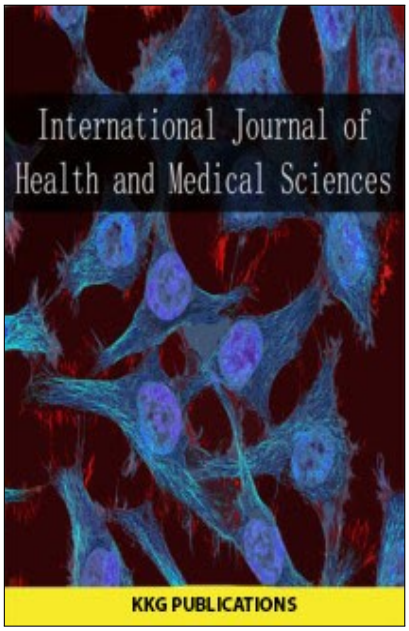

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TOXOPLASMOSIS IN IMMUNOCOMPROMISED PATIENTS: LABORATORY DIAGNOSIS

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Abstract. Toxoplasmosis is an infection largely distributed around the world caused by Toxoplasma gondii. The reactivation of the latent parasite related to profound immunosuppression constitutes a health problem, particularly in HIV patients and other immunocompromised patients. Various clinical features are observed, but the most frequent are neurotoxoplasmosis, pulmonary toxoplasmosis, and ocular toxoplasmosis. The laboratory diagnosis is not based on serology tests because of the limited results in this kind of patient. Serology can help only to predict the reactivation of infection. The confirmation of diagnosis consists of demonstrating the parasite in different samples or the detection of toxoplasma-DNA by polymerase chain reaction PCR.

INTRODUCTION

Toxoplasmosis is a disease with distribution around the world due to the protozoan parasite Toxoplasma gondii (T. gondii), that contaminates almost all warm-blooded vertebrates so imposes an important problem on human and also animal health [1]. The definitive host is represented by cats, and humans represent accidental host. Together with different warmblooded animals, humans tend to be contaminated by means of consumption of food or water infected by cat faeces which contain oocysts or by ingestion of meat including toxoplasma cysts. The protozoan may also be transmitted by means of transplantation of an organ or blood coming from an affected donor [2].

Epidemiology

The toxoplasma is very often present among the population. It is expected that 30% of human world population are holders, however only a minor percentage show some symptoms. Different studies illustrate over 95% prevalence relating to disease in distinct areas of the world [3]. Persons at risk of developing toxoplasmosis have profound immunosuppression such as solid organ or stem cell transplant or advanced HIV disease. On the other hand, cases have also been revealed in patients receving immunosuppressive therapy for inflammatory diseases, such as treatment by using anti-TNF drugs or other biologic immunosuppressive products [4].

Parasite

T. gondii is one of the phyla, Apicomplexa. There exist three infectious forms of that protozoan consisting of oocysts, tachyzoite and bradyzoites. Oocysts are formed only in felines however require sexual reproduction of T. gondii. Once sporulated, it is composed of two sporocysts, each surrounding four sporozoites.

The tachyzoite form is considered the fast replicating one, and results in systemic dissemination and later active tissue infection in intermediate hosts. Such as latent form of the parasite, the bradyzoite is related to chronic infection. That form can remain in cells of various organs for the lifelong of the host within tissue cysts [5].

Pathogenesis

It is proposed that toxoplasmosis in immunocompromised people, generally (95% of cases) comes from reactivation of latent bradyzoites cysts [6]. Cysts reactivation takes place when the person is entered into a major stage of immunosuppression.

The neurotoxoplasmosis could occur in persons who have a T-lymphocytes CD4+ count less than 200 per microliter. The danger of reactivation of cysts raises with decrease in CD4+ levels. The higher risk of developing the disease happens when the CD4 + T-cell count falls to levels below 50 cells per microliter [7].

Having the immunosuppression, a breakdown of tissue cysts formed by protozoa will take place and lead to a release of bradyzoites, that multiply in place and then migrate to some other organs. The injury by infection of Toxoplasma gondii is a result of cell invasion that begins a lysis process and therefore results in cell and tissue destruction [8].

