International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 09, Issue 12, December 2024,
https://doi.org/10.23958/ijirms/vol09-i12/1998

Clinical Case

Cerebral Toxoplasmosis with Negative Toxoplasmosis Serology in an HIV-Infected Patient: Case Report

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Received 03 October 2024; Accepted 22 November 2024; Published 06 December 2024

Abstract

Cerebral toxoplasmosis is the most common opportunistic infection of the central nervous system during HIV infection in Europe and Africa. The diagnosis is made by a set of clinical, radiological, serological, histological, molecular arguments as well as the response or not to the anti-toxoplasmosis treatment. We report the case of a 52-year-old HIV-infected patient, CD4 count at 11 / mm3, who presented a month before admission with fever and weight loss amounting to 15 kg, headache, memory problems, without signs of deficit or signs of intracranial hypertension. A lumbar puncture (LP) was performed after elimination of contraindications showed isolated hyperproteinorrachia, cerebral computed tomography scan (CT scan) was performed after its availability showed an image of abscess, anti-toxoplasmosis treatment was started, further brain MRI confirmed the abscess image, and toxoplasmosis serology was requested twice and came back negative, PCR for Toxoplasma gondii was requested in cerebrospinal fluid (CSF) and returned positive. The outcome was good clinically and radiologically. A control CT scan performed 3 months after showed almost total disappearance of the lesion. The diagnosis of cerebral toxoplasmosis must be made in HIV- infected patients in front of any neurological manifestations with suggestive radiological images even with negative serology.

Keywords: ***Cerebral toxoplasmosis, PCR, serology, HIV, case report.***

Introduction

Toxoplasmosis is an infection caused by the intracellular zoonotic parasite Toxoplasma gondii. In adults, toxoplasmosis can affect multiple sites, with the brain being the most severely impacted. Cerebral toxoplasmosis (CT) is the most prevalent opportunistic infection of the central nervous system in HIV- infected patients [1,2]. It often represents a reactivation of the parasite from a prior primary infection [1,3]. The prognosis for CT largely depends on the severity of initial clinical manifestations as well as the timeliness of diagnosis and treatment [1]. In HIV- infected patients who present with a cerebral mass, the diagnosis of cerebral toxoplasmosis is highly likely when accompanied by positive IgG serology for Toxoplasma and a CD4 count of less than 100 cells/mm³. However, if both IgM and IgG serologies are negative, the diagnosis of cerebral toxoplasmosis is usually ruled out in current practice [3].

We report a case of PCR-confirmed cerebral toxoplasmosis in a severely immunocompromised HIV-infected patient, despite negative serological results.

Case presentation

This 52-year-old male patient was referred for positive HIV serology with a one-month history of episodic headaches, memory problems, behavioural disorders, fever and weight loss (15 kg). There were no visual disturbances, vomiting, deficits or signs of intracranial hypertension. Clinical examination was normal, apart from oral-oesophageal candidiasis. In the absence of any contraindication, we performed a lumbar puncture (LP) which showed a clear macroscopic appearance, albuminorachy at 1.07g/l, glucorachy at 0.46g/l, concomitant glycemia at 0.93 g/l, glucorachy/glycemia ratio at 0.5, the elements were <3/mm3, with absence of bacteria, yeast and Mycobacterium tuberculosis on direct examination, the culture was sterile.

The following day, a cerebral CT scan was performed, which revealed a spontaneously hypodense right deep parietal lesion, discreetly enhancing in the periphery after injection of contrast medium (CM), associated with a patch of peri-lesional edema, all of which was responsible for a mass effect on the homolateral lateral ventricle and the midline. Magnetic resonance imaging (MRI) of the brain confirmed the image of a brain abscess (**Fig. 1.B**).

