

Neuropsychiatric Symptoms in Cerebral Toxoplasmosis with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS): Case Report

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ABSTRACT

Cerebral toxoplasmosis is often caused by the reactivation of pre-existing infections. The increasing number of HIV/AIDS increased cases of cerebral toxoplasmosis. Cerebral toxoplasmosis can show clinical symptoms of neurological and psychiatric. Psychiatric symptoms such as psychosis are often associated with cerebral toxoplasmosis infection. Hemichorea and hemiballism are movement disorders often found in cerebral toxoplasmosis, although movement disorders are less common than other neurological symptoms. We report that a 53-year-old man with complaints of whole-body weakness three days before admitted to the hospital. Patient's appetite decreased. While being treated, he saw an oriental figure walking back and forth as if watching him. Patient also heard voices and complained involuntary movements in the right hand and leg. Neurological examination revealed right hemichorea with characteristics; arrhythmic, irregular, high amplitude, and improved at rest. Psychiatric examination revealed visual and auditory hallucinations. Laboratory examination showed anemia and leukopenia. Chest X-ray revealed a left pleural effusion. Magnetic Resonance Imaging (MRI) of the head with contrast showed multiple lesions with perifocal edema, suspected cerebral toxoplasmosis. Patient received anti-toxoplasmosis and antipsychotic. Patient improved on the sixth day of treatment. Cerebral toxoplasmosis can cause serious complications

in patients with HIV/AIDS. Psychotic symptoms such as hallucinations and delusions are often associated with cerebral toxoplasmosis infection. Hemichorea is the most common type of movement disorder in toxoplasmosis cerebral patients related to HIV/AIDS. The main treatment is anti-toxoplasmosis medication. Combination with antipsychotics is effective in treating the symptoms of psychosis and hemichorea, while also inhibiting the replication of *Toxoplasma gondii*.

Keywords: Cerebral Toxoplasmosis, HIV/AIDS, Neuropsychiatric

BACKGROUND

Cerebral toxoplasmosis is an infection caused by *Toxoplasma gondii* and affects brain tissue. *Toxoplasma gondii* is an obligate intracellular parasite.[1] The resulting infection gives very varied clinical symptoms in humans and animals. *Toxoplasma gondii* infection is often caused by the reactivation of pre-existing disease and generally attacks patients with an impaired immune system. In patients with a good immune system, toxoplasmosis infection usually does not cause any symptoms.[2] With the increasing number of people living with HIV/AIDS, cerebral toxoplasmosis cases are also increasing.[3] The incidence of cerebral toxoplasmosis varies for each area, depending on the

presence of the toxoplasmosis parasite as the cause and the cleanliness of the area. In the United States and European countries, the seroprevalence rate increases with age and contact. In the United States, the seroprevalence at the age of 10-19 years ranges from 5-30%, and above 50 years, it ranges from 10-67%. It is estimated that this seroprevalence will increase by around 1% yearly. The incidence of this disease has greatly decreased after using Highly Active Antiretroviral Therapy (HAART) to treat people living with HIV. [4-5] Cerebral toxoplasmosis can cause neurological and psychiatric disorders. Neurological symptoms include headaches, decreased consciousness, seizures, hemiparesis, and sometimes found involuntary movements such as hemichorea and hemiballism. Psychosis symptoms are often associated with cerebral toxoplasmosis. Some literature also mentions that people with cerebral toxoplasmosis are more prone to suffer from schizophrenia. A definite diagnosis of toxoplasmosis infection is by finding *Toxoplasma gondii* in blood, tissue, or body fluids. Immunoglobulin M (IgM) antibody examination to detect acute infection in the first week. The recommended radiological examination is a Computed Tomography (CT) scan or MRI with contrast. An MRI examination gives better results and is more sensitive than a CT scan.[3-4] Acute phase therapy can be given pyrimethamine with sulfadiazine, or a combination of pyrimethamine with clindamycin also gives the same results. Other alternative therapies that can be given are trimethoprim-sulfamethoxazole and azithromycin.[4]

CASE REPORT

A 53-year-old man with complaints of whole-body weakness since three days ago was admitted to the hospital. The patient's appetite has decreased. He ate about 4-5 tablespoons the last few days. The patient said that while being treated in the hospital, he had seen a human figure with an oriental appearance walking back and forth around the hospital as if watching him, but only the

patient himself could see him. This condition causes the patient to be afraid. The patient also heard voices, like several people chatting, but the accompanying family said they did not hear anything. The patient also complained of involuntary movement in the right hand and leg, which had been felt since one year ago. The patient had received treatment for these symptoms, which have reduced slightly but he stopped the treatment himself. The complaint of involuntary movement is still being felt and getting worse in the last few days. There was no previous history of psychiatric disorders. The patient was diagnosed with Stage IV HIV World Health Organizations (WHO) one year ago and had received HAART. The patient was treated with anti-toxoplasmosis drugs therapy for three months for a diagnosis of cerebral toxoplasmosis ten months ago, and then the patient stopped himself.