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Clinical Features

In contrast to the setting of toxoplasmosis in immunocompetent people, the infection is constantly life menacing in immunocompromised patients. Concerning transplant patients, severe and disseminated toxoplasmosis may come from both the reactivation of latent infection in the recipient or infection may come from a seropositive donor giving cyst-containing organ to a seronegative recevor [9]. About HIV-infected patients, Toxoplasmic encephalitis (TE) is considered as the prevalent manifestation of the disease in these types of patients and can generate different symptoms, such as headache, incoordination, ataxia to hemiparesis, loss of memory, dementia, or focal to major motor seizures, generally associated with fever [10]. Other organs could be concerned, either because they are target organs for encystment and thus are subsequent potential sites for cyst reactivation or for the reason that they are secondarily infected right after the dissemination of parasites from a primary reactivation site. After the brain, the most commonly involved organs are the lungs.

Pulmonary toxoplasmosis usually results in a febrile interstitial lung disease and may progress to acute respiratory failure. It is associated with disseminated toxoplasmosis in at least half cases, and cerebral toxoplasmosis in a third of cases. Pulmonary radiology reveals bilateral infiltrates, usually thin and diffused, but often irregular and nodular [11]. Less commonly, toxoplasmic retinochoroiditis can take place separately with other signs regarding evolutive infection.

Diagnosis

Serological testing of T. gondii offers limited results in immunosupressed patients. For example, antibody production could be completely abolished concerning patients being subjected to Haematopoietic Stem Cell Transplantation (HSCT) and also serological status is generally uninterpretable in Solid Organ Transplant (SOT) recipients unless it continues to be regular, meticulous monitoring, both before and after transplantation [12], [13]. Concerning HIV infected patients, it was cited that high IgG titers may be predictive of the development of toxoplasmic encephalitis once CD_4 cell counts drop under 200 cells/μl [14]. For this reason, serology is important to estimate if the patient is susceptible to a reactivation of infection, thus the patients who are antibody-positive are at risk for reactivation of infection. The confirmation of evolutive infection is offered by the demonstration of tachyzoites in fluids or tissues via PCR or microscopic examination. The direct examination of Giemsa-stained tissue pieces or smears is the most rapid and lowest priced means of diagnosis [15].

Cerebral Toxoplasmosis

Once the neurotoxoplasmosis is considered in HIV-positive patients, imaging tests such as magnetic resonance and computed tomography, are suggested [16] to demonstrate typical lesion.

If there is doubt concerning neurotoxoplasosis diagnosis, the examination of Cerebrospinal Fluid (CSF) may be performed right after elimination of intracranial hypertension [17]. Neurotoxoplasmosis could be diagnosed by microscopic examination by the CSF technique or Giemsa stain but it is rare for T. gondii to be identified from CSF from immunocompromised patients [18].

The isolation of T. gondii's DNA in body fluids, particularly CSF acquired by lumbar puncture, by means of polymerase chain reaction (PCR) could also be executed to assist in facilitating the diagnosis of neurotoxoplasmosis having sensitivity of 33 to 65% [19]. Last of all, the conclusive diagnosis of neurotoxoplasmosis is provided by the pathological examination of brain tissue biopsy showing tachyzoites or cysts enclosed by areas of inflammation [20].

Pulmonary Toxoplasmosis

PCR detection methods are usually used to detect T. gondii DNA in Bronchoalveolar Lavage Fluids (BALFs) [21]. Direct detection of the parasite in respiratory fluids using conventional staining is regarded to be time-consuming and needs a certain level of experience on the part of the microbiologist, but it is still the most commonly used technique for detection of the parasite in the lungs [22].

Ocular Toxoplasmosis

After ophtalmological diagnosis, laboratory methods consist of parasite detection and analysis of local antibody generation in ocular fluids, with both techniques being complementary. PCR identification of parasite DNA in Aqueous Humor (AH) or vitreous fluid had been claimed with variable success [23].

CONCLUSION

While serology tests do not contribute in toxoplasmosis diagnosis, it is suggested that once toxoplasmosis is suspected, Imaging tests like magnetic resonance and computed tomography should be realized to show typical lesion of infection. The laboratory role consists of confirming diagnosis if there is a doubt by the detection of the parasite using conventionel stains or by the isolation of toxoplasma-DNA by PCR.

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