Blood toxoplasmosis serology was negative for IgG and IgM. CD4 count was 11/mm3. We started trial anti-toxoplasmic treatment with sulfamethoxazole-trimethoprim at a dose of 100mg-20mg/kg/d in view of the typical appearance of brain imaging despite negative serology, while awaiting the result of PCR, which showed a positive result for Toxoplasma gondii. No other opportune infections (tuberculosis, cryptococcosis, Cytomegalovirus CMV) were found. A second toxoplasma serology test was carried out two weeks later and remained negative. The patient progressed well on anti-toxoplasma therapy, and a follow-up CT scan performed three months later showed almost complete disappearance of the lesion

(**Fig. 1.C**). The patient commenced a Tenofovir disoproxil fumarate (TDF), Emtricitabine (FTC) and Efavirenz (EFV) based triple therapy regimen, which led to favorable immunovirological outcomes. One year after treatment initiation, the patient demonstrated a CD4 count of 324 cells/mm³ and sustained an undetectable viral load.

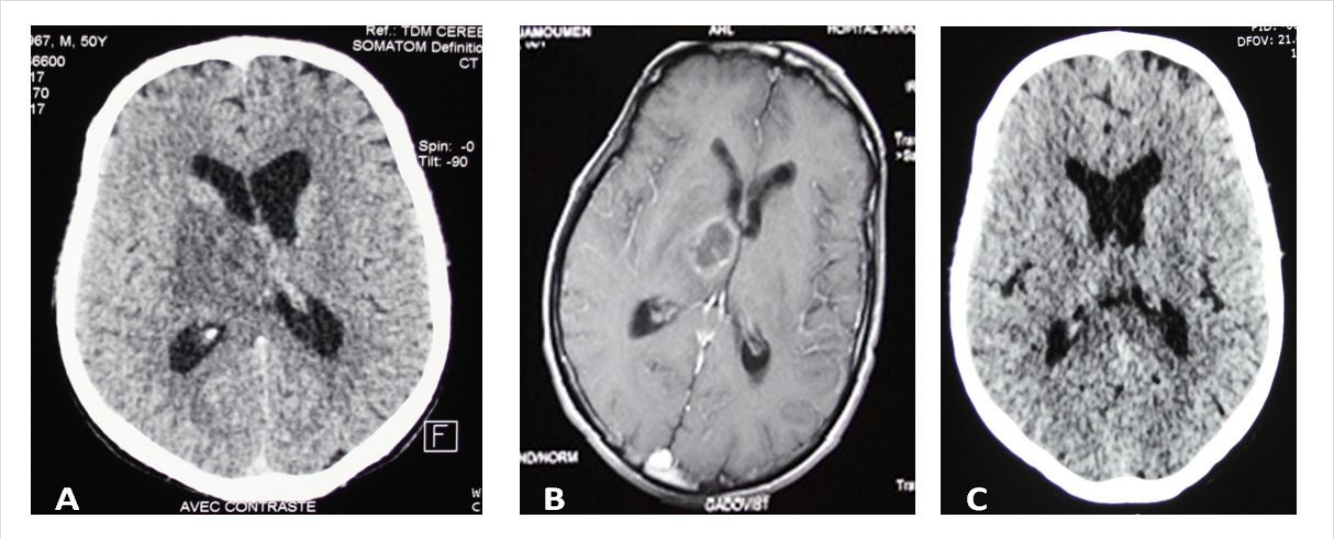

Figure 1: Radiographic Findings Before and After Therapy

A: Pre-therapeutic cerebral CT scan reveals a spontaneously hypodense lesion in the right deep parietal region, which shows subtle peripheral enhancement following the administration of contrast. This lesion is accompanied by a zone of peri-lesional edema, contributing to mass effect on the ipsilateral lateral ventricle and midline structures. **B:** Pre-therapeutic cerebral MRI demonstrates multiple supratentorial lesions with extensive perilesional edema, likely indicative of cerebral abscesses. **C:** Post-therapeutic cerebral CT scan, conducted three months later, shows complete resolution of the previously identified lesions.

Discussion

Cerebral toxoplasmosis is the most common opportunistic infection of the central nervous system during HIV infection in Europe and Africa [1,2,4]. In *Toxoplasma gondii* seropositive patients, the risk of cerebral toxoplasmosis is around 30% [4]. This is often a reactivation of the parasite present since a previous primary infection [1,3,4]. Its frequency has been greatly reduced by the introduction of antiretrovirals and sulfamethoxazole-trimethoprim chemoprophylaxis in profoundly immunocompromised patients (CD4<200/mm3) [1,5]. HIV-associated toxoplasmosis manifests mainly as non-specific encephalitis [6].

