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Case Report

Late presentation of toxoplasmosis in renal transplant recipients

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Abstract

Toxoplasma gondii is a rare cause of infection in renal transplant recipients and usually occurs within 3 months of transplantation, this being the period of maximum immunosuppression. We report two cases of toxoplasmosis presenting several years after transplantation. One patient developed *Toxoplasma* retinitis 4 years after renal transplantation and lost peripheral vision in his affected eye. Another developed cerebral toxoplasmosis 6 years following his second renal transplant but did not survive despite treatment. These cases highlight the need for a high index of suspicion of toxoplasmosis as a potential diagnosis even during the later stages of the post-transplant period as survival is poor without early recognition and treatment.

Keywords: renal transplantation; toxoplasmosis

Background

Toxoplasma gondii is an opportunistic pathogen frequently found in AIDS and heart transplant patients, but it remains a rare cause of infection in renal transplant recipients [1]. It can result from reactivation of latent infection or from primary infection. Acute infection may be transmitted via an allograft from a seropositive donor to a seronegative recipient and tends to occur within 3 months of transplantation, which corresponds to the period of maximum immunosuppression [2,3]. We report two cases of toxoplasmosis occurring several years following renal transplantation.

Case report 1

Case 1 was a 47-year-old male with end-stage renal disease of unknown cause who received a cadaveric renal transplant in 2003. The donor was seronegative for *T. gondii*. Initial immunosuppression consisted of cyclosporin and prednisolone, along with prophylactic cotrimoxazole for 3 months. Shortly afterwards, he had an episode of borderline acute cellular rejection, requiring three doses of methylprednisolone. He had another episode of acute cellular rejection in 2006, requiring a further three doses of methylprednisolone. At this point, he was switched from cyclosporin to tacrolimus. A repeat renal transplant biopsy 1 month later showed ongoing acute cellular rejection, so he received a course of rabbit anti-thymocyte globulin and mycophenolate mofetil (MMF) was added to tacrolimus and prednisolone for immunosuppression.

In 2007, he presented with distorted vision in the right eye and was treated for anterior uveitis. His vision continued to worsen with a decrease in visual acuity in the right eye to 6/18. Dilated fundoscopy revealed significant vitritis with punched-out white retinal lesions in the nasal retina, consistent with *Toxoplasma* retinitis. Treatment with azithromycin was commenced. Two weeks later, visual acuity had decreased to 6/36 in the right eye with unchanged fundoscopic appearances. He underwent a vitreous biopsy. Vitreous PCR was positive for *Toxoplasma* and the patient also had a positive IgM Ab for *T. gondii* with a dye test of 4000 IU/mL. He continued azithromycin along with an increased dose of prednisolone. After 3 months, the *Toxoplasma* retinitis was quiescent and treatment was stopped; however, the patient had lost peripheral vision in his right eye and was unable to distinguish fine details.

Case report 2

Case 2 was a 49-year-old male butcher with focal and segmental glomerulosclerosis (FSGS) who received his second cadaveric renal transplant in 2003. The donor was seropositive for *T. gondii*. Initial immunosuppressive treatment comprised tacrolimus and prednisolone. He received prophylactic cotrimoxazole at a dose of 480 mg three times weekly for 3 months. In 2004, recurrence of FSGS in the allograft was demonstrated on a renal transplant biopsy. At this point, he was commenced on MMF, in addition to tacrolimus and prednisolone. Tacrolimus was stopped in 2008.

He was admitted in 2009 with lethargy and anorexia. On examination, the patient was confused with a right-sided pronator drift and hemiparesis. Blood tests revealed stable allograft function with a serum creatinine of 342 μmol/L with a normal white cell count (7.4×10^9/L) and C-reactive protein of 26 mg/L. An unenhanced cranial CT scan showed areas of low attenuation affecting the white matter of both

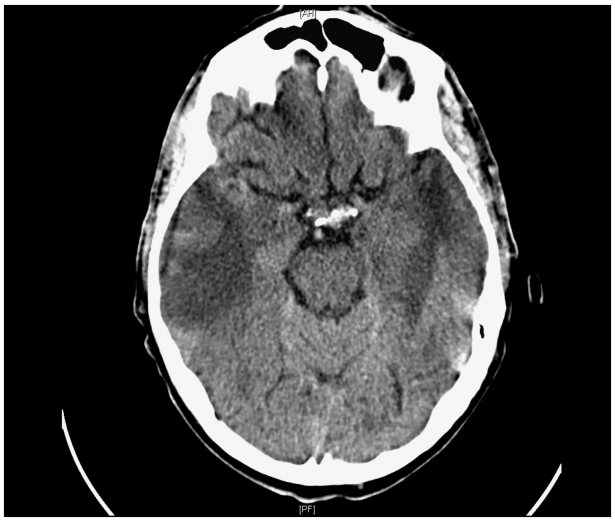

Fig. 1. Unenhanced CT scan of the brain showing areas of low attenuation affecting the white matter of both temporal lobes and the left frontoparietal lobe, with mild mass effect.

