Serological Study of *Toxoplasma gondii* in Kidney Recipients

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Abstract

Toxoplasma gondii IgG antibodies were determined in 200 kidney recipients by the Sabin-Felmand dye test. Twenty-two (11%) cases were positive for antibody detection. There was a statistically significant difference in the history of taking under-cooked meat, between the number of sero-positive cases and that of sero-negative subjects (63.6% *vs* 28.8%, p = 0.02). No such significant difference was evident regarding cat ownership (13.6% *vs* 22.0%, p = 0.3).

Sixteen (72.6%) of the 22 subjects with positive *T.gondii* antibody had undergone kidney transplantation less than one year ago during which a high dose of immunosuppressive drugs were prescribed. The remaining six (27.3%) cases had had transplantation more than one year ago and were on a lower dosage of immunosuprresants. Toxoplasma reactivation seemed to be higher in the former group, which should thus be closely followed-up. Preventive chemoprophylaxis should be considered if there is any indication of toxoplasma reactivation.

Since there have been occasional reports of donor-to-host transmission of toxoplasmosis in kidney transplant recipients, serological screening of toxoplasma antibody in kidney donors is advisable. Potential donors with positive toxoplasma antibody should be rejected; but if that is unavoidable, 6-week prophylactic treatment of primary infection in kidney recipients should be administered.

Key word : *Toxoplasma Gondii* Antibody, Kidney Recipients

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In Thailand, toxoplasmosis has become an increasingly important health problem with the advent of the HIV/AIDS pandemic. The prevalence of *Toxoplasma gondii* antibodies in pregnant women with and without HIV infection, in blood donors and in the newborn has been studied[1-3]. Apart from a

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report on HIV/AIDS patients[4], there is, as yet, no data on toxoplasma infection in other immunocompromised conditions in Thai people. We, therefore, studied the sero-prevalence of *T.gondii* antibody and risk factors for disease transmission in kidney recipients.

Transplantation has been increasingly performed for end-stage renal failure since the introduction of the immunosuppressant, cyclosporine [5]. Awareness of toxoplasma reactivation during immunosuppressant treatment would provide better management for those kidney recipients.

MATERIAL AND METHOD

A prospective, cross-sectional study was conducted at the Renal Clinic of Ramathibodi Hospital from April to December 1999. With informed consent, two hundred consecutive kidney recipients (139 males and 61 females) were enrolled. The age-range of those 200 kidney recipients was 18 to 65 years, with 82.5 per cent being between 31 and 60 years old. One hundred and twenty two patients received kidneys from cadavers, whilst the remaining 78 did so from living donors. The following steps were performed:

1. Demographic information about personal data, food-taking habit, cat ownership, drug treatment as well as the duration after organ transplant were recorded.

2. Venous blood samples were taken from the kidney recipients and sera were stored at -4°C until tested. Determination of IgG toxoplasma antibody was carried out using the Sabin-Felmand dye test[6], at the Department of Protozoology, Faculty of Tropical Medicine.

3. The data were analyzed for the prevalence of toxoplasma IgG antibody, and the information concerning cat ownership and food taking habit were compared between the sero-positive and sero-negative groups using Chi-square test to demonstrate the statistically significant difference. Also, some other specific characteristics in patients who had toxoplasma antibody were recorded.

RESULT

Twenty-two (11%) of 200 kidney recipients were positive for *T.gondii* IgG antibody (Table 1). Sixteen (72.6%) of 22 subjects with *T.gondii* antibody had been transplanted within one year during which high doses of cyclosporin and corticosteroid were prescribed. Only 6 (27.3%) cases who had been transplanted for longer than one year and had taken lower doses of immunosuppressants possessed *T. gondii* antibody. Prevalence of *T.gondii* antibody between the two groups was statistically different (Table 1; $p = 0.05$). However, during the study period, acute toxoplasmosis was not observed in any kidney recipient.

There was a statistically significant difference between subjects who were positive and negative for toxoplasma antibody with regard to history of taking undercooked meat (63.6% *vs* 22.8%, $p = 0.02$). No significant difference was found concerning cat ownership, 13.6% *vs* 22.0%, $p = 0.3$ (Table 2).

DISCUSSION

Even though infection is a well-known complication after kidney and other organ transplantation, kidney transplantation has increasingly been employed for the treatment of end stage renal failure worldwide including Thailand. Two patterns of toxoplasmosis observed in the organ transplant recipients are either the primary infection, in which the donor's graft contains the pseudocyst which is transmitted to the seronegative recipient or the reactivation of latent infection in the host. In the West, approximately 40 per cent of prospective recipients

Table 1. Duration of undergoing kidney transplantation and toxoplasma antibody.

Duration of undergoing kidney transplantation	Positive toxoplasma IgG antibody	%	Negative toxoplasma IgG antibody	%
Within 1 year	16	72.7*	86	48.3
More than 1 year	6	27.3*	92	51.7

* p-value = 0.05

Table 2. Risk factors for toxoplasma infection.

Risk factors	Number of cases tested	Number of cases with positive toxoplasma IgG antibody	%	Number of cases with negative toxoplasma IgG antibody	%	p-value
History of taking undercooked meat	53	14	63.60	39	28.8	0.02
Cat ownership	34	3	13.6	31	17.5	0.3

who were scheduled for organ transplantation were seropositive for *T.gondii* and thus harboured cysts containing viable forms of the organism that can be reactivated, particularly during immunosuppression (8). From the present study, only 11 per cent of kidney recipients were positive for *T.gondii*. Thus, the amount of toxoplasma reactivation in Thai recipients should be lower than in the West.

