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Seropositivity of *Toxoplasma Gondii* Among Blood Donors and Patients with Hematologic Malignity

Saadet Yıldız[1], Ramazan Esen[2], Kamuran Karaman[3], Yunus Emre Beyhan[1*]

[1]*Department of Medical Parasitology, Van Yuzuncu Yil University Faculty of Medicine, Van, Turkey*
[2]*Department of Internal Medicine, Van Yuzuncu Yil University Faculty of Medicine, Van, Turkey*
[3]*Department of Child Health and Diseases Van Yuzuncu Yil University Faculty of Medicine, Van, Turkey*

ABSTRACT

Toxoplasma gondii (*T. gondii*) is an opportunistic parasite. Transmission from *T. gondii*-infected donors to recipients is possible through blood and organ transplantation. In this study, it was aimed to investigate the presence of *T. gondii* antibodies in healthy donors and in blood recipients with immunosuppressed hematological malignancies. A total of 92 patients included in the present study (46 donors and 46 patients). Sixteen of the hematological patients had lymphoblastic leukemia and 14 had acute myeloblastic leukemia. The presence of IgG and IgM Toxoplasma antibodies and IgG avidity values were investigated by ELISA. Twenty-two (47.8%) of patients and 11 (23.9%) of the donors were found to be positive for *T.gondii* IgG antibodies. IgG positivity was detected in all patient groups except those with aplastic anemia. The highest IgG positivity was found in acute myeloblastic leukemia (8) and lymphoblastic leukemia (5). IgM seropositivity was detected totally three cases (3.3%), two of 46 patients (4.3%) and one 46 of donors (2.2%). Although the number was low, all patients with chronic myeloid leukemia were detected both IgG and IgM positive (100%). Low avidity was found in all three of the IgM positive cases. Considering that toxoplasmosis is an infection that causes severe clinical symptoms and death, routine diagnostic methods that detect the presence of parasites in donor and patient groups will be beneficial for the prevention of *T.gondii* transmission.

Keywords: Blood donors; hematologic malignity; leukemia; Toxoplasma gondii

Introduction

Toxoplasmosis is a zoonotic infection caused by *Toxoplasma gondii* (*T.gondii*), a single-celled obligate intracellular parasite that affects humans and many vertebrates (1,2). The infection affects one third of the world's population, with prevalence rates ranging from 30% to 60% in developing countries, and is predominantly seen in tropical and subtropical regions (3,4). It has been reported that the seroprevalence of infection in humans in Turkey varies between 18% and 100% (5). Toxoplasmosis can be transmitted to humans by oocysts in cat feces, meat containing tissue cysts, and congenitally. In addition, it is possible to be transmitted to recipients by blood and organ transplantation from infected donors (6). After the ingestion of the parasitic oocysts, sporozoites are released in the digestive tract, enter the tissue from the small intestinal epithelium. If the immune system does not respond adequately and in a timely manner, they reproduce rapidly by asexual division.

The infection is generally subclinical in immunocompetent adults, rarely fever, malaise, headache, and cervical lymphadenopathy occurs. Congenital toxoplasmosis may present with stillbirth, hydrocephalus, microcephaly and chorioretinitis, depending on the trimester of infection (7,8). Serious clinical pictures such as encephalitis, myocarditis and pneumonia may occur in immunosuppressed cases. Since the infection can also be transmitted by transfusion from blood donors, it remains a serious concern for immunocompromised blood recipients such as thalassemia, hemophilia, dialysis, organ transplant recipients, and patients with neonatal jaundice (9).

Biological, serological, cultural, histopathological or molecular methods are used in the diagnosis of toxoplasmosis (10). With serological methods, specific antibodies against the parasite can be detected with high sensitivity. Nowadays, IgG and IgM ELISA (Enzyme-linked Immunosorbent Assay) and IgG avidity tests are widely used which also helps in the differentiation of acute and chronic infections (11). The avidity value is the ratio of the serum sample

*Corresponding Author: Yunus Emre Beyhan, Department of Medical Parasitology, Yuzuncu Yil University Faculty of Medicine, 65080, Campus, Van, Turkey
E-mail: yebeyhan@gmail.com, Phone:+90 (506) 995 25 25
ORCID ID: Saadet Yildiz: 0000-0003-1566-2931, **Ramazan Esen:** 0000-0003-1242-2852, **Kamuran Karaman:** 0000-0003-2991-3551, **Yunus Emre Beyhan:** 0000-0002-1696-4803
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between that which is exposed to urea and that which is not. If the antigen-antibody binding is newly formed, a low avidity value occurs. Generally, in high avidity, is thought to have received the infection at least 3-5 months ago. While low avidity is considered an indication of a new infection, it does not always mean a newly acquired infection.

