The Therapeutic Diagnosis of Toxoplastic Encephalitis and Myelitis

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ABSTRACT
A 51-year-old man with advanced HIV infection presented with progressive paraparesis for 2 weeks and then developed confusion and repetitive generalized tonic clonic seizure. The physical examination revealed fever, disorientation, weakness, decreased sensation, absence of deep tendon reflexes of both lower extremities and loss of sphincter tone. The MRI of brain and spinal cord demonstrated multiple intracerebral hemorrhages involving both sides of cerebral hemisphere and enlargement of spinal cord with high signal intensity in the central column at level of T10 down to conus medullaris. His clinical symptoms were dramatically improved after a therapeutic trial of antitoxoplasmosis treatment for 7 days. There might be an argument that other infectious causes may be responsive to sulfamethoxazole treatment and may be the alternative diagnosis. However, performing brain biopsy in this case might be a greater risk than benefit. The therapeutic diagnosis of toxoplasmic encephalitis and myelitis was the most appropriate option for this patient. (J Infect Dis Antimicrob Agents 2014;31:107-13.)

INTRODUCTION
Toxoplastic encephalitis is the major opportunistic infection in AIDS patients. Diagnosis of cerebral toxoplasmosis can be made in a patient who presents with typical clinical manifestations and pathology or serology are compatible with this infection. However, in many areas where diagnosis cannot be made due to limited resources, the therapeutic response might be an important tool for diagnosis. We reported a case of toxoplasmic encephalitis and myelitis in an AIDS patient that diagnosed by a therapeutic response to antitoxoplasmosis drugs.

CASE REPORT
A 51-year-old man, an electrician, lived in Chonburi Province. He had been diagnosed with HIV infection 7 years ago when he had pulmonary tuberculosis and he also had received antiretroviral therapy with anti-tuberculosis drugs for six months. Then he was lost to follow-up. This time he was referred to King Chulalongkorn Memorial Hospital because of progressive paraparesis for 2 weeks.

Eight weeks before referral, he had felt numbness in both of his feet, then gradually progressed to the shins. Five weeks later he had experienced difficulty in walking and that slowed him down when climbing up and down stairs. He also had a diffuse headache. An acetaminophen 1 g could relieve his symptoms. He did not recognize a fever or other constitutional symptoms.
Two weeks before referral, he woke up in the morning and observed prominent weakness of his legs and could not stand up. He was admitted to a provincial hospital. His body temperature was 38.8°C. Blood pressure 140/80 mmHg and heart rate 96 bpm. The neurological examination revealed that his lower extremities had motor power grade 3/5 both sides with impaired pinprick sensation below both knees and loosening of sphincter tone. The basic laboratory was done and CBC showed Hb 7.4 g/dL, Hct 23.9%, MCV 61.3 fL, WBC 2,920/mm³ (N 75%, L 13%, M 8%, E 2%, atypical lymphocytes 2%), platelets 41,000 cell/mm³. Anti-HIV was confirmed positive with CD4 T cell count was 19 (5%) cells/mm³.

He had received an empirical treatment for fever with intravenous ceftriaxone 2 g once daily and oral fluconazole 200 mg twice daily.

The MRI of the T-L spine showed enlargement of the spinal cord with high signal intensity in the central column at the level of T10 down to conus medullaris and heterogeneous low signal intensity on T2 in conus medullaris. There was decreased signal intensity of all lumbar intervertebral disks with slight bulging disks at L2-3, L3-4, L4-5 and small disk protrusion at L5-S1 without root compression. At L1 level, central high signal with rim-low signal on T2 was seen which might represent blood components and post-contrast study, a small enhanced dot in the central column of conus medullaris was demonstrated. (Fig 1 and 2)

The CT of the brain with contrast was performed before lumbar puncture for CSF analysis and revealed multiple small hematomas scattered in bilateral cerebral hemispheres with no sign of

![Image](https://via.placeholder.com/150)

**Figure 1.** Sagittal view of the T-L spines (T2 with contrast, short TI inversion recovery) (STIR), (T1 with fat saturated and contrast), showed enlargement of spinal cord with high signal intensity in the central column at level of T10 down to conus medullaris and heterogeneous low signal intensity on T2 in conus medullaris.
brain herniation. The MRI brain showed multiple intracerebral hemorrhages involving both sides of cerebral hemisphere. The largest one was 3.3 cm in diameter with surrounding edema in the right occipital lobe and this finding might represent a recent hemorrhage. No restricted diffusion on DWI was observed and post-contrast study showed no abnormal enhancement. (Fig. 3)

The lumbar puncture revealed opening pressure/closing pressure 12/6 cmH₂O, WBC 20 cells/mm³ (no differential count), RBC 1,480 cells/mm³, protein 96 mg/dL, sugar 72 mg/dL, plasma glucose 137 mg%, Gram stain was no organism seen and no bacterial growth on CSF culture.

