

Cerebral Toxoplasmosis in an HIV Positive Patient: A Case Report and Review of Pathogenesis and Laboratory Diagnosis

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Toxoplasmosis is a worldwide infection. It may have acute or latent clinical presentations. Because of defective cell mediated immunity, patients are at a higher risk of developing toxoplasma encephalitis. We report the first biopsy diagnosed case of cerebral toxoplasmosis in an HIV positive patient from the Kingdom of Bahrain and review the pathogenesis, pathology and laboratory diagnosis.

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Toxoplasmosis is caused by *Toxoplasma gondii*, an obligate intracellular protozoan of worldwide distribution. The prevalence of seropositivity for antibodies against *T. gondii* has been estimated at 3% to 67% and the rate of seroprevalence as high as 90% in Western Europe and tropical countries¹. Transmission to humans occurs primarily by ingestion of undercooked meat that contains tissue cysts or by exposure to Oocysts either through ingestion of contaminated vegetables or direct contact with cat faeces¹. Other modes of transmission are transplacental route, blood product transfusion and organ transplantation.

The development of cell mediated immunity after acute infection with *T. gondii* result in the control of the disease, but not the eradication of the infection¹. The ensuing chronic or latent phase of infection is characterized by the presence of the organism in the tissues of the infected individual (brain, skeletal muscle and heart). A chronically infected individual who develops defect in cell-mediated immunity is at risk of reactivation of the infection and toxoplasma encephalitis^{1,2}.

We report the first biopsy diagnosed case of cerebral toxoplasmosis in an HIV positive patient from Bahrain and review the pathogenesis, pathology and laboratory diagnosis.

Case Report

Forty-four year-old Bahraini male patient presented in July 2003 with history of headache, recurrent attacks of tonic-clonic convulsions and dysarthria of five days duration. On examination, the central nervous system showed reduced muscle tone and an upgoing plantar reflex on the right side. Cranial nerves were normal. There were no signs of meningeal irritation. Other systems did not show any significant findings.

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A CT scan of brain was done, see figure 1, which showed multiple ring enhancing intra-cerebral space occupying lesions in the left parietal, frontal, temporal lobes and in the right thalamic region. The largest lesion measured 2 cm in diameter. He underwent a frontal lobe biopsy, which showed areas of coagulative necrosis bordered by macrophages and lymphocytes, Figure 2.

Characteristic pseudo cysts of *T. gondii* containing many tachyzoites were detected. Some pseudocysts have ruptured with spilling of the tachyzoites into the surrounding tissue.

Investigations showed raised liver enzyme levels. Toxoplasma serology revealed raised IgG antibody levels of 69 IU/ml. It was subsequently discovered that the patient tested positive, in December 2002, for HIV and hepatitis C virus, during a followed-up for malunited wrist fracture. The CD4 cell count was 27/microlitre and was started on antiretroviral therapy, which he opted to discontinue. Based on histological diagnosis of toxoplasmosis, the patient was restarted on antiretroviral drugs and was given Cotrimoxazole and antiepileptic.

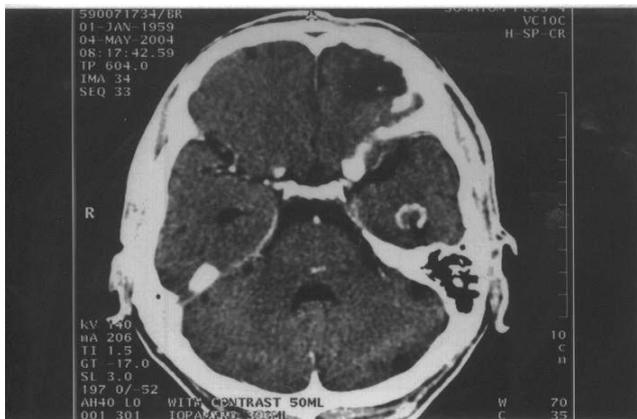


Figure 1: CT Scan Image Showing Ring Enhancing Intra-cerebral Lesion in the Left Parietal Lobe of the Brain

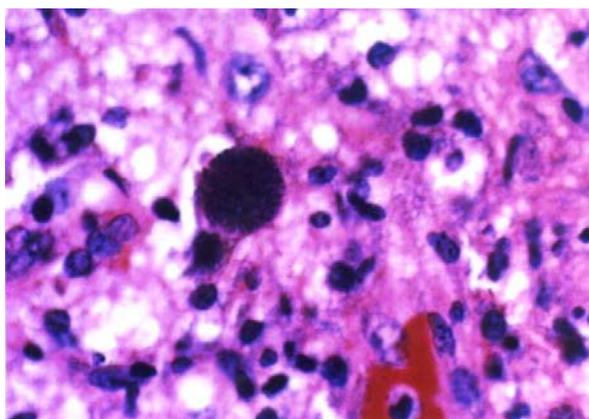


Figure 2: Frontal Lobe Biopsy Showing Areas of Coagulative Necrosis Bordered by Macrophages, Lymphocytes and Characteristic Pseudo cysts of *T. gondii* Containing Many Tachyzoites (H&E stain, x 400)

