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Case report

Rare cardiac complication of toxoplasmosis in immunocompetent host

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ABSTRACT

Myocarditis is a rare complication of toxoplasmosis, especially in immunocompetent individuals. We present a case of a 28-year-old man with a history of fever and chest pain suggestive of myocarditis. Fever, along with lymphadenopathy, electrocardiography, imaging, and serologic testing, showed *Toxoplasma gondii* as the probable etiology. An excellent response to treatment confirmed the diagnosis.

Introduction

Toxoplasma gondii is an intracellular protozoan, which is able to infect a wide variety of vertebrates. Feline is the primary host, where *T gondii* completes its life cycle. This parasite infects the feline's intestinal cell, which then excreted at the infectious oocysts stage. Once oocysts are ingested by humans, they will infect the intestinal epithelia and spread throughout the body. Another means of Toxoplasma infection in humans is vertical transmission from an infected mother to her fetus [1, 2].

Toxoplasma infection is commonly found in immunocompromised patients, especially those with low absolute CD4 count (<100) [3]. On the contrary, most immunocompetent hosts frequently come up with asymptomatic cases of toxoplasmosis [4]. Myocarditis caused by *T gondii* is rarely reported in immunocompetent hosts, which made the diagnosis of cardiac toxoplasmosis challenging [5]. Here, we present a case of a 28-year-old man with the diagnosis of myocarditis due to *Toxoplasma gondii* infection.

Case presentation

A 28-year-old male came to our outpatient clinic with a history of fluctuating fever for about eight weeks prior to visitation. The most frequent temperature was 38° C and controllable by acetaminophen. One week after fever occurred, the patient complained of chest pain, with a sharp characteristic, aggravated by inspiration, relieved with rest, and the pain was not localized. Accompanying symptoms such as shortness of breath, anorexia, and sweating were not found. The patient has no history of promiscuity and intravenous drug abuse. No other risk factor was found remarkable.

After a week of fluctuating fever and chest pain, the patient sought medical aid. The physical examination showed lymphadenopathy in neck region. Several laboratory and imaging workups were performed. The laboratory workup showed lymphopenia, elevated liver function test (AST 114 U/l, ALT 112 U/l), elevated high sensitivity troponin T (571 ng/ml), elevated CK-MB (41 IU/l), hypercholesterolemia (Total Cholesterol 194 mg/dl), hyponatremia (104 mEq/l). The patient underwent cardiac MRI, and cardiac MRI showed a normal LV volume with normal systolic function, global normokinetic, but there was a myocardial necrosis in several segments. The patient was then referred to a cardiovascular center and was admitted for about six days.

The vital sign on the first-day admission was slight tachycardia (104 bpm), the general examination was unremarkable. The patient underwent several laboratory and imaging workups upon admission. Chest radiograph was within normal limit, electrocardiography (ECG) showed small q wave in II, III, aVF, and V4-V6 and t wave flattening in II, III, aVF. The laboratory result showed that hematologic study and CRP level was within normal limit. There were elevated liver function test (AST 114 U/l, ALT 112 U/l), elevated LDH (518 U/l), elevated high sensitivity troponin T (571 ng/ml), elevated NT pro BNP (88 pg/ml). Evaluation of

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common infectious causes such as dengue, typhoid fever, and malaria came out negative. The patient was diagnosed with acute myocarditis and received methylprednisolone 72 mg/day, lansoprazole 30 mg b.i.d., bisoprolol 10 mg per day, ramipril 10 mg per day. On the third day of admission, the chest pain was improved, and electrocardiography was performed and showed no significant anatomical and functional abnormality. Chest X-ray showed no sign of cardiomegaly. Cardiac MRI showed Late Gadolinium Enhancement (LGE) areas consistent with myocardial necrosis, depicting transmural and subepicardial involvement at the basal anteroseptal segment, as well as midwall, subepicardial involvement at the mid anterolateral, and inferior segment. (Fig. 1). Laboratory workup was reperformed on the sixth-day admission and was within normal limit. The patient was then discharged with a tapering dose of methylprednisolone, lansoprazole, bisoprolol, and ramipril, and with several education materials such as bed rest and activity limitation for six weeks, echocardiography, and MRI reevaluation in 3 months.

