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Case Report

Molecular diagnosis of toxoplasmosis at the onset of symptomatic primary infection: A straightforward alternative to serological examinations

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\textbf{A B S T R A C T}

Myopericarditis is a rare but well-documented clinical presentation of primary \textit{Toxoplasma gondii} infection in immunocompetent patients. Here, early detection of \textit{Toxoplasma} DNA in the peripheral blood by PCR allowed the diagnosis of acute toxoplasmosis while serological tests were negative. Additional serological evaluations 2 weeks later confirmed the diagnosis and showed that cardiac manifestations occurred before seroconversion. This highlights the importance of a second serological control in the case of a suspected active infection. Overall, we show here that PCR testing for \textit{Toxoplasma} is a sensitive and straightforward alternative to serological examinations.

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\textbf{Introduction}

\textit{Toxoplasma gondii} is the causative agent of toxoplasmosis and one of the most prevalent zoonotic agents. It infects approximately one-third of the human population globally (Montoya and Liesenfeld, 2004). This parasite spans distinct biological barriers during acute infection and eventually persists as tissue cysts to escape the host immune system. Humans are generally infected through the consumption of undercooked meat or vegetables and water contaminated by cat faeces.

Uncontrolled parasite replication during primary infection in the foetus and reactivation of tissue cysts in the immunocompromised host can lead to life-threatening involvement of one or more organs. Myocarditis is a well-known complication of toxoplasmosis, most often associated with HIV infection (Kirchhoff et al., 2004). Cardiac clinical manifestations result from active parasite invasion of the pericardium and myocardium, producing local inflammatory responses and potential subsequent cardiomyopathies (Nunes et al., 2017).

This article reports the diagnosis of \textit{Toxoplasma} myopericarditis, occurring before seroconversion for \textit{T. gondii}, by detection of parasite DNA in the peripheral blood of a patient with no laboratory or clinical evidence of immunosuppression. The diagnosis of acute toxoplasmosis in immunocompetent subjects is discussed.

\textbf{Case report}

A 23-year-old man was admitted to the Emergency Room of the Academic Hospital of Montpellier on March 13, 2018. He complained of intense chest pain not relieved by paracetamol, which had started 2 days ago. At the time of admission, a physical examination was normal and the patient appeared febrile, with normal blood pressure and a rhythmic heart beat of 87 bpm. The pain was typical of pericarditis: it was retrosternal, constrictive,
increased with deep inspiration, and was relieved by anteflexion
and after treatment with acetylsalicylic acid 1 g. There was no
evidence of pericardial friction, which is usually fickle, fleeting,
and does not eliminate the diagnosis if absent. An electrocardiogram
and echocardiogram showed no particular abnormality. Troponin,
a marker of myocardial necrosis, was elevated at 31.3 ng/l
(reference value <14 ng/l) as was C-reactive protein (CRP) at
76.1 ng/l (reference value <5 mg/l), suggesting an infectious
myopericarditis in the absence of an alternative aetiology.

The patient was transferred to the cardiology intensive care unit
the day after admission. Serological and molecular testing was
negative for herpes simplex virus 1 and 2, hepatitis B and C virus,
HIV, and human herpes virus 6 and 8, and consistent with past
exposure to rubella virus, cytomegalovirus, parvovirus B19, and
Epstein–Barr virus. The results of immunological analyses were
normal (lymphocytes, plasma immunoelctrophoresis, autoantibodies).

Three days after the appearance of the symptoms, serological
tests for toxoplasmosis were negative; however, PCR to detect T.
gondii DNA in the peripheral blood was positive (Table 1). Recent
primary infection by the parasite was therefore considered the
aetiological factor of the myopericarditis. The patient did not
present any symptoms of cervical lymphadenopathy or myalgia,
which may occur during the initial stages of T. gondii infection
(Montoya and Liesenfeld, 2004). However, he complained of
intermittent abdominal pain a few days before his admission to the
emergency room.

During his hospitalization, the patient’s clinical condition
improved and levels of troponin and CRP normalized 3 days after
the appearance of the cardiac symptoms. Treatment based on
acetylsalicylic acid 1 g three times a day for 1 month, lansoprazole
15 mg once a day for 1 month, colchicine 1 mg once a day for 3
months, and bisoprolol 1.25 mg once a day for 3 months was
prescribed. The patient did not receive any drugs for toxoplasmosis
and was discharged 4 days after admission with an appointment
for cardiac magnetic resonance imaging. This revealed probable
lateral myocarditis. To confirm the diagnosis of toxoplasmosis,
biochemical follow-up was requested. Two weeks after the paracic-
ditis episode with elevation of troponin levels, PCR no longer
detected T. gondii DNA in the peripheral blood (Table 1), suggesting
that the circulation of parasites had been very transient. However,
IgG and IgM were found positive, with a consistent low antigen
affinity of IgG at 0.14 index (high >0.6), confirming a recent
Toxoplasma seroconversion (Table 1).

Discussion

Toxoplasma primary infection is asymptomatic and harmless
for the vast majority of healthy individuals, causing mononucleosis-
like symptoms with cervical lymphadenopathy in 10% of subjects
(Montoya and Liesenfeld, 2004). Primary infections with atypical
strains from South America can be associated with severe clinical
involvement in the immunocompetent host (Sobanski et al., 2013).
In the case presented here, the patient’s history revealed that he
had eaten raw horse meat at a restaurant less than 2 weeks before
the appearance of his cardiac symptoms, while no other risk factor
was found. The meal served at the restaurant during this period
of time had come from Europe and was, therefore, unlikely
contaminated by atypical strains. Despite the attempt to genotype
the Toxoplasma DNA isolated from the patient’s blood, it was not
possible to confirm this assumption due to the low parasite load.

Toxoplasma pericarditis and myocarditis have already been
documented in immunocompetent patients (Bousquet et al., 2016;
Chandrier et al., 2000; Montoya et al., 1997; Mroczek-Czernecka
et al., 2006; Paspalaki et al., 2001; Pergola et al., 2010; Roubille
et al., 2012; Sano et al., 2000), although the number of cases is low.
In these previous cases, serological testing was generally used to
link the cardiac complications to toxoplasmosis. Indeed, guidelines
for the diagnosis of acute toxoplasmosis in immunocompetent
patients state the requirement for two serological tests separated
by 3 weeks. However, as illustrated here, a number of symptomatic
primary infections may be undiagnosed at the first serological
examination, due to the delayed synthesis of specific antibodies.

This case highlights the importance of performing blood PCR
analysis, which is likely to be the first positive biological test, soon
after the appearance of the cardiac symptoms. Indeed, serological
conversion for toxoplasmosis was evidenced after the patient’s
recovery from his cardiac disorders (i.e., relief of chest pain and
normalization of troponin levels). Therefore, in the absence of
molecular diagnosis and the second serological control, the
patient’s transient disorders would not have been associated with
active toxoplasmosis. The identification of Toxoplasma as the
aetiological factor of myopericarditis is, however, necessary in
order to exclude other probably more severe diagnoses.

In conclusion, when symptomatic Toxoplasma primary infection
is suspected, physicians should consider blood PCR as a sensitive
and straightforward approach for diagnosis.

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Ethical approval

We read and complied with the policy of the journal on ethical consent. The study was conducted in accordance with the regulations of the local medical ethics committee of the Hospital University Centre (CHU) of Montpellier, France, in line with the revised Declaration of Helsinki.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Study design: MFL and YS; data collection: MFL, DC, CG, SA, AI, PF, YS; data analysis: MFL, DC, PF, YS; writing: MFL, DC, CR, LI, PF, YS.

References