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LETTER TO THE EDITORS

Successful treatment of ocular toxoplasmosis that developed four years after kidney transplantation

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Dear Sirs,

Toxoplasmosis after solid organ transplantation is associated with high morbidity and mortality rates and is usually diagnosed after the first month post-transplantation [1,2]. Approximately one-third of humans worldwide are chronically infected with *Toxoplasma gondii* [3,4]. However, the prevalence of the disease and the sources of infection vary between geographic regions, with differences in toxoplasmic environments, climates, eating habits and hygiene status [5].

Ocular toxoplasmosis is caused by *Toxoplasma gondii* through congenital or acquired routes. Although several studies have reported on patients who developed toxoplasmosis after kidney transplantation, only a few have reported on ocular toxoplasmosis after transplantation. Here, we report a rare case of ocular toxoplasmosis that developed 4 years after kidney transplantation.

A 39-year-old Paraguayan man with chronic renal failure caused by IgA nephropathy had undergone kidney transplantation from a living-related donor in March 2007. The blood type was compatible, and human leucocyte antigen typing had shown a 2/6 locus mismatch. The standard complement-dependent cytotoxicity cross-match test was negative. Induction therapy for immunosuppression comprised tacrolimus (TAC), mycophenolate mofetil (MMF), methylprednisolone (mPSL) and basiliximab. Subsequent maintenance immunosuppression therapy comprised TAC, MMF and mPSL. His serum creatinine (S-Cr) level was 1.8 mg/dl immediately after kidney transplantation, and he did not present proteinuria or microhaematuria. However, in September 2009, his S-Cr level increased to 2.1 mg/dl, and he presented proteinuria of 4.59 g/day and microhaematuria 20–29/high-power field (HPF). Based on a renal biopsy performed in February 2010, we diagnosed recurrent IgA nephropathy and chronic active antibody-mediated rejection. The patient underwent tonsillectomy in April 2010 and had received steroid pulse therapy 3 times, and he was administered i.v. mPSL 500 mg/day for three consecutive days in addition to his maintenance immunosuppressive therapy (TAC 2.5 mg/day, MMF 1000 mg/day, and mPSL 4 mg/day). Subsequently, his S-Cr level, proteinuria and microhaematuria were at 2.3 mg/dl, 2.23 g/day and 0–1/HPF, respectively. In April 2011, the vision on his left eye became blurry. He revisited our hospital in May 2011. The visual acuity of his left eye reduced from a minimum angle of resolution (log MAR) −0.3 to +1.0. Initially, we diagnosed uveitis with iritis and purulent accumulation in the anterior chamber of his left eye and suspected herpes zoster ophthalmia; therefore, we administered valacyclovir 500 mg/day and decreased MMF to 500 mg/day. However, visual acuity of his left eye deteriorated from log MAR +1.0 to +1.7, and his left eye pain exacerbated; therefore, we increased the dose of mPSL from 4 mg/day to 20 mg/day as a treatment for uveitis, increased the administration of valacyclovir to 1000 mg/day, and stopped MMF. Test results showed significantly high levels of serum toxoplasma IgG antibodies (×40960) and toxoplasma antigen (×2048) using a serum latex agglutination method; therefore, in May 2011, we started the administration of clindamycin (CLDM) 2400 mg/day. Furthermore, later in May 2011, polymerase chain reaction (PCR) test results of the anterior chamber aqueous humour were positive for *Toxoplasma gondii* [Fig. 1 (I)]. We confirmed that he had been living in South America where the infection rate of *Toxoplasma* is high, and he had a history of frequent contact with cats, an animal frequently associated with *Toxoplasma* infection. We finally made the definitive diagnosis of ocular toxoplasmosis. On 28 May 2011, in addition to CLDM, we administered pyrimethamine (25 mg/day) and folinate (10 mg/day) 3 times a week. CLDM, pyrimethamine and folinate were administered for 28 days (Day 74 after the development of eye symptoms); treatment concluded in June 2011. His intra-ocular findings improved markedly, and his visual acuity recovered to log MAR +0.52 on 24 June 2011. Further, we tapered PSL gradually from 20 mg/day to 5 mg/day in 4 months. The TAC trough level was adequately maintained at 3.0–5.0 ng/ml during his follow-up. The subsequent clinical course was good, and the visual acuity of his left eye improved to log MAR +0.22 after 5 months [Fig. 1 (II)]. Figure 1 (III) shows the fundus and

anterior segment before and after treatment. His left eye findings improved with the course of treatment.

Oniki proposed the following diagnostic criteria for acquired ocular toxoplasmosis [6]. Unlike that in primary infection, the definitive diagnosis of ocular toxoplasmosis can be difficult in the case of relapse. In two-thirds of patients, *Toxoplasma gondii*-specific antibodies are produced sometime after the first clinical appearance of symptoms. We suspect that our patient may have had *Toxoplasma gondii*-specific antibodies because he owned