One week after discharge, fluctuating fever and chest pain were reappeared and worsened within one month, which made the patient visited our clinic to undergo a thorough examination. The physical examination showed no significant finding. Several laboratory workups were then performed. Hematologic study was within normal limit. Due to the clinical manifestation of previous lymphadenopathy and myocarditis, we performed anti-Toxoplasma immunoserology and found reactive IgM anti-Toxoplasma (30.9 IU/ml) and IgG anti Toxoplasma (2.99 IU/ml) with low avidity (21,0 %Avi). The patient then diagnosed with toxoplasma myocarditis and was treated with pyrimethamine and clindamycin for eight weeks. The patient was encouraged to visit our clinic every two weeks. The symptom then improved after about one-month medication.

Discussion

Toxoplasma gondii is an obligate intracellular parasite infecting approximately one-third of the human population. It exists in nature as three form, oocysts, bradyzoites, and replicating tachyzoites. When humans consumed food or water contaminated with oocyst or meat containing tissue cyst, bradyzoites from tissue cyst or sporozoites from oocyst are released in intestine and invade surrounding cell, and becoming tachyzoites. Tachyzoites were the hallmark form of active disease, which can disseminate through blood and lymphatic vessels causing necrosis lesion and acute inflammatory reaction. The humoral immune response is capable of killing extracellular tachyzoites, but some of them formed tissue cysts in muscle, myocardium, central nervous system, et al., which causing a latent infection [6].

Study about the prevalence of *Toxoplasma gondii* mainly focuses on special populations such as pregnant women or HIV patients [3,7]. The data of seroprevalence of *Toxoplasma gondii* in general population is limited but is predicted around 20–62 % [8,9].

The most common clinical sign of toxoplasmosis in immunocompetent hosts is cervical lymphadenopathy accompanied by constitutional symptoms, such as fever, chills, and sweats [4,10]. Although rare, complications such as pneumonitis, myocarditis, pericarditis, polymyositis, hepatitis, and encephalitis have been reported in immunocompetent individuals [11].

Because toxoplasmosis might come with atypical presentation and may inflict a heavy burden due to its morbidity and mortality, a careful and thorough investigation must be conducted. Our patient came with fluctuating fever, chest pain, and lymphadenopathy. There is no history of intravenous drug abuse and promiscuity to rule out the possible risk factors of immunocompromised state due to HIV infection. Acute onset of fever, chest pain, along with increased cardiac enzymes and T-wave changes found in electrocardiography suggest acute myocarditis, reaffirmed by MRI. Myocarditis is an inflammatory cardiac disorder induced predominantly by viruses but also by another infectious agents, including bacteria, parasites [12,13]. However, optimal treatment given by previous health centers could only relieve the symptoms for a while. Recurrence of fever and chest pain indicates other opportunistic infections as an alternative etiology.

Fever and lymphadenopathy that occurred as the initial complaint may suggest Toxoplasma infection, which needed to be confirmed by serologic testing. Several methods are used for diagnosis of

