Diagnosis and Epidemiology of Toxoplasmosis in Korea

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Abstract: Toxoplasma gondii can cause congenital as well as postnatal toxoplasmosis in humans and animals, and thereby elicit various kinds and grades of clinical manifestations. In the human host, especially the congenital type gives rise to serious complications and sequelae such as blindness and hydrocephalus. Serological tests such as Sabin-Feldman dye test, indirect hemagglutination test, indirect fluorescent antibody test, indirect latex agglutination test, agglutination test, enzyme-linked immunosorbent assay, and detection of circulating antigens or antibodies are popularly used for the diagnosis of toxoplasmosis. In Korea, several local surveys during the past 20~30 years have shown that the antibody positive rates of patients in general hospitals ranged from 1.9% to 7.2%. Special clinical attention should be paid to immunocompromised patients, since immunosuppression is known to activate and aggravate latent toxoplasmosis, and in such cases the patients are often led to encephalitis, coma and death.

Key words: Toxoplasma gondii, toxoplasmosis, serological test, epidemiology, immunosuppression

INTRODUCTION

Toxoplasmosis is a typical zoonosis of Toxoplasma gondii which infects mammals and birds with very low specificity. Felidae, both domestic and wild, are pivotal in the epidemiology of toxoplasmosis because they are Toxoplasma's only definitive hosts. Congenital toxoplasmosis can result in meningoencephalitis, which may have serious sequelae such as blindness, hydrocephaly, and mental retardation. Postnatal, ingestion-acquired toxoplasmosis in adults is generally mild or asymptomatic; cysts are formed in the brain, musculature, or elsewhere, but they do not elicit an inflammatory response.

IMMUNOSEROLOGIC DIAGNOSIS

Diagnosis of toxoplasmosis is performed by the isolation of Toxoplasma from patients, or by histopathological and serological tests, but serological tests are widely used to diagnose toxoplasmosis in general. Many serological tests have been developed for the detection of antibodies of Toxoplasma. Of these, the most reliable is the cytoplasm-modifying or “dye” test of Sabin and Feldman (1948). It is a sensitive and so far the most specific test for toxoplasmosis. The indirect fluorescent antibody test (IFAT) overcomes some of the dye tests using killed Toxoplasma as antigen. Each of the other serological tests—namely, indirect hemagglutination test (IHA), indirect latex agglutination test (ILA), agglutination test, and enzyme-linked immunosorbent assay (ELISA), has some advantages. IHA and agglutination tests are easy to perform, but they need further evaluation for specificity for titers. The complement fixation test and ELISA are also useful, but these depend upon the purity of the
antigenic preparation. Recently, some trials have been made to detect immunoglobulin M or *Toxoplasma* antigen itself in the sera of early-phase infections or immune-compromised persons.

1) **Dye test**

In 1948, Sabin and Feldman first described the dye test method, which improved specificity dramatically compared to the neutralization test or complement fixation test. Under the presence of accessory factor and complement-like factor, tachyzoites of *Toxoplasma* were transformed and left unstained by alkaline methylene blue after the reaction with antisera. This method was evaluated as a basic method with specificity and sensitivity. In the case of acute toxoplasmosis, the dye test titers increased rapidly to 1:1,024, 1:4,096, or higher in 1 month and decreased thereafter over several years; to 1:16 after 10 years.

2) **Indirect hemagglutination test**

*Toxoplasma* antibody can be detected at lower concentrations by this method, which relies on the ability of the antibody to cross-link red blood cells by the antigen on their surface. Jacobs and Lunde (1957) developed a method using sheep erythrocytes as a carrier. Lewis and Kessel (1961) used human erythrocytes. Chicken or turkey erythrocytes were also used by other workers. In the case of toxoplasmosis, the IHA antibody appeared later, but higher than the DT antibody, approaching a titer of 1:4,096 to 1:64,000, but the specificity was lower than the DT. Kobayashi *et al.* (1971) compared the agreement of the DT and IHA antibodies to be 95.9% by the Jacobs and Lunde method and 95.4% by the Lewis and Kessel method.

3) **Indirect fluorescent antibody test**

In the conventional IFA test, whole, killed tachyzoites are incubated with serum, and antibody detection is enhanced by adding fluorescent-labeled antispecies IgG and viewing it with a fluorescent microscope. The IFA titers generally correspond with those of the DT of 99.1% according to Kobayashi *et al.* (1971).

It also has some disadvantages: the need for a fluorescent microscope, for species-specific conjugates, and for cross-reaction with rheumatoid factor (RF) and antinuclear antibodies (ANA).

4) **Indirect latex agglutination test**

In this test, soluble antigen is coated on latex particles, and the pattern of agglutination is observed when the serum to be tested is added. It is easy to perform and does not require special training or equipment. Titers in the ILA test compared favorably with the DT, and the test was judged to be useful for screening human sera.

