

Research Article

Seroprevalence of *Toxoplasma gondii* Infection among HIV-Infected Patients in Tokyo, Japan

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Abstract

The seroprevalence of IgG antibodies against *Toxoplasma gondii* was assessed in 169 adult non-hemophilic Japanese patients infected with human immunodeficiency virus. The seroprevalence of *T. gondii* infection was only 14.2%, which was similar to findings from the USA and lower than that reported for most other countries. The positive ratio of *T. gondii* IgG antibodies was significantly higher in patients aged ≥ 40 years (21.0% vs. 7.9%, $p=0.01$) with < 200 CD4⁺ cells / μ L (20.5% vs. 9.4%, $p=0.04$). Group analysis showed that seropositivity did not differ according to sexuality. The ratios of positivity for hepatitis B surface antigen, hepatitis B surface antibody, hepatitis C antibody, serological findings for syphilis and the findings of the *Treponema pallidum* hemagglutination test were not associated the seroprevalence of IgG antibodies against *T. gondii*.

These results indicate that patients in Japan with lesions of the central nervous system and antibodies against *T. gondii* are highly likely to have toxoplasmosis. Infection with *T. gondii* should be carefully assessed in elderly Japanese patients who are infected with human immunodeficiency virus.

INTRODUCTION

Toxoplasma encephalitis (TE) represents an important opportunistic infection in patients infected with human immunodeficiency virus (HIV). Measuring IgG antibodies to *T. gondii* is crucial, because the risk of developing cerebral toxoplasmosis is high among HIV-seropositive individuals. Therefore, HIV-infected patients with Toxoplasma antibodies must start oral pharmacotherapy as toxoplasmosis prophylaxis. Nissapatorn et al. reported that almost half (44.4%) of patients who are infected with HIV or have acquired immunodeficiency syndrome (AIDS) in Malaysia are seropositive for Toxoplasma [1], and seropositive ratios are also high in other countries except the USA [2-6]. We previously reported a very low seroprevalence (5.4%) in non-symptomatic Japanese patients [7].

However, differences such as age, sexuality or number of

CD4 positive cells among subgroups of patients have not been discussed. Also, relationships between these seroprevalence of Toxoplasma antibodies and seropositivity to HBV, HCV and syphilis remains unclear. Seroprevalence might differ with race, region and era and thus, these issues should also be investigated in Japan. The results of such an investigation would help to determine clinical diagnoses. In present study, we investigated the prevalence of antibodies against Toxoplasma among Japanese patients infected with HIV.

PATIENTS AND METHODS

The Department of General Medicine at Juntendo University provided care to 257 patients with documented HIV infection from 1990 to 2012 in central Tokyo. Test for IgG antibodies to *T. gondii* has been a routine part of the initial assessment of all HIV-infected patients since 1990. Patients who missed the test were

excluded from the statistical analysis. The study group comprised only Japanese patients living in Japan who were infected with non-hemophiliac HIV.

Serological test for IgG anti-Toxoplasma antibodies was employed by using enzyme-linked immunosorbent assays (ELISA) at a commercial testing laboratory (SRL, Tokyo, Japan). Chemiluminescence enzyme immunoassays (CLEIA) were used to test for HIV antibody, hepatitis B surface antigen (HBs Ag), hepatitis B surface antibody (HBs Ab) and hepatitis C virus antibody (HCV Ab), and *Treponema pallidum* was assessed by hemagglutination (TPHA) assays.

Statistical comparisons were done by using the chi-square test. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Toxoplasma IgG antibody results were available from 169 (male, $n = 163$; female; $n = 6$; mean age, 33 y; range, 21 - 75 y) of the 257 patients. Table 1 shows details of the patients. Most of them had acquired HIV through a sexual route, 49.7% being men who have sex with men (MSM) and 19.5% being heterosexual. Only one patient had a history of intravenous drug use. Of the 169 patients, 43.2% had a baseline CD4⁺ lymphocyte count $< 200/\mu\text{L}$ (mean \pm SD, $274.9 \pm 248/\mu\text{L}$).

