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Case Report

Reactivation of Latent Toxoplasmosis in a Schizophrenia Patient: A Case Report

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Abstract

Schizophrenia is a serious mental disorder characterized by chronic relapsing episodes of psychosis. The disease is multifactorial, where infections, genetic vulnerability and environmental factors are involved in the development of the illness. *Toxoplasma gondii* is one of the parasites that has long been known associated with schizophrenia in many studies. To date, there is growing evidence of association between *T. gondii* infections and schizophrenia. Herein we report a rare case of reactivated toxoplasmosis in a schizophrenia individual. This patient was incidentally diagnosed with reactivated *T. gondii* infection. He denied any symptoms of toxoplasmosis but experienced a mild psychiatric auditory hallucination. Serology test for *T. gondii* immunoglobulin antibodies measured a high positive IgG titer (135.9 IU/ml) and negative for IgM. Interestingly, nested PCR exhibited a positive result for the type I strain of *T. gondii* dense granular (GRA) 7 gene (*GRA7*). This case highlights the detection of probable reactivation of toxoplasmosis in an immunocompetent schizophrenic patient without psychiatric treatment-resistant and remains asymptomatic for toxoplasmosis. Both serology and molecular tools have been a helpful aid in establishing the diagnosis. Nonetheless, early detection as in this case may aid the patient management in the future.

Introduction

Toxoplasmosis is one of the commonest protozoan infections caused by an intracellular parasite, *Toxoplasma gondii*. Even so, the main form of toxoplasmosis is latent and asymptomatic. *T. gondii* infection in immunocompromised patients can be life-threatening and often affects the central nervous system. But in an immunocompetent host, the immunity is often able to contain the infection and had a good prognosis (1).

Immunocompetent individuals with latent toxoplasmosis may not be completely asymptomatic, instead of the emergence of neuropsychiatric manifestations and behavioural changes (2,3). For instance, a study by Emelia et al. (2012) demonstrated that schizophrenia individuals had a higher prevalence of anti-*T. gondii* antibodies compared to controls (4).

Herein we report a rare case of probable reactivated toxoplasmosis in an immunocompetent patient, with a known psychiatric illness of schizophrenia.

Case Report

A 40-yr-old, Malaysian male was diagnosed with schizophrenia at the age of 25 years old. During that time, he presented with headache, vomiting, and auditory hallucinations for two years. He received oral risperidone 4 mg once daily together with intramuscular depot injection of fluphenazine 25 mg monthly. Despite the current regime of treatment, he was still experiencing residual mild psychiatric symptoms such as auditory hallucination. However, he is able to tolerate it and does not affect his basic daily functioning. He can sleep at night and his appetite remains good. For the past medical history, he had a short duration of admission history in a psychiatric ward which was about 6 years ago. He had no history of major surgical procedure. However, he had histories involved in minor motor vehicle accidents, which he sustained, minor wound for 6 times in the past 10 years.

He is single and currently stays with his mother. They live in an urban area and came from a middle-income family. He had a basic primary level of education. None of his family had a history of psychiatric illness. He previously worked as a cafe helper but remains unemployed for the past year due to lack of interest. He had no history of travel or petting cats. He is a heavy smoker and casual alcohol drinker. He had a history of using a psychoactive substance such as ecstasy 10 years ago.

Upon physical examination, he was comfortable, calm and able to give full cooperation. His speech was coherent and relevant. His mood was euthymic, while his affect was appropriate to his thought. There was a minimal auditory hallucination in which he could not elaborate further. Otherwise, central nervous system examinations were normal. No lymph nodes were palpable and other systemic examination was unremarkable. He was recruited from the Psychiatric Clinic for research on toxoplasmosis among psychiatric patients in the year 2018.

The study was approved by the Research Ethics Committee, the National University of Malaysia (UKM PPI/111/8/ JEP-2018-281). He fully understood the research and consented for participation.

