

# Cerebral Toxoplasmosis Mimicking Subacute Meningitis in HIV-Infected Patients; a Cohort Study from Indonesia

A. Rizal Ganiem<sup>1</sup>, Sofiati Dian<sup>1</sup>, Agnes Indriati<sup>2</sup>, Lidya Chaidir<sup>3</sup>, Rudi Wisaksana<sup>4</sup>, Patrick Sturm<sup>5</sup>, Willem Melchers<sup>5</sup>, Andre van der Ven<sup>6</sup>, Ida Parwati<sup>2</sup>, Reinout van Crevel<sup>6\*</sup>

**1** Department of Neurology, Hasan Sadikin Hospital, Bandung, Indonesia, **2** Department of Clinical Pathology, Hasan Sadikin Hospital, Bandung, Indonesia, **3** Health Research Unit, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia, **4** Department of Internal Medicine, Hasan Sadikin Hospital, Bandung, Indonesia, **5** Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, The Netherlands, **6** Department of Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands

## Abstract

**Background:** HIV-associated subacute meningitis is mostly caused by tuberculosis or cryptococcosis, but often no etiology can be established. In the absence of CT or MRI of the brain, toxoplasmosis is generally not considered as part of the differential diagnosis.

**Methodology/Principal Findings:** We performed cerebrospinal fluid real time PCR and serological testing for *Toxoplasma gondii* in archived samples from a well-characterized cohort of 64 HIV-infected patients presenting with subacute meningitis in a referral hospital in Indonesia. Neuroradiology was only available for 6 patients. At time of presentation, patients mostly had newly diagnosed and advanced HIV infection (median CD4 count 22 cells/mL), with only 17.2% taking ART, and 9.4% PJP-prophylaxis. CSF PCR for *T. Gondii* was positive in 21 patients (32.8%). Circulating toxoplasma IgG was present in 77.2% of patients tested, including all in whom the PCR of CSF was positive for *T. Gondii*. Clinically, in the absence of neuroradiology, toxoplasmosis was difficult to distinguish from tuberculosis or cryptococcal meningitis, although CSF abnormalities were less pronounced. Mortality among patients with a positive CSF *T. Gondii* PCR was 81%, 2.16-fold higher (95% CI 1.04–4.47) compared to those with a negative PCR.

**Conclusions/Significance:** Toxoplasmosis should be considered in HIV-infected patients with clinically suspected subacute meningitis in settings where neuroradiology is not available.

**Citation:** Ganiem AR, Dian S, Indriati A, Chaidir L, Wisaksana R, et al. (2013) Cerebral Toxoplasmosis Mimicking Subacute Meningitis in HIV-Infected Patients; a Cohort Study from Indonesia. *PLoS Negl Trop Dis* 7(1): e1994. doi:10.1371/journal.pntd.0001994

**Editor:** Judd L. Walson, University of Washington, United States of America

**Received:** July 13, 2012; **Accepted:** November 16, 2012; **Published:** January 10, 2013

**Copyright:** © 2013 Ganiem et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Funding:** This study was financially supported by the Royal Academy of Arts and Sciences (KNAW, www.know.nl; 07-MP-10), the Netherlands; and by IMPACT, a 5-year HIV program supported by the European Commission (SANTE/2005/105-033). Ahmad Rizal Ganiem, Lidya Chaidir and Rudi Wisaksana are supported by fellowships from Radboud University Nijmegen Medical Center. Reinout van Crevel has a VIDI-grant from the Netherlands Organization for Scientific Research (NWO, www.nwo.nl; 017.106.310). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

\* E-mail: r.vancrevel@aig.umcn.nl

## Introduction

In settings of Africa and Asia, the most common cause of subacute meningitis in patients with advanced HIV infection is either tuberculous or cryptococcal infection [1,2]. However, in many patients, the etiology of subacute meningitis cannot be established [1,3]. In line with a large retrospective cohort of adult meningitis patients in South Africa, where 52.8% had no definite diagnosis despite extensive microbiological testing [1], we could not identify the causative pathogen in 48.9% of HIV-infected meningitis patients in an Indonesian setting [4].

Toxoplasmosis is a common and serious central nervous system (CNS) infection in patients with advanced HIV infection [5–8], although its incidence has decreased with introduction of antiretroviral treatment (ART) [6,9]. Cerebral toxoplasmosis mostly presents as cerebral mass lesions with headache, confusion, fever, lethargy, seizures, cranial nerve palsies, psychomotor changes, hemiparesis and/or ataxia [10]. Some of these symptoms may also mimic meningitis, but cerebral toxoplasmosis is generally

not considered as a differential diagnosis of subacute meningitis in HIV-infected patients. This is especially the case in low-resource settings where no CT or MRI can be performed. We have therefore examined if toxoplasmosis can be diagnosed in HIV-infected patients presenting with subacute meningitis of unknown origin in Indonesia, using cerebrospinal fluid (CSF) PCR for *T. gondii*.

## Methods

### Ethics statement

Anonymized CSF and blood samples were used from an already-existing hospital collection, from a cohort of patients collected as part of a project ‘Optimization of diagnosis of meningitis’, approved by the Ethical Committee of Hasan Sadikin Hospital/Medical Faculty of Universitas Padjadjaran, Bandung, Indonesia (No. 85/FKUP-RSHS/KEPK/Kep/EC/2006). As this study was done using already existing sample collection, no separate consent was asked for this study. HIV testing is done