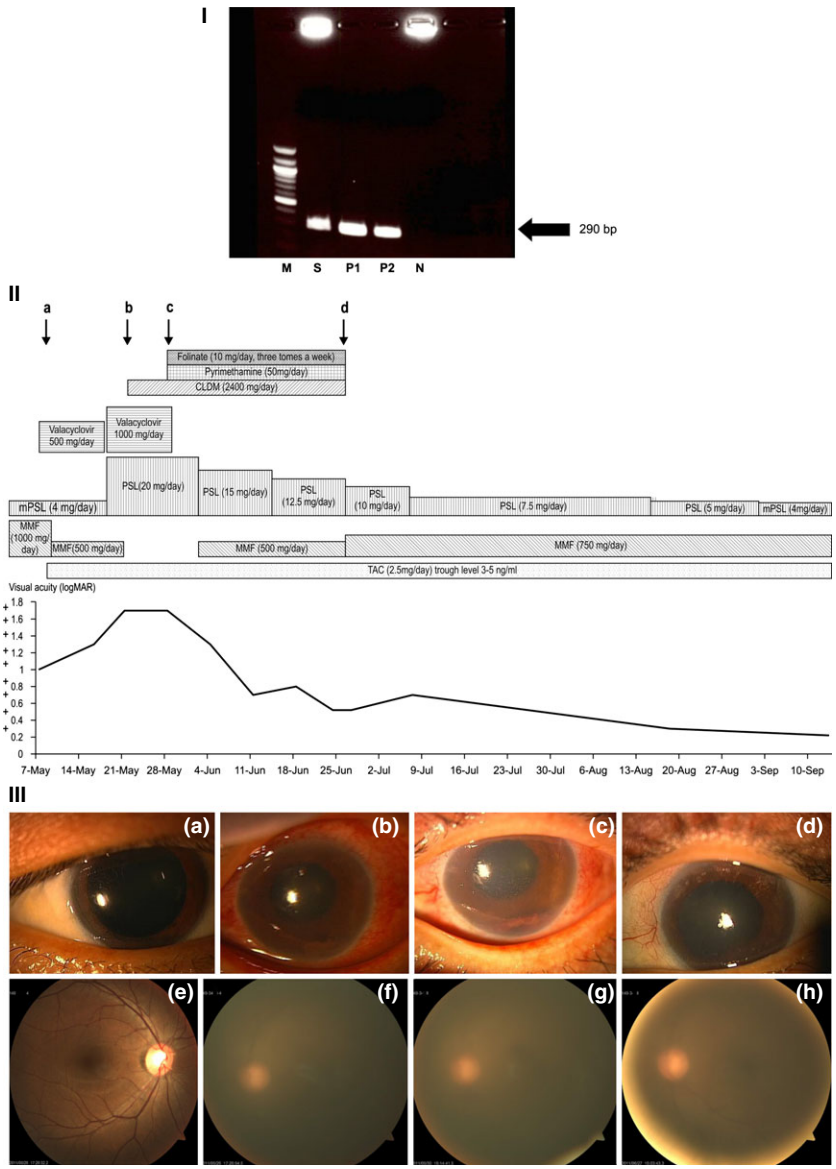

Figure 1 (I) Nested-polymerase chain reaction of the anterior chamber aqueous humour to determine the presence of *Toxoplasma gondii* specimens. The patient's anterior chamber aqueous humour showed 290 bp gene fragments in lane S. M, marker; S, sample; P1, positive control 1/10; P2, positive control 1/100; N, negative control. (II) Clinical course. (a) Diagnosis of uveitis. (b) Examination showed significantly high serum toxoplasma IgG antibodies (×40960), and toxoplasma antigen (×2048) using the serum latex agglutination method. (c) The definitive diagnosis of ocular toxoplasmosis. (d) End of treatment with CLMD, pyrimethamine and folinate after 28 days. CLDM, clindamycin; PSL, prednisolone; mPSL, methylprednisolone; MMF, mycophenolate mofetil; log MAR, minimum angle of resolution. (III) The anterior segment and fundus of the patient's eyes. (a) Anterior segment of his right (not affected) eye. (b) Anterior segment of his left (affected) eye before treatment. (c) Anterior segment of his left (affected) eye on Day 14 after the administration of pyrimethamine. (d) Anterior segment of his left (affected) eye on Day 28 after the administration of pyrimethamine. (e) Fundus of his right eye (not affected). (f) Fundus of his left (affected) eye before treatment. (g) Fundus of his left (affected) eye on Day 14 after the administration of pyrimethamine. (h) Fundus of his left (affected) eye on Day 28 after the administration of pyrimethamine.

many cats during his childhood. In addition, he had no overseas travel history. Risks of reactivation for transplant recipients are closely related to degree and duration of immunosuppression and type of transplantation. The risk for transmission is >50% in heart transplant recipients, <20% in liver, <1% in kidney, intestinal and renal/pancreas transplant recipients [1]. Furthermore, the diagnosis of ocular toxoplasmosis is difficult when patients are in an immunosuppressive state because IgM antibodies for *Toxoplasma gondii* do not appear in the blood. As our patient did not have IgM antibodies for *Toxoplasma gondii* in his blood, we treated him for herpes zoster ophthalmia.

Currently, there are many tests for detecting *Toxoplasma gondii,* including indirect latex agglutination, indirect fluorescent antibody method, dye test and PCR. Among these, PCR for *Toxoplasma gondii* in the anterior chamber aqueous humour is the most useful, with 53% sensitivity and 83% specificity [7]. Several studies in foreign countries have reported on the diagnosis of *Toxoplasma gondii* using PCR. We targeted the '18S rDNA region' that is considered to have the highest number of copies and specificity, and our diagnosis was based on the nested-PCR method [8,9].

Regarding ocular toxoplasmosis treatment, combined therapy with pyrimethamine (100 mg loading dose, then 25–50 mg/day) and sulfadiazine of (2–4 g/day) is recommended in other countries [10]. In Japan, combination therapy with pyrimethamine and CLDM is commonly used to avoid sulfadiazine side effects. Others prefer to use calcium folinate to avoid bone marrow suppression by pyrimethamine. In our case, successful treatment was achieved with CLDM 2400 mg/day, pyrimethamine 25 mg/day and folinate 10 mg/day, 3 times a week for 28 days.

In conclusion, ocular toxoplasmosis should be considered in the differential diagnosis of patients with a history of kidney transplantation who present with ocular problems. PCR testing of the anterior chamber aqueous humour is useful in the definitive diagnosis of ocular toxoplasmosis.

Conflicts of interest

The authors have declared no conflicts of interest.

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