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# Cerebral toxoplasmosis in an HIV-negative immunocompetent young man

Regin Filamel R. Escalada *MD*, Norman D. Pagar *MD FPCP*, Patricia B. Olarte *MD FPNA*, Herminigildo H. Gan *MD FPCP*

*Department of Neurology, Jose Reyes Memorial Medical Center, Manila, Philippine*

### *Abstract*

This is a case of a 20-year old male, who was previously healthy, presenting to the emergency room with generalized seizures. Prior to this, he has been observed to be withdrawn and lacking in drive to do wilful activities as he used to. On neuroimaging, there were multiple rim-enhancing lesions in the right basal ganglia and caudate nucleus. The patient's serum also tested highly positive for *Toxoplasma* IgG but HIV testing was negative and CD4+ count was equal to 625 cells/mm3. Along with other findings, a clinical impression of cerebral toxoplamosis was made and he was started on the available antibiotic treatment. Response to such treatment was observed as well as regression of the lesions on neuroimaging. The patient was eventually discharged improved. This patient shows that cerebral toxoplasmosis may rarely occur in patients without HIV infection or state of immunosuppression.

## INTRODUCTION

*Toxoplasma gondii* is an obligate intracellular protozoan that infects up to a third of a world's population. Human beings may acquire such infection by ingestion of tissue cysts in the undercooked meat of intermediate hosts (e.g. pig, cattle, sheep, etc.) or by ingestion of food or water contaminated by feces containing oocysts from the definitive host which are the members of the feline family. Generally, it is an opportunistic infection which primarily affects and becomes clinically symptomatic in immunocompromised hosts – patients infected with human immunodeficiency virus (HIV) or post-transplant patients receiving drug immunosuppression. Primary toxoplasmosis in immunocompetent individuals was found to be very minimal.[1] In the majority of patients who are immunocompetent, *T. gondii* infection may present only as nonspecific self-limiting illness or may remain asymptomatic in most cases.[2] In the Philippines, from 1977-2000, a wide range of prevalence of antibodies to *T. gondii* among healthy persons was found to be <2 to 61.2% for 1977-2000.[3] To date, there has been no published documentation of symptomatic cerebral toxoplasmosis in an otherwise healthy population. Primary infection may at times have lymphadenopathy.[4] Rarely, some immunocompetent individuals develop chorioretinitis and pulmonary forms.[5] It may also present with CNS (central nervous system) involvement. We found only a few reports on immunocompetent patients who presented with CNS involvement. One of which was a middle-aged man who presented with long-standing headache for five years.[6,7]

A key feature of *T. gondii* is the microorganism's ability to cross biological barriers and may reach the brain, eyes, and the placenta. Cerebral toxoplasmosis typically manifests as cerebral mass lesions with headache, confusion, fever, lethargy, seizures, cranial nerve palsies, psychomotor changes, hemiparesis, and/or ataxia. Usual radiological findings may be bilateral, multiple, ring enhancing lesions on the basal ganglia and corticomedullary junctions of cerebral hemisphere.[8] This report is a case of a cerebral toxoplasmosis in a patient without HIV infection or any history of immunosuppression. Written informed consent was obtained from the patient and this case report was approved by the institutional Ethics Review Board.

## CASE REPORT

A 20 year-old male, single, previously healthy man from an agricultural province with no history of prior hospitalization, presented with generalized tonic-clonic seizure at the emergency room. He had four pets, three cats and a dog. He worked as a caretaker in a chicken farm. He had two sexual

*Address correspondence to:* Dr Regin Filamel R. Escalada, Jose R. Reyes Memorial Medical Center, Rizal Avenue, Sta. Cruz, Manila, Philippine. Tel: +632-711-9491 Loc. 292, Email: reginfilamelr.escalada@gmail.com

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partners with prior sexual practices unknown to the patient.

On the second week of May 2017, the patient was noted to have lack of will and initiative to do his daily tasks. He was observed to have decreased drive to mingle with his family and friends. On the following month, he was often drowsy. During the same time, he had his first episode of stiffening of all extremities with upward rolling of eyeballs, lasting for approximately 2 minutes with impairment of consciousness. He was brought to a neurologist. An electroencephalogram (EEG) was done showed epileptiform discharges over the right fronto-temporal area with slowing over the bilateral frontal area. Valproic 500 mg twice daily was started. A contrast-enhanced cranial magnetic resonance imaging (MRI) was requested but was not immediately done due to financial constraints.

