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Fatal disseminated toxoplasmosis after liver transplantation: improved and early diagnosis by PCR

KEYWORDS

Liver transplantation, real-time PCR, toxoplasmosis

Disseminated toxoplasmosis after liver transplantation is a rare, but often fatal, event.[1] The high mortality rate is generally due to a delay in diagnosis and initiation of therapy.[2] The classical diagnosis of toxoplasmosis based on serological tests can be unreliable in transplant patients. Therefore, the diagnosis is usually based on the direct demonstration of the parasite in tissues or biological fluids.[2,3] However, these techniques are time-consuming and lack sensitivity. We report a case of disseminated toxoplasmosis after liver transplantation, evaluating the use of quantitative polymerase chain reaction (PCR) as an early diagnostic tool.

A 36-year-old Dutch male underwent an orthotopic liver transplantation on 29 October 2002. The immunosuppressive regimen included mycophenolate mofetil, prednisone and cyclosporine. At 21 days post-transplantation the patient presented with fever. Cytomegalovirus infection was diagnosed and treated with ganciclovir. Despite this therapy, the fever persisted, with ascitis and splenomegaly. Antibiotics were started because of suspicion of peritonitis, although cultures remained negative. In the following days pancytopenia and renal insufficiency developed. At day 44, the patient developed acute respiratory failure. A bronchoalveolar lavage (BAL) was performed and a few hours later the patient died due to cardiac arrest. Microscopic examination of the BAL fluid revealed several *Toxoplasma* tachyzoites. *Toxoplasma* serology remained negative. A real-time PCR with *T. gondii* specific primers and detection probe which amplify and detect a 100-bp fragment within the *T. gondii* B1 gene[4] was performed on DNA isolated from plasma and other clinical samples. For quantification, a tenfold dilution series of *T. gondii* DNA from a known number of parasites was included in the amplification run. Simultaneous isolation, amplification and detection of a standard amount of phocid herpes virus was used as an internal control of inhibition.[5] *Toxoplasma* DNA was detected in the BAL fluid and in lung, pleura, liver and spleen samples obtained after obduction. Plasma samples showed increasing levels of *Toxoplasma* DNA, first detectable on day 37 after transplantation (*figure 1*). In retrospect, the donor had serological evidence of a prior *Toxoplasma* infection, suggesting *Toxoplasma* transmission via an infected allograft. In conclusion, real-time PCR on plasma proved to be a simple, rapid, and highly sensitive method to diagnose disseminated toxoplasmosis. Since early initiation of specific anti-*Toxoplasma* therapy is a critical prognosis factor, highly sensitive PCR methods that can be applied directly to plasma samples could be of great help in cases of unexplained fever in immunocompromised recipients.

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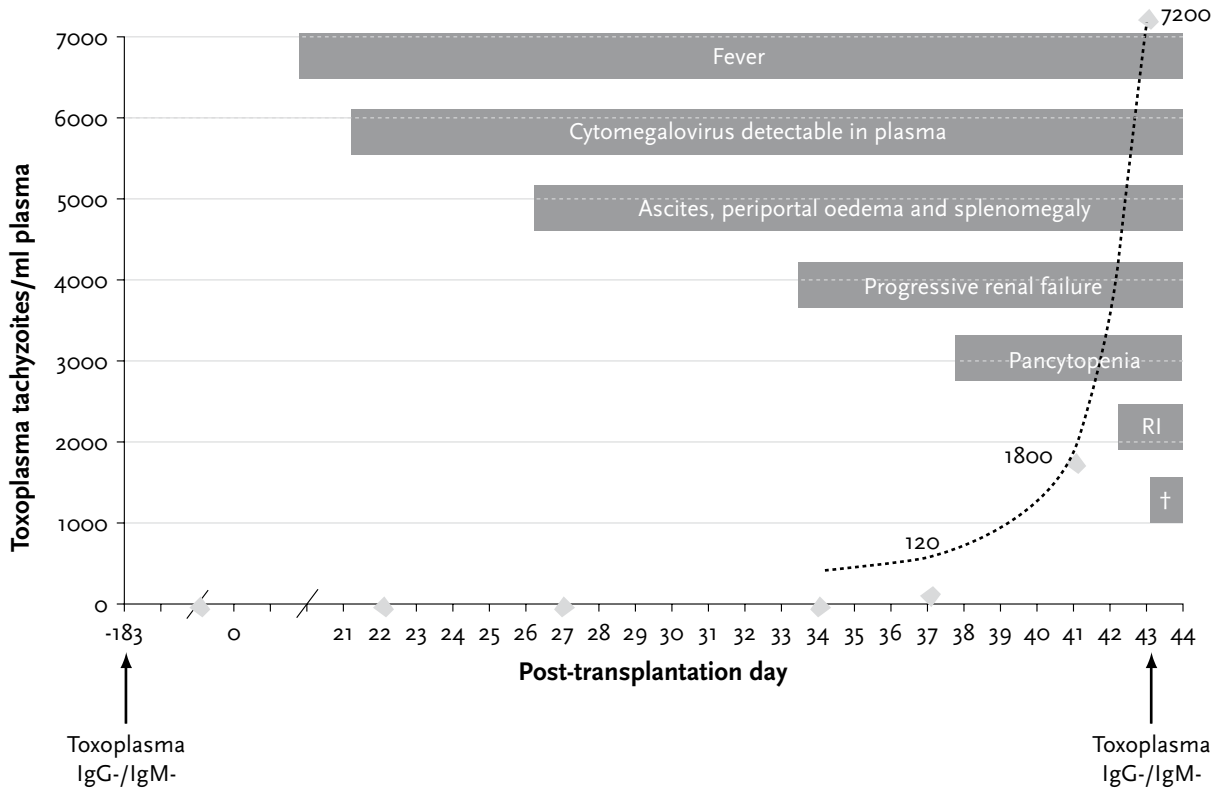
Figure 1. *Serology and quantitative Toxoplasma gondii real-time PCR test analysis of sequential plasma samples from a patient with disseminated toxoplasmosis after orthotopic liver transplantation*



RI = respiratory insufficiency. †Death.

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