Twenty four (14.2%) of the 169 patients had serological evidence of *T. gondii* infection. Figure 1 shows that the prevalence was increased by advancing age, especially in those > 40 y. The probability of being seropositive to *T. gondii* was significantly higher for patients whose age was greater than 40 years (21.0% vs. 7.9%: $p=0.01$; Table 2). The numbers of CD4⁺ cells were statistically significant; 20.5% and 9.4% of patients had < 200 and ≥ 200 CD4⁺ cells/ μL , respectively ($p=0.04$). Sexuality did not significantly differ among the groups.

Seroprevalence did not significantly differ among positive ratios of HBs Ag, HBs Ab, HCV Ab, serological outcomes of syphilis (STS) and the TPHA test (Table 3). However, the seroprevalence of *T. gondii* seemed higher in patients with positive STS ($p=0.09$).

DISCUSSION

With the emergence of individuals infected with HIV in Japan, *T. gondii* has become an important opportunistic pathogen, especially in the central nervous system. *T. gondii* can reactivate and cause cerebral toxoplasmosis, usually when the CD4⁺ lymphocyte count falls less than $100/\mu\text{L}$ [8-10]. The incidence of TE in patients infected with HIV depends mainly on the existence of latent anti-Toxoplasma antibodies in the population [11,12].

Table 1: HIV-infected patients who were infected by *Toxoplasma gondii* infection.

Factor	n	
Median age (range; y)	169	33 (21 - 75)
Mean CD4 (\pm SD; cells/ μL)	169	274.9 ± 248
Mean HIV RNA (range; copies/mL)	124	3.4×10^4 ($0 - 3.4 \times 10^5$)

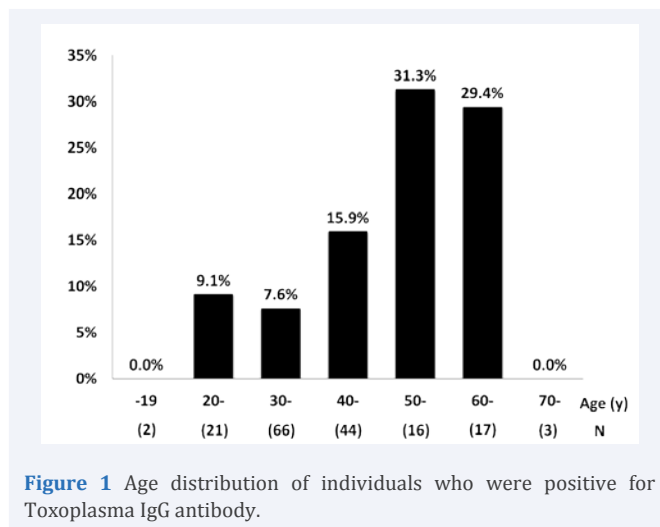


Figure 1 Age distribution of individuals who were positive for Toxoplasma IgG antibody.

Table 2: Seroprevalence of anti-Toxoplasma gondii antibody according to age, sexuality and CD4⁺ cells.

Factor	n	Toxoplasma IgG % (n)		P	Odds ratio
Age (y)	169	< 40 7.9 (7)	≥ 40 21.0 (17)	0.01*	3.16
Sexuality	122	MSM 10.1 (9)	Hetero 18.1 (6)	0.23	0.51
CD4 ⁺ cells ($/\mu\text{L}$)	169	< 200 20.5 (15)	≥ 200 9.4 (9)	0.04*	0.40

Table 3: Association between *Toxoplasma gondii* and other infections.

Factor	n	Toxoplasma IgG % (n)		P	Odds ratio
		Positive	Negative		
HBs Ag	147	5.3 (1)	7.0 (9)	0.84	0.73
HBs Ab	69	142.9 (3)	48.4 (30)	0.90	0.80
HCV Ab	147	5.3 (1)	3.1(4)	0.84	1.72
STS	142	43.8 (7)	123.8 (30)	0.09	2.49
TPHA	131	50.0 (7)	144.4 (52)	0.69	1.25

HBs Ab, hepatitis B surface antibody; HBs Ag, hepatitis B surface antigen; HCV Ab, hepatitis C virus antibody; STS, serological test for syphilis; TPHA, *Treponema pallidum* hemagglutination.

