting the central nervous system in patients with acquired immunodeficiency syndrome (AIDS). Approximately 30-50% of human immunodeficiency virus (HIV)-positive patients infected with *T. gondii* will develop in to cerebral toxoplasmosis.<sup>1,2</sup> The ability of *T. gondii* to asymptotically persist in the central nervous system of an immunocompetent individual is extremely rare, as in other microbes that penetrate the central nervous system, this disease will manifest and has a high morbidity.<sup>3</sup>

Human are exposed to *T. gondii* mainly via contaminated water or food through vertical transmission. During the acute phase of infection, *T. gondii* will spread in the host's body as a tachyzoite, a fast replicating form of the parasite which is a target for host immune response. When the infection progresses, the transition of the acute infection phase of *T. gondii* to chronic infection as bradyzoite, the form of cysts that will not be detected by the immune system and cause a persistent infection. In the body of human and mice, the brain is the primary organ in which persistent cyst will form.<sup>3</sup>

In patients with HIV/AIDS, there is increasing number of cases of meningoencephalitis due to *T. gondii* through reactivation mechanism of persistent cysts in the central nervous system (CNS).<sup>4</sup> Early diagnosis and treatment of cerebral toxoplasmosis can improve survival and mortality rate. Brain MRI is essential in determining diagnosis and differentiating cerebral toxoplasmosis from other diseases such as primary CNS lymphoma and tuberculoma. A characteristic appearance such as "eccentric target sign" and "concentric target sign" has often been described, however atypical MRI finding are common, making diagnosis more

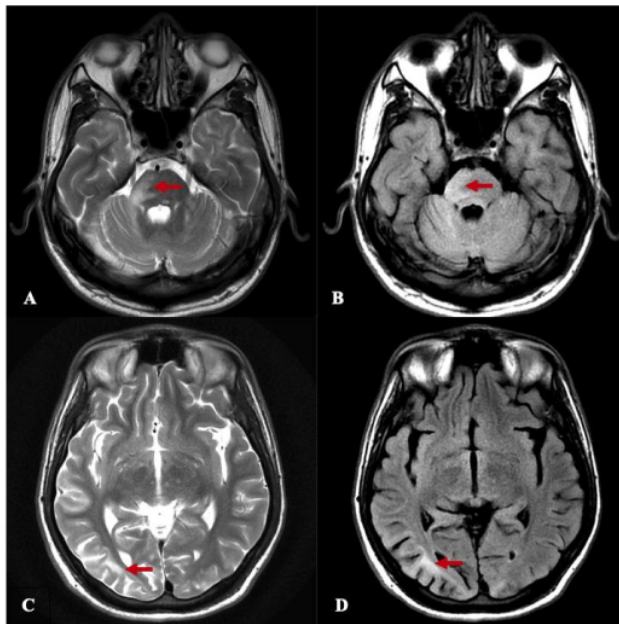
challenging.<sup>5-8</sup> In this case report, we described a case of cerebral toxoplasmosis with atypical MRI finding as an acute disseminated encephalomyelitis (ADEM).

### Case Illustration

A 40-year old male patient presented with complaint of unstable gait for two months which worsen within last week, accompanied with progressive headache, right side weakness of the body, drooping face, slurred speech, and history of intermittent fever for the last one month. History of promiscuity was unclear and history of drug use was denied. The patient was fully alert with Glasgow Coma Scale E4M6V5, no neck rigidity, there was bidirectional nystagmus, right side central type facial and lingual palsy, with dysmetria, dysdiadokinesia, ataxia, and increased physiologic reflexes on the right extremities.

Laboratory tests showed a reactive result for three methods HIV test, with CD4 count of 59 cells/uL. Serologic test for *T. gondii* showed a result of IgG 234.4 IU/ml and IgM 0.22 IU/ml. Chest x-ray examination was within normal limits. Brain MRI showed a hyperintensity on T2 and FLAIR in the right and left inferior cerebellar peduncle, right and left pons, subcortical temporo-occipital, and right parietal lobe which represented a case of ADEM.

After seven days of therapeutic regiments using combination of pyrimethamine and clindamycin, the patient showed a good response with clinical improvement of dysmetria, dysdiadokinesia and ataxia symptoms.



**Figure 1.** Brain MRI of a people living with HIV with a cerebral toxoplasmosis infection showing hyperintensity on T2 (A,C) and FLAIR (B,D) in the pons and subcortical of right temporo-occipital (red arrow) suggesting as an ADEM case.