On the 2nd week of July 2017, he developed left hemiparesis and had another episode of seizure. On the following month, the patient had multiple episodes of seizure. At the emergency room, a contrast-enhanced cranial computed tomography (CT) scan was done which showed almost symmetrical moderate low density changes probably representing edema of the cerebral white matter in the frontal lobes including the internal and external capsules as well as in the caudate-lentiform. Two small contrast-enhancing nodules in the basal ganglia and one in the head of the caudate nucleus were seen. The cerebral sulci are effaced (right more than the left) and the midline structures were not displaced (Figure 1).

In the post-ictal state, vital signs were within normal limits. General physical examination was unremarkable and there was no palpable lymphadenopathy. He could be awakened by repeated shoulder tapping and name calling, moaned to pain and had spontaneous movement of all extremities. His pupils were 3 mm equally and briskly reactive to light. Fundoscopic examination was unremarkable. His primary gaze was at midline and had brisk corneal reflexes. He had left central facial palsy on grimace with preferential use of the right upper and lower extremities. Tendon reflexes were all within normal limits. There was no nuchal rigidity, Kernig's, or Brudzinski sign. Plantar reflexes were normoreactive. Baseline complete blood count, serum electrolytes and liver function tests were within normal limits. Chest X-ray was also normal. The erythrocyte sedimentation rate (ESR) was elevated at 100 mm/hr (reference normal value for men aged less than 50 years: 1-10 mm/h). CD4+ count was equal to 625 cells/mm$^3$.

Based on the history, clinical presentation and initial neuroimaging done, he was managed as having seizure disorder, secondary to multiple intracranial masses, probably secondary to neurotoxoplasmosis. Trimethoprim sulfamethoxazole (160/800) mg tablet thrice daily was immediately started. An HIV-antibody chemiluminiscence-linked immunosorbent assay (CLIA) test was done which revealed negative result. His serum was also tested for Toxoplasma IgG which was positive at 200 IU/ml (Reference: ≤9 IU/ml = negative, 10-11IU/ml = equivocal, ≥12 IU/ml = positive) via enzyme-linked fluorescence assay (ELFA). Lumbar puncture was also done. Cerebrospinal fluid (CSF) microscopy and culture were negative for bacterial, fungal, and acid-fast bacilli infection. CSF fluid polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* and Cryptococcal Latex Agglutination System (CALAS) yielded negative results. Cerebrospinal fluid (CSF) glucose and protein levels were within normal values. The patient's stool was also examined through Kato Katz method and revealed positive for hookworm ova. The patient was given Mebendazole for three days.

After three weeks of hospital stay, he become alert and coherent. The right hemiparesis resolved and he was able to walk independently. Due to financial limitations, a contrast-enhanced cranial MRI was done only in the 4th week of antibiotic treatment. Imaging revealed partial resolution of the bilateral edema involving the bilateral basal ganglia, frontal, and parietal periventricular white matter areas. There is also is reduction in size of the contrast-enhancing nodule in the right basal ganglia with resolution of the lesion in the head of the caudate nucleus (Figure 2). The patient was eventually discharged improved and continued taking the antibiotic for 8 more weeks.

## DISCUSSION

The prevalence of *T. gondii* infection in humans worldwide varies according to the environment, eating habits, and age.[9] With the concurrent HIV/AIDS pandemic, toxoplasmosis was shown to be highly prevalent in HIV-infected patients. Our patient had no indications of immunocompromised state. He had no history of transplant and screening test (CLIA) for HIV was negative. In the diagnosis of HIV infection, utilization of either enzyme-linked immunosorbent assay (ELISA) and chemiluminescence (CLIA) immunoassay was found to have no significant difference. The positive rate of chemiluminescence immunoassay