After 12 days of treatment at a provincial hospital, his weakness of lower limbs progressed and he developed cauda equina syndrome. He had been in a state of confusion and lethargy. Finally his physician decided to refer this patient to KCMH after episodes of generalized tonic clonic seizure.

The patient gained his consciousness upon arrival at KCMH but was unable to follow simple commands. His vital signs were stable with BT 36.5°C, BP 126/88 mmHg, HR 110/min and RR 20/min. The physical examination showed mildly pale conjunctivae, no icteric sclerae, and no lymph node enlargement. The cardiovascular and respiratory systems appeared normal. The neurological examination demonstrated normal cranial nerve function and fundoscopic exam showed neither papilledema nor cytomegalovirus retinitis. The motor system was markedly abnormal at the lower extremities which had muscular atrophy and flaccid tone of both legs but no fasciculation. The motor power of hip flexors/extensors were grade III/IV, knee flexors/extensors III/IV and ankle dorsiflexors/plantar flexors II/II which were the same in both legs. The motor system of upper extremities appeared normal and deep tendon reflexes were equal. The deep tendon reflexes of both legs were absent. The clonus was negative and Babinski’s sign was plantar flexion. The sensory was abnormal with impaired pinprick sensation below both knees, impaired anal and perineum sensation, impaired vibrating sensation below L3 level, impaired proprioception in both feet, ankles and knees. The autonomic systems showed loss of sphincter tone and bulbocavernous reflex. The cerebellar signs were intact. He had no stiffness in his neck.

The CBC showed pancytopenia again with Hb 8.2 g/dL, Hct 27.0%, MCV 66 fl, WBC 4,410/mm³ (N 82.8%, L 8.1%, M 6.5%, E 0.1%, B 2.5%) and platelet 20,000/mm³. The peripheral blood smear revealed hypochromic microcytic RBC, few ovalocytes, few target cells, decreased number of white blood cells,
and markedly decreased number of platelets. The iron study was normal. The hemoglobin typing was hemoglobin H disease but could not explain pancytopenia cause. Then a bone marrow study was performed with the results showing normal trilinage cellular marrow with no opportunistic pathogen detected.

The renal and liver function appeared normal. Several serological tests were done and showed negative for cryptococcal antigen, serum galactomannan, toxoplasma IgG and IgM antibody by ELISA. The blood for CMV and EBV viral load were less than 600 copies/mL. The cerebrospinal fluid analysis was also negative for CMV IgG and IgM.

Figure 3. MRI showed multiple intracerebral hemorrhages involving both sides of cerebral hemisphere. The largest one was 3.3 cm in diameter with surrounding edema in the right occipital lobe and this finding might represent a recent hemorrhage. No restricted diffusion on DWI was observed and post-contrast study showed no abnormal enhancement. (T1-weighted, T1 weight with contrast and fluid attenuated inversion recovery) (FLAIR).
From clinical and laboratory information, this patient presented with progressive paraparesis caused by scatter intramedullary spinal cord lesions and multiple intracerebral hemorrhages of both cerebral hemispheres. The presumptive diagnosis was Toxoplastic encephalitis and myelitis with intraregional bleeding. The differential diagnoses were disseminated tuberculosis, nocardiosis, fungal infection and CNS lymphoma. While awaiting for neurosurgical consultation, we decided to start antitoxoplasmosis drugs: pyrimethamine 200 mg once daily, sulfadiazine 1,000 mg 4 times daily and leucovorin 15 mg once daily. We also prescribed oral phenytoin 300 mg once daily for control of seizures. A corticosteroid was not administered.