Toxoplasma infection is asymptomatic in most adult humans because of effective protective immunity; this is due to antibody acting extracellularly and T-cell factors acting intracellularly. After the first infection, lifelong immunity develops, IgG positivity continues and re-infection is not observed in individuals with intact immune system. Tissue cysts occur in the human body, the tachyzoites inside invade almost all types of nucleated cells and proliferate. With the rupture of these cysts, tachyzoites reach the central nervous system, eye, skeletal and cardiac muscle via blood and lymph. It can cross the blood-brain and blood-placental barriers and reach the brain and fetus. In chronic infections these tachyzoites transform into bradyzoites. With the rupture of the cyst in immunosuppressed individuals, bradyzoites are released and the immunity is insufficient to destroy them, tachyzoites are formed again and the infection recurs (12).

Transfused patients are at risk for *T. gondii* infection due to both acute infection transmission from donors and re-activation of existing cysts (13). In order to prevent this situation and to adopt appropriate strategies, it is important to know the presence of infection.

The purpose of this study is to investigate T. gondii antibody positivity in healthy donors and blood recipients with hematological malignancies.

Materials and methods

This study was conducted on healthy donors (18-60 years old) admitted to the Medical Center Blood Transfusion Unit and blood recipients (0-80 years old) who were immunocompromised and hospitalized with hematological malignancies and received more than one course of chemotherapy and/or radiotherapy. Sixteen of the hematological patients had lymphoblastic leukemia and 14 had acute myeloblastic leukemia. All malignancy diagnoses are given in Table 1.

A total of 92 patients, including 46 volunteer donors and 46 patients, were included in the study. There were 27 male and 19 female patients in the patient group, and 44 males and two females in the donor group. The study was approved by the non-interventional clinical research ethics committee (2020/03-42). A tube blood sample was obtained from peripheral blood from each blood donor and blood recipient. After centrifugation at 3000 rpm for 10 minutes, serum and buffy-coat were separated. Serum samples were stored at −20 °C until used. In order to investigate IgG and IgM antibody levels in all serum samples, Human TOX-IgG and Human TOX-IgM ELISA kits (Wuhan Fine Biotech Co., Ltd., Wuhan, China) were used in accordance with the manufacturer's recommendations. The results were interpreted by calculating cut-off values according to the criteria of the kit used. In IgM positive cases, Elecsys Toxo IgG avidity test (COBAS E and ELECSYS are trademarks of Roche, Germany) was performed to investigate whether toxoplasmosis was in the acute or chronic phase. According to the kit protocol, it was evaluated as >80% high avidity, 70%-79% cutoff avidity, and <70% low avidity. All blood samples were routinely examined for Hepatitis B virus (HBV), Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), and Treponemapallidum (Syphilis) before being used for transfusion.

The Fisher Exact chi-square test was used to examine the differences between the groups and the results were presented with frequency of occurrence and percentages. SPSS 15.0 Windows package program was used in the statistical analysis of the study and $p \leq 0.05$ was accepted as the statistical significance limit.

Results

In this study, 22 (47.8%) of 46 patients and 11 (23.9%) of 46 donors were found to be positive for *T.gondii* IgG antibodies. A positivity was detected in all patient groups except those with aplastic anemia. IgG positivity was highest in acute myeloblastic leukemia (8 patients) and lymphoblastic leukemia (5 patients). (Table 1).

IgG positivity was found to be 19.5% (9/19) in women and 28.3% (13/27) in men in the patient group (p=0.003). Eight of the nine positive cases (8/9) in female patients were found to be over the age of 40 (p<0.001), while no significant difference was found in age groups in men (p=0.306) (Table 2).

While IgG positivity was not found in women, 25% (11/44) of men were positive in the donor group. Since the number of female patients in the donors was only two, no significant correlation was found between antibody positivity and gender (p=0.659) (Table 3).

Table 1. Patient Groups With Hematological Malignancies and IgG Positivity

Disease	Total	IgG-	IgG+
Acute lymphoblastic leukemia	16	11	5 (31.3%)
Acute myeloblastic leukemia	14	6	8 (57.1%)
Hodgkin's disease	3	2	1 (33.3%)
Non hodgkin lymphoma	3	2	1 (33.3%)
Multiple myeloma	2	1	1 (50%)
Chronic myeloid leukemia	2	0	2 (100%)
Chronic lymphocytic leukemia	2	1	1 (50%)
Adrenal gland malignant neoplasm	1	0	1 (100%)
Aplastic anemia	1	1	- (0%)
Hemophagocytosis lymphohistiocytosis	1	0	1 (100%)
Malignant neoplasm of stomach	1	0	1 (100%)
Total	46	24	22

Table 2. *T.gondii* Seropositivity In Patients With Hematologic Malignity

	Female				Male				Total
	age				Age***				
	<20	20-40	> 40	Total	<20	20-40	> 40	Total	
IgG+	1	0	8**	9 (19.5%)*	5	3	5	13 (28.3%)*	22 (47.8%)
IgG-	3	7	0	10	7	2	5	14	24
Total	4	7	8	19	12	5	10	27	46