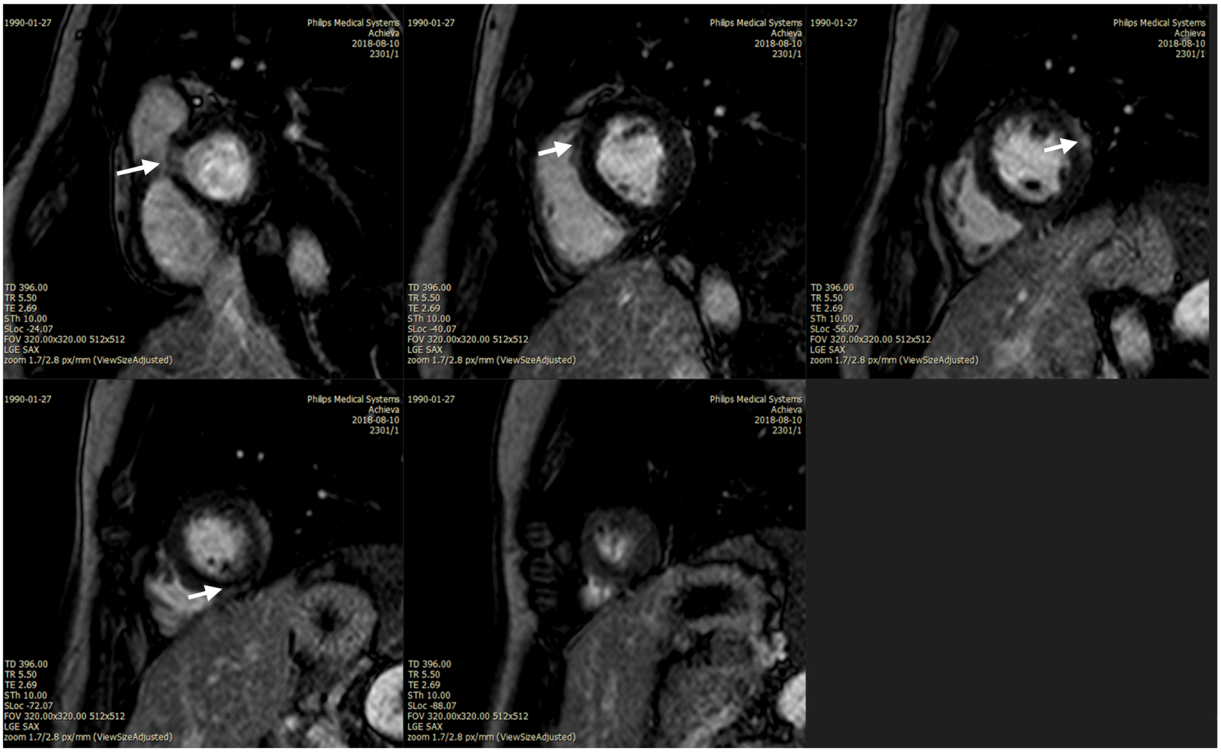

Fig. 1. Cardiac MRI showed myocardial necrosis in multiple sites (white arrows).

Toxoplasmosis Gondii infection, but gold standard tests are enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence assay (IFA) for detection of Toxoplasma-specific antibodies (IgG or IgM) [2,4]. Serologic testing performed on our patient showed reactive IgM (30.9 IU/ml) and reactive IgG anti-Toxoplasma (2.99 IU/ml). Low avidity of IgG anti-Toxoplasma in our patients may suggest the possibility of acute toxoplasmosis. These serologic findings, along with the clinical presentation, other laboratory workups, electrocardiography, and imaging, aid the construction of Cardiac toxoplasmosis diagnosis.

The report of cardiac involvement in toxoplasmosis is very limited. Toxoplasma myocarditis only has been reported in special populations such as in HIV patients. The prevalence varies according to various studies, and diagnosis is usually made postmortem since cardiac involvement is usually clinically silent. The diagnosis of toxoplasmosis relies on serology or identification of the bradyzoites in myocardial tissue [14–16]. To our knowledge, only one case reported the occurrence of Toxoplasma myocarditis in otherwise young, healthy man [17].

Our patient was then treated with pyrimethamine and clindamycin for six weeks. The symptoms improved within the first two weeks of medication, which suggests cessation of the progress of the disease and treatment success. To date, the clear indication of toxoplasmosis treatment in immunocompetent patients was only reserved in severe cases or vital organ involvement. The treatment of choice is based on a combination of pyrimethamine and sulfadiazine or pyrimethamine and clindamycin [14].

There were some limitations in our case report. First, we did not perform an endomyocardial biopsy as the gold standard and confirmatory testing of myocarditis toxoplasma, and we could not perform the PCR detection of Toxoplasma DNA due to the limited resources in Indonesia. However, the normalization of serological values and remission of myocarditis symptoms suggest the successful therapy of myocarditis toxoplasma suspected in our patient. We hope our report may add insightful perspective in evaluation of myocarditis, in which toxoplasmosis should be evaluated as the primary cause of the disease.

Conclusion

Unusual opportunistic infection such as toxoplasmosis may be obscured by the more prominent conditions such as acute myocarditis and can halt clinicians from pursuing the management necessitated, which may lead to decreased quality of life, morbidity, and mortality.

Toxoplasmosis should always be on the list of the diagnoses made by clinicians each time a patient presents with acute onset of fever and lymphadenopathy.