Therefore, to understand the seroprevalence of these antibodies in HIV-infected individuals is very important.

The local prevalence of Toxoplasma antibodies in HIV-infected patients might depend on that in healthy adults. Yamaoka and Konishi showed that the seroprevalence of IgG anti-Toxoplasma antibodies among 2,564 healthy Japanese was 9.3% in 1993 [13]. Our previous study found a similar seroprevalence (7.1%) as compared to that reported [7]. *T. gondii* typically infects humans who have ingested tissue cysts in undercooked meat from an infected animal, or by ingesting infectious oocysts from the environment, usually from soil contaminated with feline feces [14-16]. Lower prevalence might be related to a lower risk in exposure to *T. gondii* infection, reflecting the dietary habits and better sanitary conditions in Japan.

These results might also explain the lower incidence of TE

in Japan. One study found that only 1.07% of Japanese patients infected with HIV had toxoplasmosis [17]. TE is often difficult to distinguish from malignant lymphoma or progressive multifocal leukoencephalopathy in patients infected with HIV. However, the present results suggest that patients in Japan with lesions of the central nervous system and antibodies to *T. gondii* have a high probability of having TE.

It has been indicated that up to one third of the global population is infected with *T. gondii* [18]. As most toxoplasma infections among humans arise due to consuming undercooked or raw meat containing tissue cysts or by exposure to oocysts through ingesting food and water contaminated with cat feces. However, the incidence of toxoplasmosis among patients with AIDS with and without cats does not significantly differ [19]. One study from the USA indicates that persons who have HIV with ages ≥ 50 years were more likely to have antibodies to *T. gondii* [20]. Our data confirmed a similar tendency in a Japanese population.

Our present study found the seroprevalence of anti-Toxoplasma IgG antibody was higher among patients with low CD4⁺ cell counts (Table 2). Mice deficient in CD4 have impaired resistance to tachyzoites and HIV infection increases susceptibility to *T. gondii* infection [21]. The present findings are also compatible with those of a Nigerian study [22].

The relationship between *T. gondii* infection and sexual contact that can result in HBV, HCV or syphilis is unclear. We did not find a statistical relationship between toxoplasmosis and the seroprevalence of HBV, HCV or syphilis.

This retrospective study did not have information regarding basic risk factors such as cat ownership, dietary habits, soil exposure and other important risk factors for disease acquisition. Moreover, the number of serum samples was insufficient due to limited resources, and thus, the statistical power is lower. The present findings should be interpreted in light of these limitations.

CONCLUSIONS

The seroprevalence of anti-Toxoplasma IgG antibody among Japanese persons infected with HIV was determined. Although the rate was relatively lower than those elsewhere, our findings indicated that 14.2% of HIV positive patients in Japan are at risk of developing life-threatening, secondary reactivation of cerebral toxoplasmosis in association with AIDS. The seroprevalence of *T. gondii* significantly varies among subpopulations of patients with HIV, especially age groups. Therefore, individual subgroup analyses are required. Youth should also be educated to minimize risk and prevent new Toxoplasma infections arising.