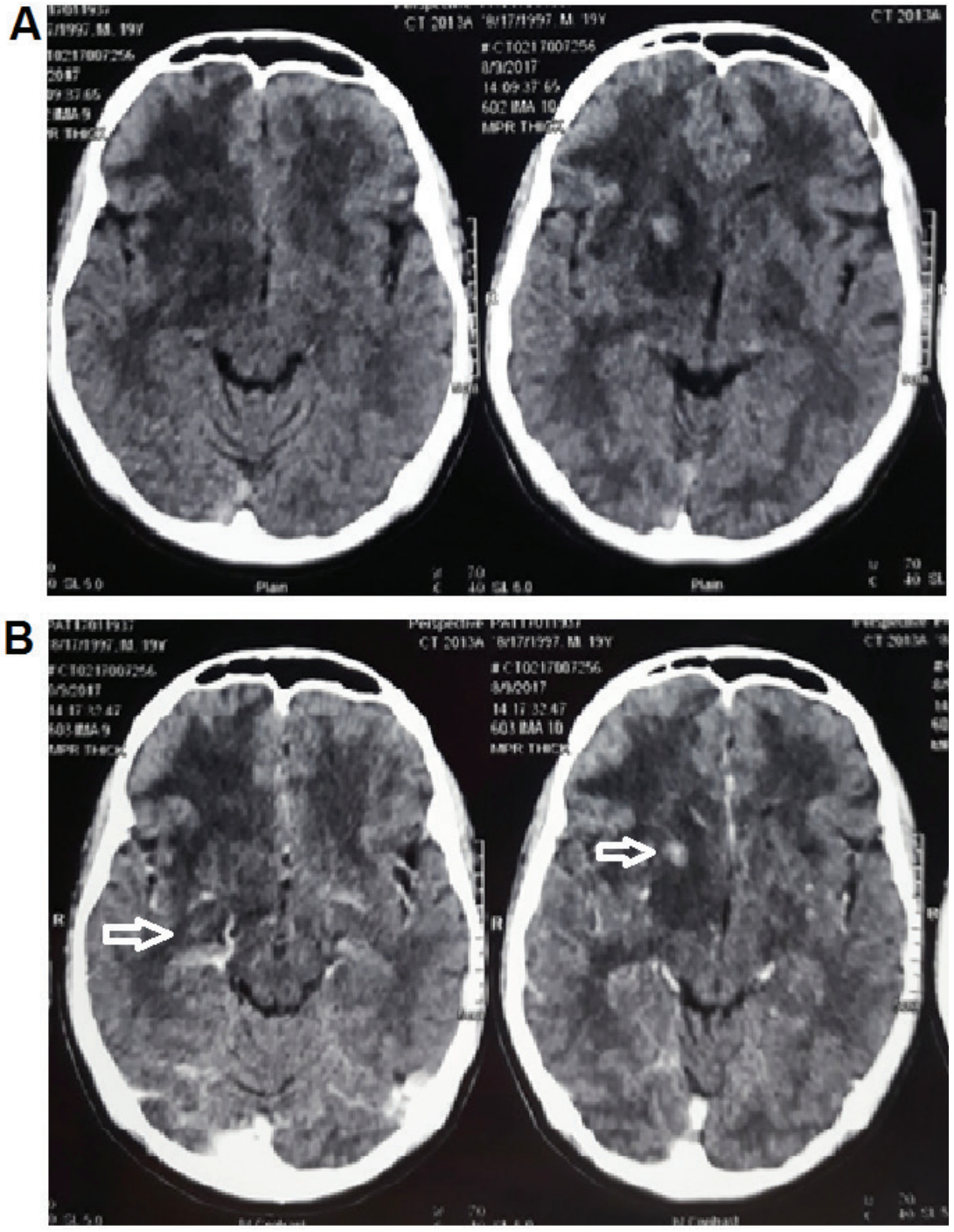


Figure 1. *Plain and contrast-enhanced cranial CT scan in axial view*. There is presence of almost symmetrical moderate low density changes or edema of the cerebral white matter especially in the frontal lobes including the internal and external capsules as well as edema in the caudate-lentiform nuclei and right anterior temporal white matter. Two (2) rim-enhancing nodules post-contrast in the putamenmeasuring 0.5 x 0.5 cm and 0.8 x 0.8 cm were noted (*white arrow, left image*). Another lesion (0.5 x 0.4 cm) is seen in the head of the caudate nucleus (*white arrow, right image)*

