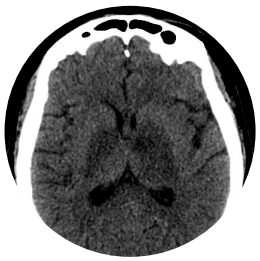

Atypical imaging presentation of neurotoxoplasmosis

Neurotoxoplasmosis con presentación imagenológica atípica

Marco Antonio Bula Álvarez[1]
Estephania Sáenz Sandoval[2]

DOI: https://doi.org/10.53903/01212095.167

Summary

Cerebral toxoplasmosis or neurotoxoplasmosis is one of the most frequent infections by opportunistic agents in HIV-infected patients and is associated with severe immunodeficiency. In these patients, it causes high-grade neurological lesions and even death. It usually appears as multiple foci of lesions with gangliobasal predominance and annular enhancement. We present a clinical case of neurotoxoplasmosis in a HIV patient with an unusual radiological pattern.

Resumen

La toxoplasmosis cerebral o neurotoxoplasmosis es una de las infecciones por agentes oportunistas más frecuentes en pacientes infectados por virus de inmunodeficiencia humana (VIH) y se relaciona con inmunodeficiencia severa. En estos pacientes causa lesiones neurológicas de alto grado e incluso la muerte. Suele aparecer como múltiples focos de lesión de predominio gangliobasal y con realce anular. Se presenta un caso clínico de neurotoxoplasmosis en paciente VIH con un patrón radiológico poco frecuente.

Key words (MeSH)

Immunosuppression therapy
Toxoplasmosis, cerebral
HIV
Diagnostic imaging

Palabras clave (DeCS)

Terapia de inmunosupresión
Toxoplasmosis cerebral
VIH
Diagnóstico por imagen

Introduction

Toxoplasmosis is a zoonotic infection caused by the protozoan Toxoplasma gondii, an intracellular parasite with a natural reservoir in cats. Carrier status is acquired by direct consumption of oocysts from cat feces and/or food and water contaminated with them (1, 2). It is one of the most common infections in humans; it is estimated that one third of the world's population has this latent infection; in low-income countries the co-infection of toxoplasmosis with HIV is 55% and it is an AIDS indicator disease. In the general Colombian population, the seroprevalence is approximately 45-47% and its incidence in HIV-AIDS patients is 7,000-10,000 new cases each year. There are no significant differences in the proportion of infected women and men (1, 3).

Acute toxoplasmosis frequently presents with subclinical pictures of non-specific or mild symptomatology such as general malaise, fever and adenopathies; however, in reserved cases it can lead to encephalitis with high mortality. After acute infection, the parasite disseminates and persists chronically in the form of cysts in organs such as the heart, brain and musculoskeletal system without causing any symptoms in healthy individuals. Its reactivation, spread and complication depend on the immunological profile of the host, and neurotoxoplasmosis or cerebral toxoplasmosis is the first complication of this infection in patients with immunosuppression (4).

Toxoplasma gondii is the opportunistic agent that most frequently causes encephalic lesions and neurological dysfunction in HIV-positive patients in the world; except in the African continent, where Cryptococcus neoformans infection is most frequently reported. The prevalence of cerebral toxoplasmosis is approximately 15% in AIDS patients (2, 3) and is associated with poor or non-adherence to antiretroviral treatment or late diagnosis of HIV infection. In these patients the morbimortality rate is high (1).

Clinical Case

A 41-year-old female patient with a history of untreated hypothyroidism, a clinical picture of 20 days of evolution characterized by asthenia, hyporexia, headache, abdominal pain, diarrhea, weight loss of 20 kg, global aphasia, disorientation and somnolence. Paraclinical examinations showed anemia and leukopenia, and HIV+ serology. Due to the patient's condition and the suspicion of encephalitis due to opportunistic disease, a simple cranial computed axial tomography (CT) scan was performed, which revealed low density of bilateral localization of lenticular nuclei, thalami, posterior arm of the external capsule and anterior arm to a lesser degree. A contrast-enhanced CT scan was performed to improve diagnostic accuracy, but no contrast enhancement of the lesions was evident (Figures 1 and 2). In images the lesions were compatible with anoxic ischemic encephalopathy; a magnetic resonance imaging (MRI) was performed under sedation.

[1]Resident of Radiology and Diagnostic Imaging, Universidad Autónoma de Bucaramanga. Bucaramanga, Colombia.

[2]Medical Student of the Autonomous Universidad de Bucaramanga. Bucaramanga, Colombia.