General physical examination within normal limits. Neurologic examination revealed right hemichorea with arrhythmic, irregular, high amplitude characteristics and improved at rest. Psychiatric examinations have shown dysphoric mood, visual and auditory hallucinations, mixed-type insomnia, and grade 4 insight. Laboratory tests showed hemoglobin 9.7 g/dl and leukocytes 2,950/mm³. Chest X-ray examination in Figure 1 has shown a left pleural effusion. MRI examination of the head with contrast, as shown in Figure 2 has shown well-defined lesions in the subcortical right and left frontal lobes, right and left centrum semiovale, right and left corona radiata, left internal capsule, and left basal ganglia accompanied by perifocal edema, leading to a process suspected cerebral toxoplasmosis infection.

Multidisciplinary specialists treat patients to get the best results. Treatment with haloperidol 0.5 mg every 24 hours orally and valproic acid 250 mg every 12 hours orally was administered by a neurologist for complaints of hemichorea. The psychiatrist added lorazepam 0.5 mg every 24 hours along with haloperidol therapy that the

neurologist had given for hallucinations. The internal medicine gave HAART, co-trimoxazole 960 mg every 24 hours orally, paracetamol 500 mg every 8 hours orally, fluconazole 200 mg every 24 hours orally, cefepime 2 g every 8 hours IV for viral

infections and opportunistic symptoms. On the sixth day, the patient was discharged in stable condition. Symptoms of anemia, leukopenia, hallucinations, and involuntary movements improved during treatment.



Figure 1. Thorax AP revealed left pleural effusion

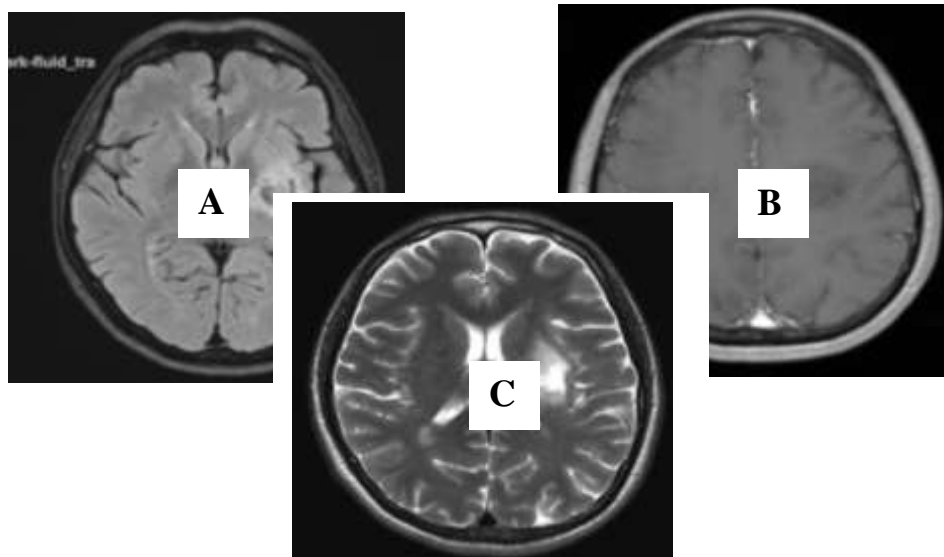


Figure 2. Head MRI with contrast: A. FLAIR, has shown iso-hypointense lesion; B. T1WI, has shown hypointense lesion; C. T2WI, has shown hyperintense lesion

DISCUSSION

Toxoplasma gondii is an intracellular protozoan that can cause zoonotic infections. Acute *Toxoplasma gondii* infection is usually subclinical in most immunocompetent individuals. Cerebral toxoplasmosis is caused almost exclusively by the reactivation of latent brain cysts and can cause severe complications in immunocompromised patients, especially those with HIV/AIDS. Toxoplasmosis is one of the most common infections in

humans with a worldwide distribution; it is estimated that about one-third of the global population is infected with latent toxoplasmosis. The prevalence of coinfection in low-income, middle-income, and high-income countries is 55%, 34%, and 26%, respectively. High prevalence occurs in Latin America, Eastern or Central Europe, Middle East, Southeast Asia, and Africa.[6-7]

Diagnosis of cerebral toxoplasmosis is based on clinical symptoms, level of risk,

examination of immunoglobulin G (IgG) antibodies against *Toxoplasma gondii*, and radiological examinations.[8] Typical findings of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) in patients with cerebral toxoplasmosis are multiple lesions in the basal ganglia (48%), frontal lobes (37%), and parietal lobes (37%), occipital lobes (19%), temporal lobe (18%), and brainstem/cerebellum (5-15%) with surrounding edema. Approximately 30% to 40% and 15% of patients with cerebral toxoplasmosis have a single lesion seen on CT and MRI studies. Although ring-enhancing lesions with perilesional edema are the most common pattern (44%-82%), non-enhancing lesions (6%-20%) may occur.[7]