DISCUSSION

Following oral infection, the tachyzoites of *T. gondii* disseminate throughout the body and infect any nucleated cell, where they multiply resulting in cell destruction and production of necrotic foci surrounded by inflammation. The onset of cell-mediated immunity against *T. gondii* is accompanied by transformation of the parasite into tissue cysts resulting in life long chronic infection. Cellular immunity mediated by T cells, macrophages and activity of type -1 cytokines (interleukin 12 and interferon gamma) is necessary for maintaining quiescence of chronic *T. gondii* infection³.

The mechanism by which HIV induces susceptibility to toxoplasmosis appears to be multifactorial. These include depletion of CD4 T cells, impaired production of IL-2, IL-12, IFN-gamma and impaired cytotoxic T- lymphocytic activity⁴.

Toxoplasma encephalitis usually occurs in HIV- infected patients with CD4 T cell counts less than 100/microlitre² and it is usually caused by reactivation of a chronic infection as observed in our case. Early studies indicated that 24-47% of *T. gondii* seropositive AIDS patients ultimately developed toxoplasma encephalitis^{2,5,6}.

Toxoplasmosis associated with HIV infection primarily manifests as encephalitis and is an important cause of focal brain lesions as in our case². It has a subacute onset with focal neurologic abnormalities frequently accompanied by headache, altered mental status and fever^{7,8}. Toxoplasmosis rarely presents as a rapidly fatal form of diffuse encephalitis.

Diffuse toxoplasma encephalitis should be considered in patients with positive or raised anti-*T.gondii* immunoglobulin G (IgG) antibodies and CD4 T-cell counts of less than 100/microlitre who present with unexplained neurologic disease; these findings were notably present in our case. Extra cerebral sites of involvement in such HIV-infected patients are ocular and pulmonary. The former present with chorioretinitis, vitritis and anterior uveitis while the latter present with fever and sepsis like syndrome with hypotension, disseminated intravascular coagulation, elevated lactic dehydrogenases and pulmonary infiltrates (similar to pneumocystis carinii pneumonia)^{9,10,11}.

T. gondii infection is suspected on serology and confirmed by the demonstration of tachyzoites in tissue biopsies or cytologic preparations of body fluids, isolation of organism from body fluids or blood or amplification of parasitic DNA by Polymerase chain reaction (PCR).

The most commonly used serologic test for the detection of toxoplasmosis is the estimation of anti *T. gondii* IgG and IgM. IgG titres, which characteristically show a peak within 1-2 months following infection and remain elevated for life. On the other hand, the absence of IgM antibodies virtually excludes recent infection in immunocompetent patients. Although the level typically disappears in a few weeks or months, they can remain elevated for more than a year. Thus, the presence of anti *T. gondii* IgM antibodies does not necessarily indicate a recently acquired infection¹. Between 97% to 100% of HIV infected patients with toxoplasma encephalitis have anti-*T.gondii* IgG antibodies^{5,7,12}. Thus, the absence of antibodies against *T. gondii* makes the diagnosis of toxoplasmosis unlikely in these patients. On the other hand, excisional brain biopsy can provide a definitive diagnosis in such cases.

Histopathological findings range from granulomatous reaction with gliosis and microglial nodules to necrotizing encephalitis^{7,13}. In the present case, the presence of tachyzoites and cysts surrounded by inflammation was considered a diagnostic feature.

Immunohistochemistry can be used for the detection of the parasite¹⁴. Wright-Giemsa stain of CSF, bronchoalveolar lavage and touch preparation of tissue biopsy specimens may reveal the parasite. Furthermore, CSF examination may reveal mild pleocytosis of mononuclear predominance and protein elevation¹. Intrathecal production of anti *T. gondii* IgG can be estimated to supports the diagnosis¹.

PCR based detection of *T. gondii* DNA can also be useful in the diagnosis of toxoplasmosis in CSF, bronchoalveolar lavage fluid, amniotic fluid, vitreous and aqueous humour and brain tissue. Blood samples have a low sensitivity for the diagnosis of toxoplasma encephalitis in AIDS patients^{15,16,17,18}.

CONCLUSION

We report the first biopsy diagnosed case of cerebral toxoplasmosis in an HIV positive patient from the Kingdom of Bahrain.

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