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REFERENCES

- Nissapatorn V, Lee C, Quek KF, Leong CL, Mahmud R, Abdullah KA. Toxoplasmosis in HIV/AIDS patients: a current situation. *Jpn J Infect Dis.* 2004; 57: 160-165.
- Meisheri YV, Mehta S, Patel U. A prospective study of seroprevalence of Toxoplasmosis in general population, and in HIV/AIDS patients in Bombay, India. *J Postgrad Med.* 1997; 43: 93-97.
- Israelski DM, Chmiel JS, Poggensee L, Phair JP, Remington JS. Prevalence of Toxoplasma infection in a cohort of homosexual men at risk of AIDS and toxoplasmic encephalitis. *J Acquir Immune Defic Syndr.* 1993; 6: 414-418.
- Holliman RE. Serological study of the prevalence of toxoplasmosis in asymptomatic patients infected with human immunodeficiency virus. *Epidemiol Infect.* 1990; 105: 415-418.
- Sýkora J, Zástěra M, Stanková M. Toxoplasmic antibodies in sera of HIV-infected persons. *Folia Parasitol (Praha).* 1992; 39:177-80
- Uneke CJ, Duhlińska DD, Njoku MO, Ngwu BA. Seroprevalence of acquired toxoplasmosis in HIV-infected and apparently healthy individuals in Jos, Nigeria. *Parassitologia.* 2005; 47: 233-236.
- Naito T, Inui A, Kudo N, Matsumoto N, Fukuda H, Isonuma H, Sekigawa I. Seroprevalence of IgG anti-toxoplasma antibodies in asymptomatic patients infected with human immunodeficiency virus in Japan. *Intern Med.* 2007; 46: 1149-1150.
- Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. *Clin Infect Dis.* 1992; 15: 211-222.
- Renold C, Sugar A, Chave JP, Perrin L, Delavelle J, Pizzolato G, Burkhard P. Toxoplasma encephalitis in patients with the acquired immunodeficiency syndrome. *Medicine (Baltimore).* 1992; 71: 224-239.
- Porter SB, Sande MA. Toxoplasmosis of the central nervous system in the acquired immunodeficiency syndrome. *N Engl J Med.* 1992; 327: 1643-1648.
- Grant IH, Gold JW, Rosenblum M, Niedzwiecki D, Armstrong D. *Toxoplasma gondii* serology in HIV-infected patients: the development of central nervous system toxoplasmosis in AIDS. *AIDS.* 1990; 4: 519-521.
- Holliman RE. Serological study of the prevalence of toxoplasmosis in asymptomatic patients infected with human immunodeficiency virus. *Epidemiol Infect.* 1990; 105: 415-418.
- Yamaoka M, Konishi E. Prevalence of antibody to *Toxoplasma gondii* among inhabitants under different geographical and climatic conditions in Hyogo Prefecture, Japan. *Jpn J Med Sci Biol.* 1993; 46: 121-129.
- Dawson D. Food borne protozoan parasites. *Int J Food Microbiol.* 2005; 103: 207-227.
- Weigel RM, Dubey JP, Dyer D, Siegel AM. Risk factors for infection with *Toxoplasma gondii* for residents and workers on swine farms in Illinois. *Am J Trop Med Hyg.* 1999; 60: 793-798.
- Dubey JP. Toxoplasmosis - a waterborne zoonosis. *Vet Parasitol.* 2004; 126: 57-72.
- Kano S, Genka I, Yoshida K, et al. Parasitic disease complicated with HIV/AIDS patients in Japan. *Clinical Parasitology.* 15: 95-98,2004.
- Montoya JG, Liesenfeld O. Toxoplasmosis. *Lancet.* 2004; 363: 1965-1976.
- Wallace MR, Rossetti RJ, Olson PE. Cats and toxoplasmosis risk in HIV-infected adults. *JAMA.* 1993; 269: 76-77.
- Falusi O, French AL, Seaberg EC, Tien PC, Watts DH, Minkoff H, Piessens E. Prevalence and predictors of Toxoplasma seropositivity in women with and at risk for human immunodeficiency virus infection. *Clin Infect Dis.* 2002; 35: 1414-1417.
- Johnson LL, Sayles PC. Deficient humoral responses underlie

susceptibility to *Toxoplasma gondii* in CD4-deficient mice. *Infect Immun.* 2002; 70: 185-191.

22. Osunkalu VO, Akanmu SA, Ofomah NJ, Onyiaorah IV, Adediran AA,

Akinde RO, Onwuezobe IA. Seroprevalence of *Toxoplasma gondii* IgG antibody in HIV-infected patients at the Lagos University Teaching Hospital. *HIV AIDS (Auckl).* 2011; 3: 101-105.

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