Thorough observation of clinical manifestation is of paramount importance in ushering clinicians to better understand and treat the patients' condition comprehensively.

CRediT authorship contribution statement

EJN proposed the case report and obtained informed consent from the patient. EJN, SS, GC, FNH, DYH write and revise the article. JP revise and provide the insight for image included in the article. All authors contributed to drafting and revising the article, have agreed and gave final approval on the final article to be submitted.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

Ethics approval was not required for this study.

Conflict of interest

The authors declare that there is no conflict of interest

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References

[1] Kochanowsky JA, Koshy AA. Toxoplasma gondii. Curr Biol 2018;28(14):R770–1.
[2] Liu Q, Wang Z-D, Huang S-Y, Zhu X-Q. Diagnosis of toxoplasmosis and typing of Toxoplasma gondii. Parasites Vectors 2015;8(1):292.
[3] Basavaraju A. Toxoplasmosis in HIV infection: an overview. Trop Parasitol 2016;6(2):129–35.
[4] Basit KA, Nasir S, Vohra E, Shazlee MK. Toxoplasmosis in an immunocompetent patient. Pak J Med Sci 2018;34(6):1579–81.
[5] Montoya, J.G.,Boothroyd, J.C., Kovacs, J.A. Toxoplasma gondii. In: Infectious Disease Essentials. New York: Elsevier; p. 424–425.
[6] Schwartzman, JDM JH. Systemic Coccidia. In: Tropical Infectious Disease. 2nd ed. China: Elsevier; p. 1141–1148.
[7] Bigna JJ, Tochie JN, Tounouga DN, Bekolo AO, Ymele NS, Youda EL, et al. Global, regional, and country seroprevalence of Toxoplasma gondii in pregnant women: a systematic review, modelling and meta-analysis. Sci Rep 2020;10(1):12102.
[8] Wilking H., Thamm M., Stark K., Aebischer T., Seeber F. Prevalence, incidence estimations, and risk factors of Toxoplasma gondii infection in Germany: a representative, cross-sectional, serological study. Sci Rep [Internet]. 2016 Mar 3 [cited 2021 May 19];6. Available from: ⟨https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4776094/⟩.
[9] Passos ADC, Bollela VR, Furtado JMF, Lucena MM de, Bellissimo-Rodrigues F, Paula JS, et al. Prevalence and risk factors of toxoplasmosis among adults in a small Brazilian city. Rev da Soc Bras De Med Trop 2018;51(6):781–7.
[10] Taila AK, Hingwe AS, Johnson LE. Toxoplasmosis in a patient who was immunocompetent: a case report. J Med Case Rep 2011;5(1):16.
[11] Sobanski V, Ajzenberg D, Delhaes L, Bautin N, Just N. Severe toxoplasmosis in immunocompetent hosts: be aware of atypical strains. Am J Respir Crit Care Med 2013;187(10):1143–5.
[12] Tschöpe C, Ammirati E, Bozkurt B, Caforio ALP, Cooper LT, Felix SB, et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol 2021;18(3):169–93.
[13] JCS Joint Working Group. Guidelines for diagnosis and treatment of myocarditis (JCS 2009): – digest version. Circ J 2011;75(3):734–43.
[14] Franco-Paredes C, Rouphael N, Méndez J, Folch E, Rodríguez-Morales AJ, Santos JI, et al. Cardiac manifestations of parasitic infections part 2: parasitic myocardial disease. Clin Cardiol 2007;30(5):218–22.
[15] Cuervo G, Simonetti AF, Alegre O, Sanchez-Salado JC, Podzamczer D. Toxoplasma myocarditis: a rare but serious complication in an HIV-infected late presenter. AIDS 2016;30(14):2253–4.
[16] Hofman P, Drici MD, Gibelin P, Michiels JF, Thyss A. Prevalence of toxoplasma myocarditis in patients with the acquired immunodeficiency syndrome. Br Heart J 1993;70(4):376–81.
[17] Pergola G, Cascone A, Russo M. Acute pericarditis and myocarditis by Toxoplasma gondii in an immunocompetent young man: a case report. Infez Med 2010;18(1):48–52.