temporal lobes and the left frontoparietal lobe, with mild mass effect (Figure 1). MRI with contrast highlighted multiple ring-enhancing lesions, which were thought to be due to metastatic disease or lymphoma (Figure 2). Treatment with dexamethasone was initiated. He continued to deteriorate and had several generalized tonic–clonic seizures. He was started on IV cotrimoxazole to cover potential toxoplasmosis. Results showed a strongly positive dye test at 1000 IU/mL for *T. gondii* along with a positive IgM Ab. As these were suggestive of active toxoplasmosis, treatment with pyrimethamine (200 mg stat followed by 50 mg daily), sulphadiazine (500 mg qds) and folinic acid (10–25 mg daily) was commenced. He developed aspiration pneumonia and died. Post-mortem examination of the body was not performed according to the wishes of the family.

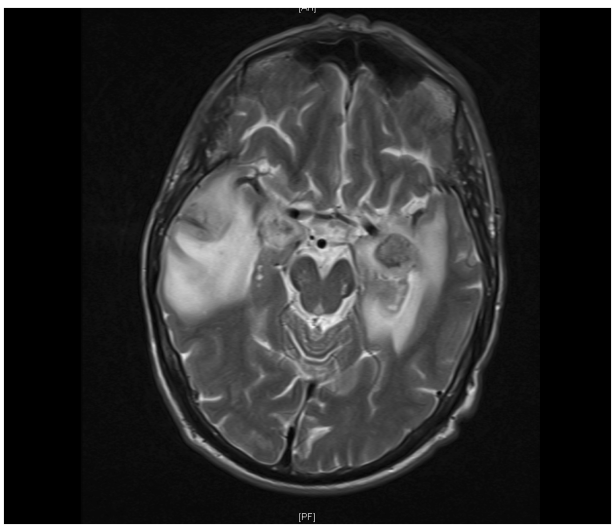

Fig. 2. MRI of the brain with contrast highlighting multiple ring-enhancing lesions.

Discussion

T. gondii is an intracellular protozoan parasite, with members of the cat family being the definitive hosts. Transmission to humans is usually by ingestion of undercooked meat containing tissue cysts or ingestion of infectious oocysts via food or water contaminated with feline faeces. In transplant patients, transmission of *T. gondii* from a seropositive donor to a seronegative recipient is an important potential cause of disease [2]. Therefore, toxoplasmosis in transplant patients can arise from reactivation of latent infection or from primary infection. Wulf *et al*. [4] reviewed 35 cases of toxoplasmosis following renal transplantation, and of these, 7 (20%) occurred in seropositive recipients and 16 (46%) in seronegative recipients; in 12 cases (34%), the serology was not known. Of the 16 cases resulting from a primary infection, 15 had a seropositive donor and were considered to be transplant-related [4]. In the two cases presented here, the first patient may have developed primary infection after eating undercooked meat whilst on holiday in Tenerife shortly before developing symptoms. The second case was most likely due to reactivation of latent infection as he had previously worked as a butcher and would almost certainly have handled raw meat containing tissue cysts.

Toxoplasmosis tends to occur within 3 months of transplantation, this being the period of maximum immunosuppression. In a review of 29 renal transplant recipients with toxoplasmosis [3], 25 of 29 patients developed the infection within 3 months of transplantation. In two cases, infection occurred after more than 1 year, and in another case, more than 2 years had elapsed. The two cases that we present are unusual in that there is a much greater duration between renal transplantation and infection, 4 and 6 years post-transplantation, respectively.

Toxoplasmosis following renal transplantation is associated with mortality in up to 65% of recipients [3,4]. This is most likely due to both a lack of clinical awareness and difficulties in confirming the diagnosis. The symptoms are often non-specific, but patients usually present with neurological disturbances or pneumonitis. Constitutional symptoms and signs, such as fever and malaise, are variable. More rarely, patients may also develop chorioretinitis, myocarditis, haemolytic anaemia and haemophagocytic-related pancytopaenia [2,5]. Concomitant infection with another pathogen is common and can add to diagnostic confusion [1]. Diagnostic tests include serology, isolation of the parasite from infected tissues or nucleic acid amplification by PCR. However, antibody titres can be hard to interpret in immunocompromised patients and correct interpretation of PCR tests is difficult, with varying sensitivity and specificity results reported from different laboratories using the same probes [6]. Therefore, the diagnosis of toxoplasmosis requires a high index of suspicion as prompt recognition and early treatment are key to increasing patient survival [1].

In summary, *T. gondii* remains a rare but significant pathogen in renal transplant recipients. Although most cases of toxoplasmosis occur shortly after transplantation, the two cases reported here were unusual in that they occurred at least 4 years later. This highlights the need for

increased awareness and early diagnosis at all stages of the post-transplant period to improve an otherwise poor outcome of toxoplasmosis in renal transplant patients.

Conflict of interest statement. None declared.

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