After antitoxoplasmosis treatment for 7 days, his clinical symptoms were dramatically improved, cauda equina syndrome was absent and his legs could voluntarily raise up with motor power grade IV. He gained full consciousness and had no headache. When considering between risk and benefit about diagnostic investigation by brain biopsy again, we thought that the patient had responded well to antitoxoplasmosis drugs and should not undergo surgery. After 2 weeks of treatment, the MRI brain was performed again and found marked decrease in size of hemorrhagic lesions along corticomedullary junction. (Fig 4)

In conclusion, the presumptive diagnosis of abnormalities of CNS in this case was toxoplastic encephalitis and myelitis. The patient also had HIV-related pancytopenia and Hb H disease.

DISCUSSION

The presence of multiple brain abscesses is the most characteristic feature of toxoplastic encephalitis (TE) in severely immunodeficient patients, particularly in patients with AIDS. A wide range of clinical findings including altered mental state, seizures, weakness, cranial nerve disturbances, sensory abnormalities, cerebellar signs, meningismus, and movement disorders are seen in toxoplastic encephalitis. Spinal cord involvement by T. gondii in AIDS patients manifests as motor or sensory disturbances of single or multiple limbs, bladder or bowel dysfunctions, or both. Local pain has been published and also spinal cord necrotizing lesions are seen at autopsy in approximately 6% of patients with TE.1 Brain abscesses in AIDS patients are characterized by three histologic zones. The central area is avascular zone, surrounding this area, is an intermediate hyperemic area with a prominent inflammatory infiltrate and perivascular cuffing by lymphocytes, plasma cells and macrophages. In the areas around the abscesses, edema, vasculitis, hemorrhage, and secondary to vascular involvement may also be present. Levy RM, et al reviewed 200 HIV patients with symptoms and signs of CNS abnormalities, 44 in 200 cases had abnormal CT findings. Fifty percent of patients who had focal CNS lesions were TE confirmed by histopathology and 10% of TE patients had cerebral hemorrhage.2 Even though the clinical and neuroradiologic findings in AIDS patients were consistent with toxoplastic encephalitis and myelitis, the definite diagnosis is isolation of Toxoplasma gondii from blood or body fluids. The histologic finding of tachyzoites in tissue sections or smears of body fluid or the PCR amplifications for detection of T. gondii DNA were another tool for the diagnosis of infection. In this case we could not perform the isolation by culture due to the resource limited institution and had not performed surgery for tissue pathology. The serologic tests for the
demonsstration of specific antibody to *T. gondii* are the only available method to support the diagnosis. However, the limitation of serologic diagnosis is poor immune response to toxoplasma, especially in severely immunocompromised hosts. Luft BJ, et al reported the poor antibody response in 37 patients with AIDS with proven cerebral toxoplasmosis by pathological diagnosis. There was only 1 patient that had positive IgM antibody by enzyme-linked immunosorbent assay test. Sukthana Y, et al reviewed the prevalence of *T. gondii* antibody between 190 HIV-infected persons and 122 non-HIV persons. There was no differences of positivity in toxoplasma IgG antibody, 23.2% in HIV-infected

Figure 4. MRI of the brain showed a marked decrease in size of hemorrhagic lesions along corticomedullary junction after 2 weeks of antitoxoplamosis drugs.
persons and 29.5% in non-HIV infected persons (P=0.25). Our patient had a very poor immunologic status with CD4 count of 6%. This could explain negativity on toxoplasmosis serology. While the planning for biopsy of intracranial lesion had been in the process, the patient had very good clinical response to antitoxoplasmic drugs. Luft BJ, et al had studied how rapid clinical response to specific therapy helps to confirm diagnosis of TE. The international, multicenter study in 49 patients with TE showed that the median time to achieve 50% improvement of neurological signs and symptoms was 3 days and the median time of clinical response was 6 days. Ninety-one percent of patients had clearly improved within 14 days. The patients that did not respond within 5-12 days had lymphoma. Our patient had initial response from day 1 of treatment and significant improvement occurred within 7 days. The therapeutic diagnosis of toxoplasmic encephalitis and myelitis was the most suitable and correlated with clinical pictures of this patient. The other infectious cause which might have responsiveness to sulfamethoxazole such as nocardiosis, was the possible differential diagnosis. Nocardiosis is, however, not a common cause of myelitis.

References