Our patient presented with encephalitis, memory impairment and headache without any deficit signs, associated with fever and altered general condition. We accepted the diagnosis of cerebral toxoplasmosis, and the course of treatment was good. The diagnosis of toxoplasmosis is established on the basis of clinical, radiological, serological and histological findings, and the response or otherwise to anti-toxoplasmic test treatment. Molecular PCR is rarely feasible, but its positivity confirms the diagnosis [4,7]. Cerebral CT scan shows focal lesions, more often multiple (57 to 85%), rounded, hypo- or iso-dense, with a frequent mass effect. After injection, contrast is annular (44 to 91%), associated with a peripheral oedematous reaction creating a cocardial image [8]. Lesions preferentially involve the cerebral hemispheres (cortico-subcortical junction), the basal ganglia and, more rarely, the sub-tensor level [8]. The sensitivity of MRI in cerebral toxoplasmosis is better than that of CT scan. In particular, MRI can detect infra-centimeter lesions located at the cortico-medullary junction, which are not accompanied by a mass effect [8]. In our patient, the CT scan showed a cocardial image associated with a mass effect on the midline and lateral ventricle, while the MRI showed multiple supratentorial lesions associated with extensive peri-lesional edema related to cerebral abscesses. The absence of specific immunoglobulins makes the diagnosis of cerebral toxoplasmosis highly unlikely in routine practice, even if neurological symptoms and imaging are sometimes suggestive [9,10]. In our patient, toxoplasma serology was carried out on two occasions and proved negative despite the presence of genuine cerebral toxoplasmosis, this result was also found in a study carried out in Burkina Faso, where 15% of HIV-infected patients with cerebral toxoplasmosis had negative toxoplasma serology, and the diagnosis was retained after clinical improvement under anti-toxoplasma treatment [2]. Toxoplasma serology negativity may be explained by profound immunosuppression [1,3]; in our case, the CD4 count was 11/mm3. In our case, following the cerebral CT scan that revealed an abscess, we initiated anti-toxoplasmic treatment despite negative serology results, without awaiting the PCR confirmation, while cerebral toxoplasmosis is one of the most common causes of cerebral abscesses, and also a treatable emergency [2]. The PCR results returned positive, confirming our approach.

CSF T. gondii polymerase chain reaction (PCR) assay has a moderate sensitivity but a high specificity and positive predictive value, especially if done within the first week. Diagnosis of cerebral toxoplasmosis can be established if CSF T. gondii PCR assay is positive, but a negative result does not exclude it. Nonetheless, performing PCR for all HIV patients who are suspected of having a cerebral infection is worthwhile, as this will help to avoid needless brain biopsy/surgery and allow early management [10,11].

Conclusion

We conclude that cerebral toxoplasmosis is a prevalent complication in HIV-infected patients. Its diagnosis relies on a combination of clinical, radiological, and serological evidence. Our observation highlights the importance of not excluding cerebral toxoplasmosis in immunocompromised patients when there is a high index of suspicion, even with negative serology, and demonstrates the value of toxoplasmic PCR in confirming the diagnosis in certain situations when lumbar puncture is feasible.

List of abbreviations

HIV: Human Immunodeficiency Virus.
MRI: Magnetic Resonance Imaging.
LP: Lumbar Puncture.
CSF: Cerebrospinal Fluid.
PCR: Polymerase Chain Reaction.
CT: Cerebral Toxoplasmosis.
CT scan: Computed Tomography scan.
CM: Contrast Medium.
CMV: Cytomegalovirus.
TDF: Tenofovir disoproxil fumarate.
FTC: Emtricitabine.
EFV: Efavirenz.

Declarations

Ethics approval and consent to participate

Not applicable.

Funding Statement

The authors declare that no funding was received for the research and publication of this article

Authors' contributions

I M: Principal Author, writes the manuscript, reviews relevant literature, and ensures the overall structure and accuracy of the article.
T Z: analyzed and interpreted the patient data regarding the neurological disease and contributor in writing the manuscript.
E R and A W: were directly involved in the diagnosis, treatment, and management of the patient and contributor in writing the manuscript.
T N: Final Review and Validation

All authors read and approved the final manuscript."

Conflicts of Interest

All authors declare that they have no conflicts of interest.

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