He denied having any symptoms of toxoplasmosis such as fever, headache, vomiting, seizures, or body weakness. Laboratory investigation of his plasma samples was analyzed for *T. gondii* IgG and IgM antibodies using commercial ELISA kits, PLATELIA™ TOXO (Bio-Rad, France). The result of anti-*Toxoplasma* IgM antibody screening was negative. On the other hand, the measurement for anti-*Toxoplasma* IgG antibody level was positive at a very high titer of 135.9 IU/ml (posi-

tive cut-off value is above 9 IU/ml). Further investigation revealed positive detection of *T. gondii* DNA by nested-polymerase chain reactive (PCR) analysis. Figure 1 shows the result of nested-PCR amplification of *T. gondii* DNA from the patient's blood sample. Genotyping was done and revealed the *T. gondii* DNA of the Type I strain. Based on these findings, the diagnosis of toxoplasmosis reactivation was suggestive. Since the patient is immunocompetent and showed no symptom, the infectious disease team continue current psychiatric follow-up, medications and plan to treat the patient if symptomatic.

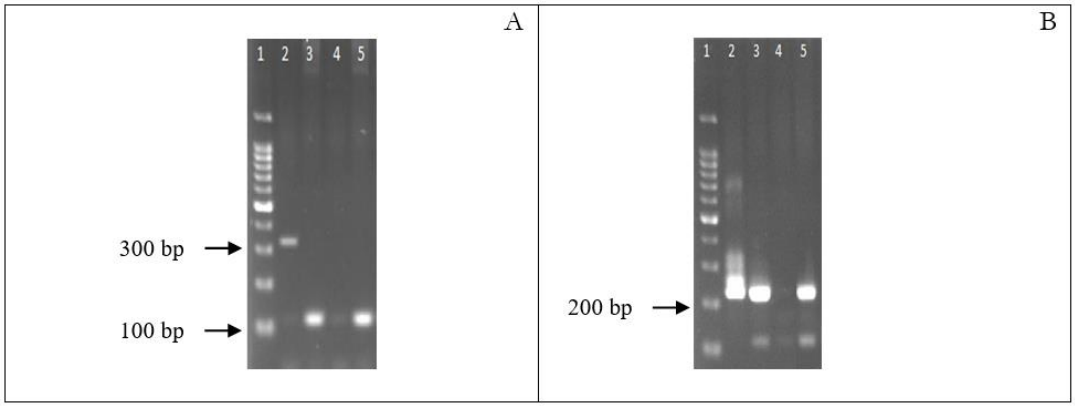

Fig. 1: Nested-PCR amplifications of *T. gondii GRA7* gene.
(A) Nest-1 PCR amplification
(B) Nest-2 PCR amplification.
Lane 1: 100 base pairs (bp) DNA ladder. Lane 2: Positive control 1 (DNA of *T. gondii* RH strain). Lane 3: Positive control 2 (IgG-negative blood sample spiked with DNA of *T. gondii*). Lane 4: Negative control (water). Lane 5: Schizophrenia patient's blood sample. Arrows show the specific bands for nested-PCR amplification

Discussion

The reactivation of latent toxoplasmosis is a result of disruption of the tissue cyst form, followed by differentiation and uncontrolled proliferation to tachyzoites and tissue destruction (5). The bradyzoites in the tissue cyst may become reactivated under immunosuppressed conditions. In the case presented here, the detection of reactivated toxoplasmosis in an immunocompetent adult is considered rare, as most of the reactivated cases are commonly occur among the immunocompromised population.

Commonly, individuals are unaware of their exposure to toxoplasmosis or may have difficulty in recalling the possible risk factors they encountered (5). This patient also was unable to recall any risk factors related to toxoplasmosis. He is from a lower socioeconomic status, claimed did not practice boiling drinking water and always buy meals from nearby stalls of his neighborhood. We postulated that the patient was most probably acquired the infection through ingestion of food or water that has been contaminated with *T. gondii* oocysts. The potential effect of vertical transmission of *Toxoplasma* in this case is also possible.

Symptoms of schizophrenia associated with *T. gondii* generally manifest in late adolescence or early adulthood (6), which supports this case study. He manifested symptoms of schizophrenia during his early adulthood. Interestingly, we noted that this patient had been involved with multiple incidences of motor-vehicle accidents. Gohardehi et al (7) highlighted several studies indicated that infected toxoplasmosis individuals aged less than 45

years old had a significantly higher risk of involving in traffic accidents. This might be the result of decreasing in psychomotor performance in those individuals (8).