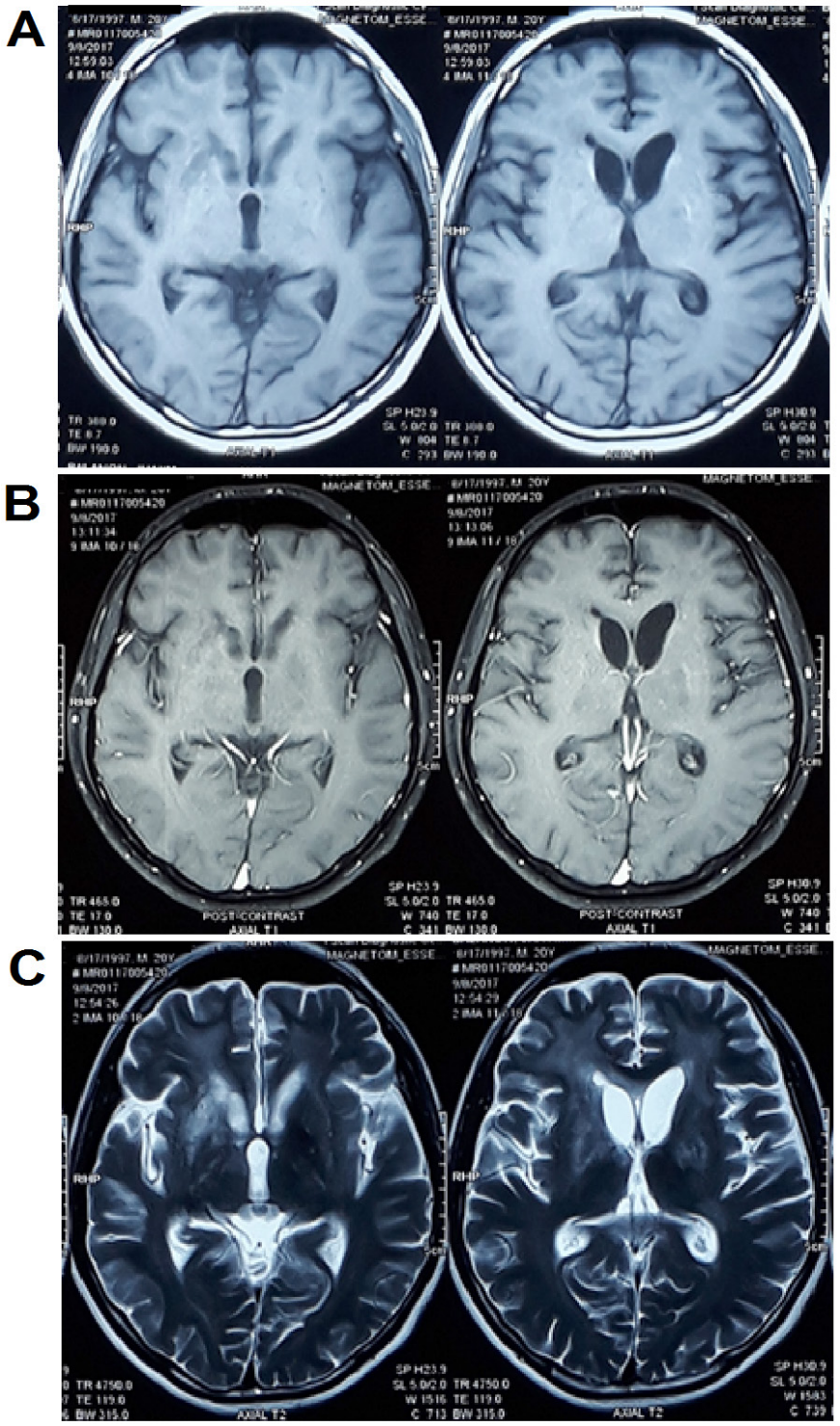


Figure 2. *T1(A) and T1 post-contrast(B) cranial MRI*. There is reduction in size of the contrast-enhancing nodule in the right basal ganglia with smaller contrast-enhancing focus measuring 0.4 x 0.4 cm (previously 0.8 x 0.8cm). The contrast-enhancing nodule in the head of the caudate nucleus in no longer appreciated. There is partial resolution of the bilateral vasogenic edema involving bilateral frontal and basal ganglial areas with minimal residual in the white matter as seen in the T2 sequence (C).

was 1.03%, while the sensitivity and specificity were 100%, 99.93%, respectively.

Immunocompetent persons with an acute primary *toxoplasma* infection does not usually present with any symptom. However, during the dormant phase of the disease, organisms may be seen within the gray and white matter of the brain.[6] Usual radiological findings may be bilateral, multiple, ring enhancing lesions on the basal ganglia and corticomedullary junctions of cerebral hemisphere. Presence of hemorrhages may occasionally be seen and would differentiate toxoplasmosis from lymphoma.[8] The common presenting symptom of cerebral toxoplasmosis is headache, often accompanied by fever and altered mental status. Our patient did not have any febrile episode, he initially presented with abulia and subsequent drowsiness. Individuals may also present with seizures and sensorimotor deficits as seen with our patient. Other common symptoms like visual disturbances and cranial nerve abnormalities were not seen.[4]

Behaviors such as contact with cats and consumption of uncooked meat were found to be the main sources of infection. Ingestion of food or water contaminated with cat feces containing oocyst, transplacental infection of the fetus, white blood cell transfusion or organ transplantation are other modes of transmission of the *T. gondii*.[3]

Recent reports have shown that the disease has a higher prevalence among men (79% versus 63.4% in women) and that age-dependent seroprevalence reaches > 92% in the age 40 to 50 group.[10]

In conclusion, this case demonstrate that symptomatic cerebral toxoplasmosis can rarely occur in immunocompetent patients.

## DISCLOSURE

Conflict of interest: None

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