### 8 Discussion

Cerebral toxoplasmosis is the most common intracranial infection among patients with HIV-AIDS which occurred in 70% of cases, followed by myocarditis and pneumonitis.<sup>4</sup>

Toxoplasma infection in immunocompromised patients can result in fatal infection with high mortality rate if not treated immediately, so earlier diagnosis is urgently needed. However, serological tests are often unable to support diagnosis, therefore radiologic imaging can be an important consideration in the diagnosis of cerebral toxoplasmosis.<sup>7</sup>

Clinical manifestations of cerebral toxoplasmosis are typically subacute, sometimes it can rapidly progress to diffuse encephalitis, ventriculitis, and there may be no focal brain lesion on brain imaging. The most common neurological symptoms include headache (38-93%), focal neurological deficits (22-80%), fever (35-88%), altered mental status (15-52%), seizure (19-58%), behavioral and psychomotor changes (37-42%), cranial nerve palsy (12-28%), ataxia (2-30%) and visual disorder (8-19%).<sup>9</sup>

Initial diagnosis of cerebral toxoplasmosis is usually made empirically, diagnosis can be confirmed by finding of multiple ring-enhancing lesions on brain MRI, a positive result on serologic test for anti-*T. gondii* immunoglobulin G (IgG) in the cerebrospinal fluid or blood, and clinical and radiologic improvement after treatment with anti-toxoplasma regimen. Nevertheless, empiric diagnosis can be a dilemma because increased level of serum anti-*T. gondii* IgG can be seen in the general population without an active infection.<sup>7</sup>

Several findings in brain imaging of cerebral toxoplasmosis has been described. The lesion is most commonly located in the basal ganglia as multiple rim-enhancing lesion. The imaging appearance is commonly known as “eccentric target sign” and is considered pathognomonic for cerebral toxoplasmosis. However, this appearance is only found in 30% of cerebral toxoplasmosis case.<sup>5,8</sup> An “eccentric target sign” appearance is characterized by area of intermediate hypointensity with peripheral area of rim enhancing hypointensity on T1 post contrast. Another more specific appearance is “concentric target sign” on T2 weighted image, this is a focal lesion in the form of concentric layers of alternating hypointensity and hyperintensity.<sup>6,10</sup>

In our patient, there were multifocal neurological deficits and the result of serologic test for *T. gondii* was positive, however radiologic finding showed an ADEM. In contrast to the typical MRI finding of cerebral toxoplasmosis, ADEM in an MRI showed multiple asymmetric bilateral patchy area on T2 weighted and proton density weighted images, FLAIR, which showed a homogenous or slightly inhomogeneous hyperintensity appearance sized larger than 4 cm, which usually involve the basal ganglia and thalamus.<sup>11</sup>

Treatment of cerebral toxoplasmosis in patients with HIV include antimicrobial therapy for *T. gondii* and antiretroviral therapy to improve the patient’s immunity. The first line treatment in cerebral toxoplasmosis is combination of pyrimethamine with sulfadiazine and leucovorin. Leucovorin is administered to reduce the toxicity of pyrimethamine. Another choice of antimicrobial treatment in patient with intolerance or those who do not response to the first line treatment is combination of pyrimethamine with clindamycin and leucovorin. Moreover, combination of trimethoprim-sulfamethoxazole has also been reported to have better tolerability than combination of pyrimethamine and sulfadiazine (Table 1).<sup>12-14</sup>

**Table 1.** Combination treatment regiments for cerebral toxoplasmosis<sup>12-14</sup>

First line treatment	Pyrimethamine 200 mg orally single dose, followed by 50 mg (body weight ≤ 60 kg) or 75 mg (body weight > 60 kg) + Sulfadiazine 1000 mg (Body
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	weight $\leq$ 60 kg) to 1500 mg (body weight > 60 kg) for each 6 hours + leucovorin (folinic acid) 10-25 mg oral per hari (up to 50 mg once or twice a day)
Alternative regimen	Pyrimethamine (same as doses listed in the first line treatment) + clindamycin 600 mg intravenous or orally every 6 hours + leucovorin (same as doses listed in the first line treatment) Trimethoprim-sulfamethoxazole (TMP-SMX) TMP 5 mg/kg and SMX 25 mg/kg orally or intravenous twice a day Pyrimethamine (same as doses listed in the first line treatment) + atovaquone 1500 mg orally twice a day + leucovorin (same as doses listed in the first line treatment), and soon.

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Antimicrobial treatment in patients with cerebral toxoplasmosis and HIV/AIDS is divided in to two phases, the first is the acute phase treatment for at least 3 weeks and can be given for up to 6 weeks if there is no complete response, and the second is maintenance phase treatment to prevent recurrence. The usual dosage in initial dose of 20 mg of pyrimethamine per day, then 50-75 mg/day and 4-8 g/day of sulfadiazine for 6 weeks. In cases of intolerance to sulfadiazine, it can be substituted with 600 mg of oral or intravenous clindamycin, 4 times per day for 3 to 6 weeks.<sup>15</sup>

In our patient, the diagnosis of cerebral toxoplasmosis was made empirically based on clinical findings of headache, focal neurologic deficits of hemiparesis and cerebellar disorder, and positive serologic test for *T. gondii*. We administered acute phase treatment for cerebral toxoplasmosis with a regiment of 200 mg loading dose of pyrimethamine followed by 75 mg maintenance dose, and 600 mg of clindamycin every 6 hours, and we observed clinical improvement after 7 days of treatment.

### Conclusion

In immunodeficiency patient who clinically and serologically suspected for cerebral toxoplasmosis, however, radiologic finding showed an appearance of ADEM, the diagnose of cerebral toxoplasmosis may be considered, and acute phase treatment for cerebral toxoplasmosis should be given with evaluation of clinical improvement periodically.

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