5) **Agglutination test**

Fulton and Turk first described the agglutination test, but it was not used until recently because of low specificity and the need for numerous tachyzoites in each test. Desmonts and Remington (1980) increased the reproducibility and sensitivity of the method by growing large numbers of tachyzoites in mouse sarcoma cells and by treating sera with 2-mercaptoethanol to remove the cross-reacting IgM. This method is popularly used in France.

6) **Enzyme-linked immunosorbent assay (ELISA)**

In the ELISA test, soluble antigen is adsorbed on a plastic surface, and the antigen-antibody reaction is enhanced by the addition of a secondary enzyme-linked antibody-antigen system. The reaction can be assessed objectively by quantitation of the color that develops. ELISA can be automated so that a large number of sera can be examined rapidly. Titers of ELISA compared favorably with the DT, IHA, and ILA of 94.9%, 92.0%, and 93.9%, respectively.

7) **Detection of anti-*Toxoplasma* IgM**

In order to diagnose early infection of *Toxoplasma*, detection of anti-*Toxoplasma* IgM was tried. There were many methods used to detect anti-*Toxoplasma* IgM, for example, IFA–IgM, ELISA–IgM, and ILA–IgM, but these could not be absolutely reliable at this time.

8) **Detection of circulating antigens**
The detection of circulating antigens or local antigens may be useful in the diagnosis of toxoplasmosis in congenital infections and in immunosuppressed patients with reduced humoral responses. Circulating antigens share some properties of both intracellular and secreted components. The ELISA system was used to detect the circulating antigens. Antigens were detected in infected tissues in addition to humoral fluids.

**TOXOPLASMOSIS IN KOREA**

Since Sob *et al.* (1960) first reported 5.6% positive human cases out of 373 subjects by skin test using toxoplasmin, there have been many reports estimating the prevalence of *Toxoplasma* antibodies among humans and animals. Moon (1965) first isolated tachyzoites from a pig. Choi (1969) also isolated tachyzoites from the pig, which were used to estimate the antibodies of pigs, and 32.7% were positive by dye test method. After the introduction of the indirect latex agglutination method, Choi *et al.* (1982) obtained 4.3% positive cases out of 412 patients of St. Mary's Hospital, and Kim and Choi (1983) obtained 7.2% positive cases out of 874 patients of Seoul Red Cross Hospital. Choi *et al.* (1983) screened 573 patients in Seoul Mental Hospital that resulted in a 1.9% positive rate, with an especially high percentage in hypochondriacs of 7.4%. Later, Choi *et al.* (1984) examined 515 swine sera from the outskirts of Seoul, which resulted in a 12.4% positive rate, and Choi *et al.* (1985) screened 377 pregnant women and 43 pelvic tumor patients of Kangnam St. Mary's Hospital, which resulted in 0.5% in the former and 7.0% in the latter. Choi *et al.* (1987) obtained 20 out of 131 (15.3%) cases in mammals, 2 out of 75 (2.7%) cases in birds, and none of 10 cases in reptiles from Seoul Grand Park. Recently, Choi *et al.* (1989) compared groups of different diseases and different localities. Patients of the general group showed higher positive rates of 1.86% (19 cases out of 1,019) than those of asthmatic group of 1.07% (11 cases out of 1,030). Patients who visited Kangnam St. Mary's Hospital (Seoul) expressed fewer cases than those who visited Cheju Medical Center (Cheju Island) of 5.77% (45 cases out of 780).

**IMMUNE-SUPPRESSION AND TOXOPLASMOSIS**

The most dangerous of the complications of toxoplasmosis are found in patients whose immunity has been depressed by malignancies and anti-tumor therapy or by the acquired immune deficiency syndrome (AIDS). Concomitant toxoplasmosis is most likely to lead to a serious result in patients given cytotoxic or immunosuppressive drugs. An example of this is to be found in Hodgkin's disease where treatment may activate latent *Toxoplasma* infections. Encephalitis is the dominant clinical manifestation in immunodepressed patients.

Transplantation of infected organs or transplantation of infected leukocytes can initiate a fatal infection in a seronegative recipient receiving immunosuppressive therapy. Transplantation of noninfected organ or leukocyte transfusion can activate latent infection in a seropositive recipient receiving immunotherapy. Ordinary whole blood transfusion is virtually free from danger but transfusion of packed leukocytes and transplantation of bone marrow has caused toxoplasmosis. It seems that the danger of transplanting an organ from a seropositive donor into a seronegative recipient is greater than that of transplanting an organ from a seronegative donor into a seropositive recipient.

Toxoplasmosis ranks high in the list of diseases which lead to the death of AIDS patients. Navia *et al.* (1986) presented clinical and pathological findings in 27 AIDS patients who developed toxoplasmosis. In nearly all of them it was characterized by encephalitis. Most of the patients had bilateral severe and persistent headaches which often woke them at night and responded poorly to analgesics. This was followed by confusion, lethargy, ataxia, and
finally coma. Seven developed retinal lesions. In the brain, the predominant lesion was necrosis, often resulting in multiple abscesses, some of which were as large as a tennis ball. These abscesses often blended with normal tissue in which numerous tachyzoites and tissue cysts were present.

REFERENCES