From 1986 to 1996, there were 344 patients who received kidney transplants at Ramathibodi Hospital(7). After transplantation, all patients received life-long corticosteroid together with one or more other immunosuppressant. The dosage of those drugs given soon after transplantation; was high and then gradually tapered after one year. Thus, the immune system was more affected during the first year after transplantation. It was well known that agents which impair T- cell function such as glucocorticoids could reactivate the latent infection both *in vitro* and *in vivo*(9). Some anti-neoplastic and immunosuppressive agents such as glucocorticoids and cyclosporine were able to cause reactivation of the latent toxoplasma infection more often than others such as vinblastine or bleomycin(9). In the present study, among 22 cases of 200 kidney recipients who had *T.gondii* seropositive, it was found that 16 cases (72.7%) had been transplanted within one year whilst the remaining 27.3 per cent (6 out of 22) were longer than one year. Toxoplasma reactivation seemed to be higher in the former than in the latter group. This may explain why recipients who had been transplanted within one year possessed a higher frequency of *T.gondii* antibody. Thus, it is advisable to closely follow-up those patients for such a complication especially in the first few weeks after transplantation. Most transplant centres advocated a low-dose trimethoprim-sulfamethoxazole regimen as prophylaxis against *P.carinii, N.asteroides* and *T.gondii*(8).

With regard to risk factors for toxoplasma infection, statistically significant difference was found with respect to a history of taking undercooked meat compared between the number of subjects with seropositive and seronegative *T.gondii* antibody (63.6 *vs* 28.8, $p = 0.02$). There was no significant difference concerning cat ownership (13.6 *vs* 22.0, $p = 0.3$). However, seronegative kidney recipients could later acquire primary infection through consuming undercooked meat or food or water contaminated with oocyst from cat excreta. It is, thus, advisable that the patients should avoid such exposures.

T.gondii pseudocyst is often found in the muscle; and the donor-to-host transmission has mainly been recorded in heart transplants(10,11). However, there have also been occasional reports in kidney transplant recipients(12,13). Serological screening for *T.gondii* antibody in kidney donors is recommended, positive potential donors should be rejected. If that is unavoidable, 6-week pyrimethamine and sulfadiazine treatment should be instituted in kidney recipients.

Since *T.gondii* antibody screening can only be done in living donors, prophylaxis drug regimen should be prescribed for those who received cadaveric kidneys as soon as the recipients develop symptoms and signs, indicating primary toxoplasma infection.

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แอนติบอดีย์ต่อเชื้อโรคขี้แมว ในผู้ป่วยที่ได้รับการเปลี่ยนไต

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โรคขี้แมว (Toxoplasmosis) เป็นปัญหาสาธารณสุขที่กำลังมีความสำคัญเพิ่มมากขึ้นเรื่อย ๆ ของประเทศโรคหนึ่ง การศึกษาข้อมูลทางระบาดวิทยา ความชุกของแอนติบอดีย์ต่อเชื้อ *Toxoplasma gondii* ในกลุ่มที่มีภูมิคุ้มกันผิดปกติมีเฉพาะในกลุ่มผู้ที่มีเลือดบวก เอ็ช ไอ วี / เอดส์ เท่านั้น ดังนั้นคณะผู้วิจัยจึงได้ศึกษาหาความชุกของแอนติบอดีย์ต่อเชื้อ *T.gondii* โดยวิธี Sabin-Feldman Dye Test และศึกษาหาปัจจัยเสี่ยงของการได้รับเชื้อนี้ในผู้ป่วยที่ได้รับการเปลี่ยนไตจำนวน 200 ราย ผลการศึกษาพบว่าร้อยละ 11 (22/200) ของกลุ่มผู้ได้รับการเปลี่ยนไตมีแอนติบอดีย์ต่อเชื้อ *T.gondii*

ร้อยละ 72.7 (16 ใน 22 คน) ของผู้ป่วยที่มีแอนติบอดีย์ต่อเชื้อ *T.gondii* ได้รับการเปลี่ยนไตภายในระยะเวลา 1 ปี หรือน้อยกว่านั้น ซึ่งเป็นระยะที่ภูมิต้านทานของผู้ป่วยจะต่ำมากเนื่องจากผู้ป่วยทุกคนได้รับยากดภูมิต้านทานขนาดสูง ดังนั้นโอกาสที่จะเกิดโรคขี้แมวรุนแรงขึ้น (toxoplasma reactivation) จึงมีได้สูงกว่ากลุ่มที่เหลือซึ่งได้รับการผ่าตัดเปลี่ยนไตมานานกว่า 1 ปีซึ่งได้รับยากดภูมิต้านทานที่มีขนาดต่ำลงมาก ดังนั้นจึงต้องติดตามและเฝ้าระวังผู้ป่วยดังกล่าวอย่างใกล้ชิด และควรพิจารณาให้ยารักษาทันทีหากมีอาการบ่งชี้ทางคลินิกของโรคขี้แมว

ปัจจัยเสี่ยงเรื่องการรับประทานเนื้อสัตว์ดิบ หรือสุก ๆ ดิบ ๆ มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติในกลุ่มผู้ที่มีแอนติบอดีย์ และไม่มีแอนติบอดีย์ต่อเชื้อ *T.gondii* (63.6% และ 28.8%, p = 0.02) แต่ไม่มีความแตกต่างกันในเรื่องการเลี้ยงแมว (13.6% และ 17.5%, p = 0.3)

คำสำคัญ : ผู้ป่วยที่ได้รับการเปลี่ยนไต, แอนติบอดีย์ต่อเชื้อโรคขี้แมว (Toxoplasmosis)

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