Often, the serodiagnosis of reactivated toxoplasmosis in the immunocompromised patient is difficult. For instance, about 3% of *Toxoplasma* IgG antibodies were not detected in HIV/AIDS patients with reactivated toxoplasmosis (9). Even though if *Toxoplasma* IgG is detected in an individual, it does not distinguish whether it is a current or past infection. Some studies even mentioned that significant change in titre may not be associated with the acute episode of reactivated toxoplasmosis (10). Generally, detection of IgM in primary toxoplasmosis indicates acute infection, but in the majority of reactivated toxoplasmosis cases, IgM is not detectable (10).

Therefore, diagnostic strategies for reactivated toxoplasmosis based on a combination of epidemiological, clinical findings and investigation (11). In our case, the patient was immunocompetent and demonstrated consistent results for both anti-*Toxoplasma* IgM and IgG antibodies in the serological screening. The IgM reading was negative, which rule out recent infection. Remarkably, the patient had a very high positive titer of anti-*T. gondii* IgG antibody. The patient also had a positive PCR result for *T. gondii GRA7* of genotype I. This gene had been detected in the *T. gondii*-infected host cells which had been developed and applied in many studies as recombinant proteins for serodiagnosis of toxoplasmosis (12). The *T. gondii* genotype I identified in this patient has been reported to be less pathogenic as compared to genotypes II and III as well as more commonly established in chronic infections (13). The latter genotypes also had higher expression of tyrosine hydroxylase genes and were strongly related to behavioral changes, in comparison with genotype I (14). Thus, both results of high titer of anti-*T. gondii* IgG antibody and the presence of *T. gondii* circulating DNA were strongly suggestive of reactivated toxoplasmosis in this patient.

The reactivation of toxoplasmosis usually occurred because of the immunosuppression phase such as acquired immune deficiencies, undergoing prolonged immunosuppressive treatment, impaired immunity or certain stress condition. However, the exact immunosuppressive status of this patient was unknown. He had no history of taking any immunosuppressive medication, no history of any organ transplant procedure and no history of recurrence infection. Otherwise, the diagnostic test for diagnosing immunosuppressive diseases such as HIV/AIDS or diabetic conditions should be tested. Immunocompetent individuals with severe symptomatic acute toxoplasmosis may experience symptoms such as fever, myalgia, lymphadenopathy or other non-specific clinical signs. Nonetheless, the majority of cases (80-90%) remains asymptomatic, similar to this patient.

Various studies have examined the potential impact of some psychiatric medication with anti-*Toxoplasma* inhibition activity and their potential implication for the treatment of *Toxoplasma*-seropositive patients (15-17). As per this case, the patient received an antipsychotic drug; fluphenazine which has a high inhibitory of anti-*Toxoplasma* activity (18). Nonetheless, the patient still developed reactivation of toxoplasmosis during the management of his psychiatric illness. On the other hand, oral risperidone which is another antipsychotic medication received by the patient had low or intermediate anti-*Toxoplasma* inhibitory activity. Treatment measures during an early stage of detection of reactivation toxoplasmosis such as in this case study remain relatively inconclusive. The immunocompetent patients do not require therapy if asymptomatic but may benefit from treatment if symptoms are severe or persist (5). On the other hand, some patients with psychiatric treatment-resistant disorders reported there were improvements after diagnosing and received treatment of toxoplasmosis (1). Even though this patient was not being diagnosed as treatment-resistant, his psychotic symptoms

remained and probably affecting his social and occupational functioning; as evident by his unemployment and limited social circle. Thus, for future reference, if he develops treatment-resistant, experience worsening of psychiatric symptoms, or develop toxoplasmosis symptoms, it is suggestive clinically to start the course of antiprotozoal treatment.

Together, this case collectively highlights the detection of probable reactivation of *T. gondii* infection in an immunocompetent schizophrenic patient without psychiatric treatment-resistant and remains asymptomatic from toxoplasmosis. Both serology and molecular methods have helped establish the diagnosis. Nonetheless, early detection as in this case may aid the patient management in the future.

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Conflict of interest

The authors have no potential conflicts of interest to disclose.

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