* p=0.003, ** p<0.001, ***p=0.306

IgM seropositivity was detected totally three cases (3/92:3.3%), two of 46 patients (4.3%) and one 46 of donors (2.2%). These two positives in patient group both were in chronic myeloid leukemia. 5.3% (1/19) of male patients, 3.7% of female patients (1/27) and 2.3% of male donors (1/44) were found positive. No positivity was found in female donors. Although the number was low, all patients with chronic myeloid leukemia were detected both IgG and IgM positive (100%). The avidity values of these three cases were found to be low at a rate of 64.9%, 64.15% and 56.19%, respectively.

Discussion

Organ transplantation and blood transfusion are potential transmission routes of *T. gondii*. If donors are infected, serious clinical outcomes such as encephalitis, brain abscess, myocarditis, and chorioretinitis may occur, as patients requiring transfusion or transplantation are usually immunosuppressed (14). In addition to acute toxoplasmosis, the prognosis may worsen and may result in death due to the risk of reactivation of cysts in individuals such as organ transplant recipients, HIV-positive people and cancer patients (9). The need for multiple transfusions, especially in patients with hematological malignancies, further increases the risk of infection. For this reason, it is important to control the presence of toxoplasmosis in donors and patients (15).

The overall prevalence of toxoplasmosis was reported as 33% in blood donors worldwide. Infection is more common in some regions due to the development of the health system of the countries and the number of infected intermediate host animals. Brazil (75%) and Ethiopia (73%) were identified as countries with high seroprevalence (16). According to data obtained from different provinces in China, the mean seroprevalence of *T. gondii* IgG was found to be 6.26% in blood donors (17). In a study conducted on 120 cancer patients (60 with hematological malignancies and 60 solid organ tumors) and 60 healthy controls receiving chemotherapy in Egypt, IgG and IgM antibody positivity were found to be 66.7% and 9.2% in the cancer group, and 33% and 6.7% in the control group (18). The prevalence of *T. gondii* was investigated in 400 volunteer blood donors in Iran using serological and molecular methods, and 73.5% IgG and 2.2% IgM positivity were detected (1.75%) (19).

Table 3. *T.gondii* Seropositivity In Donors

	Female				Male				Total
	age				age				
	<20	20-40	> 40	Total	<20	20-40	> 40	Total	
IgG+	0	0	0	0 (0%)*	0	8	3	11 (25%)*	11 (23.9%)
IgG-	0	2	0	2	2	24	7	33	35
Total	0	2	0	2	2	32	10	44	46

* p=0.659

There are few studies on blood donors and cancer patients in Turkey. In a study conducted in 385 blood donors who were considered healthy, the seroprevalence of *T. gondii* IgG and IgM antibodies were found to be 20.25% and 2.33%, respectively (20). In the group of 40 patients with hematological malignancy, IgG seropositivity was 67.5%, while IgM positivity was not detected (21). IgG positivity was found in 60% of cancer patients receiving chemotherapy (lung, breast, stomach, colon, ovarian cancer) and in 27% of the healthy control group. In another study, 60% of cancer patients receiving chemotherapy (lung, breast, stomach, colon, ovarian cancer) and 27% of the healthy control group were found seropositive. IgM positivity was detected in one person (1%) from each group (22). Yazar et al (23). determined IgG and IgM positivity in patients with neoplasia 63% and 6.5%, and 19.4% and 0.9% in the healthy control group, respectively.

In this study, IgG and IgM antibody positivity were found to be 47.8% and 4.3% in patients with hematological malignancies, and 23.9% and 2.2% in the donor group. Although a high rate of IgG positivity was detected in both groups, it is noteworthy that almost half of the patient group was seropositive. The high positivity in patients with hematological malignancies suggests that the infection may have been acquired by previous blood transfusions. The presence of IgG positivity in all malignant patients except those with aplastic anemia is very risky because of the possibility of re-activation of *Toxoplasma* cysts with suppression of the immune system.

It is an important finding that IgM positivity and low avidity values in both patients with chronic myeloid leukemia. This may be an indication that this patient group is susceptible to *Toxoplasma*. Additionally, IgM positivity and low avidity in one of the donors suggest acute infection in this person. In the presence of such an active infection, the transfer of tachyzoites from the donors to the recipient patient by blood transfusion may be possible, and serious clinical consequences may occur in the already immunosuppressed patient.

This study has shown that infection can be transmitted to particularly susceptible groups by blood transfusion. Considering that toxoplasmosis is an infection causes severe clinical symptoms and death, routine diagnostic methods that detect the presence of parasites in donor and patient groups will be beneficial for the prevention of *T.gondii* transmission.

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