It is already known that acute and latent forms of toxoplasmosis are associated with neurological and neuropsychiatric symptoms. Some neuropsychiatric disorders are schizophrenia, bipolar disorder, obsessive-compulsive disorder, depression, substance abuse disorder, generalized anxiety, and panic disorder. Neurological symptoms include hemiparesis, aphasia, cranial nerve paresis, seizures, and sometimes involuntary movements such as hemichorea, hemiballism, dystonia, athetosis and myoclonus are found. The relationship between latent toxoplasmosis and neurological disorders is stronger than psychiatric disorders.[9]

Several previous studies have estimated *Toxoplasma gondii* infection as a risk factor for developing schizophrenia and depression in humans. The genome of *Toxoplasma gondii* is known to contain 2-aromatic amino acid hydroxylases, which have the potential to affect the biosynthesis of dopamine and serotonin directly.[10-11] The potential mechanism responsible for changes in the behavior of patients with cerebral toxoplasmosis is related to the role of tryptophan metabolism and the Hypothalamic Pituitary Adrenal Axis (HPA Axis). Many cases of acute toxoplasmosis in adults are associated with psychiatric symptoms such as delusions and

hallucinations. A case report by Marchira et al., found a 20-year-old male patient with behavioral changes described as difficulty sleeping, laughing, and screaming at himself. The patient was diagnosed with toxoplasmosis based on a clinical and examination of anti-toxoplasmosis IgM and IgG. The patient has then treated with risperidone 2 mg every 12 hours and anti-toxoplasmosis pyrimethamine and clindamycin. The patient's condition improved and stabilized after two weeks of treatment.[12] In our case, the patient also complained of visual and auditory hallucinations, then received treatment with antipsychotic haloperidol 0.5 mg/24 hours and lorazepam 0.5 mg every 24 hours. Noticeable improvement was seen, the patient had no symptoms of hallucinations within a few days of treatment. Several studies have linked the administration of haloperidol to inhibiting the replication of *Toxoplasma gondii*, because the *Toxoplasma gondii* genome affects the biosynthesis of dopamine and serotonin. Involuntary movements in HIV/AIDS patients are increasingly common nowadays. Many factors are the cause, including HIV encephalopathy, Progressive Multifocal Leukoencephalopathy (PML), Whipple's disease, and due to drug use.[2,3] One of the most frequently reported causes is cerebral toxoplasmosis. The most common involuntary movement disorders are unilateral hyperkinetic disorders such as hemichorea and hemiballism. Hemichorea and hemiballism in patients with toxoplasmosis of the brain occur in approximately 7.4% of cases.[13] A case report by Rabhi et al., where a patient they observed complained of hemichorea movements in the left hand and leg. The patient has a history of HIV/AIDS with opportunistic toxoplasmosis cerebral infection. The clinical features of hemichorea associated with cerebral toxoplasmosis do not generally differ from hemichorea. Symptoms of hemichorea can be an early symptom of HIV/AIDS.[14] Most cases of chorea and ballism in

toxoplasmosis of the brain with HIV/AIDS are reported with multiple brain lesions. The structures most commonly affected are the subthalamic nucleus, thalamus, caudate nucleus, putamen, globus pallidus, midbrain, and internal capsule. Chorea and ballism usually occur due to damage to subthalamic nucleus and globus pallidus. This is consistent with our case, where there were lesions in the basal ganglia area and left internal capsule with clinical features of uncontrolled hyperkinetic movements on the right side of the body.[14]

A case report by Dimal et al., 24-year-old male patient with AIDS experiencing complaints of hemichorea and hemiballism related to toxoplasmosis infection of the brain. The patient was treated with anti-toxoplasmosis drugs and symptomatic therapy. In that case, the patient was given trimethoprim/sulfamethoxazole and risperidone. There was a marked improvement in the patient. Hemichorea associated with toxoplasmosis of the brain is generally reversible if diagnosed and treated early.[15] In our case, the patient with right hemichorea received therapy with co-trimoxazole 960 mg/24 hours together with antipsychotics. The patient's clinical condition improved within a few days and the patient was planned for outpatient care.

CONCLUSIONS

Cerebral toxoplasmosis is an opportunistic infection that most often attacks the brain in patients with HIV infection. Toxoplasmosis of the brain can cause neurological and psychiatric symptoms. Several clinical and epidemiological studies have shown a positive correlation between *Toxoplasma gondii* infection and psychosis. Research shows that any change in the level of neurotransmitters can lead to changes in a person's behavior. Changes in neurotransmitters in brain tissue occur in *Toxoplasma gondii* infection, which causes an increase in dopamine concentrations that can induce behavioral changes in humans. Several studies reported that some antipsychotic drugs could treat symptoms of

psychosis and also inhibit the replication ability of *Toxoplasma gondii* because it has a genome structure similar to dopamine.

Movement disorders that occur in patients with cerebral toxoplasmosis are rare neurological symptoms. Symptoms of movement disorders may appear as early symptoms in cerebral toxoplasmosis infection with HIV/AIDS. Hemichorea and hemiballism are the most common movement disorders in cerebral toxoplasmosis. The main treatment is anti-toxoplasmosis drugs to treat the infection because the symptoms of movement disorders in cerebral toxoplasmosis are reversible. Antipsychotics can be given in the short term and can be stopped if complaints are improved.

Declaration by Authors

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