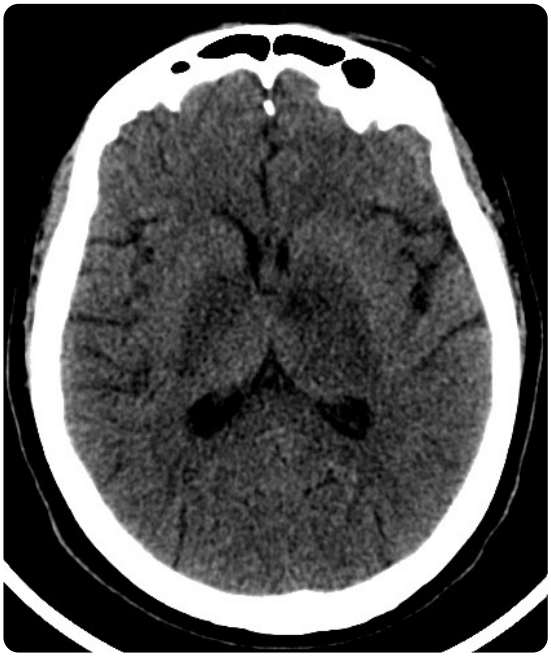

Figure 1. Simple cranial CT scan. Bilateral hypodense lesions with predominance in the left hemisphere. They are located in the left thalamus, globus pallidus and putamen, and in the right globus pallidus. Also, in the right medial frontal region, left frontal subcortical region (not visible in this axial image) with perilesional edema in some lesions. There is no midline deviation.

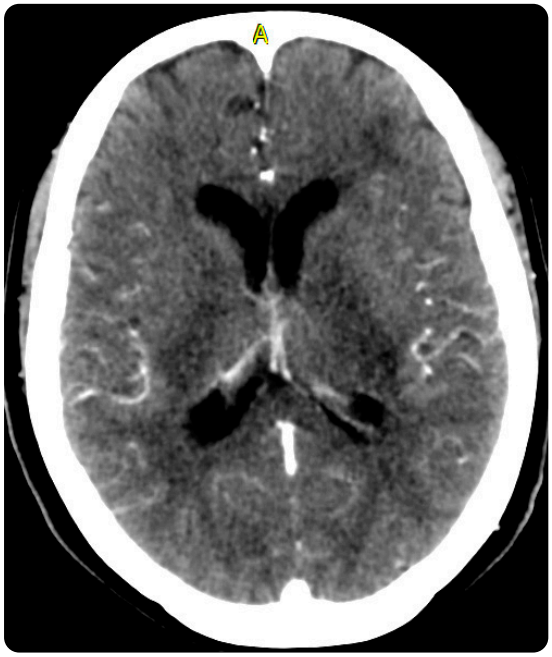

Figure 2. CT with contrast medium. There is no contrast enhancement of the lesions described in Figure 1.

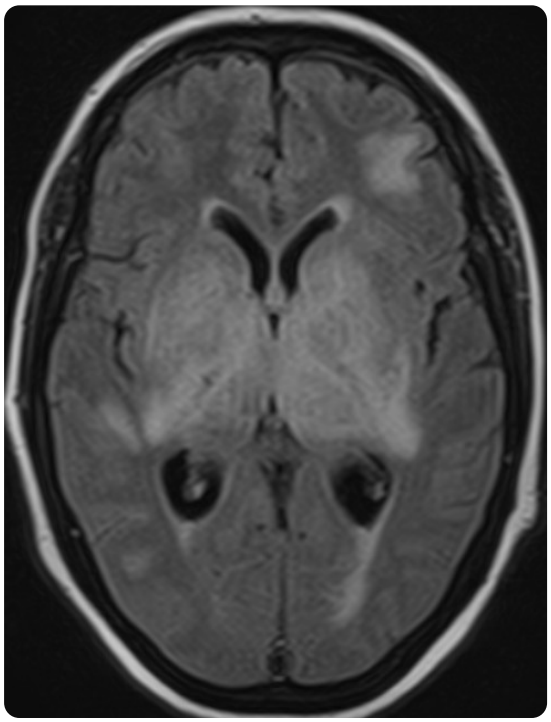

Figure 3. MRI FLAIR sequence with T2 information. Multiple high signal subcortical lesions in the left frontal and right temporooccipital region, thalamic localization and bilateral basal ganglion with vasogenic edema, without midline deviation.

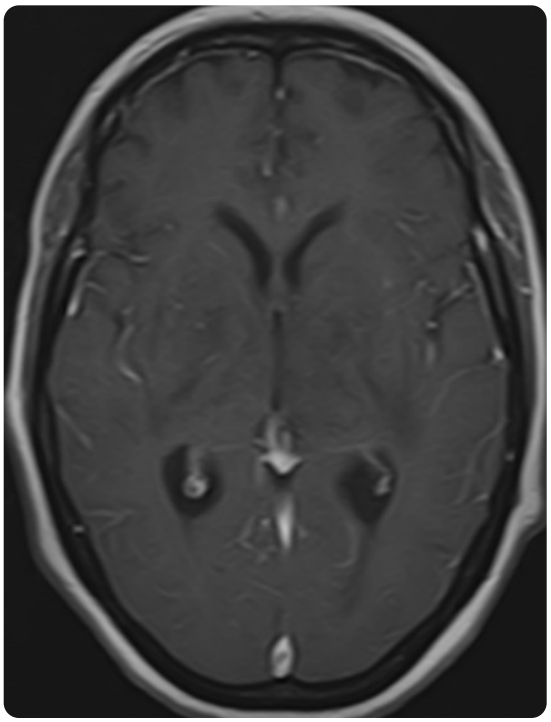

Figure 4. MR sequence with T1 information and contrast medium administration. Small rounded lesions in gangliobasal and mesial frontal location with faint enhancement with contrast medium and low signal areas in gangliobasal regions suggesting vasogenic edema.

Three days later, the patient was admitted to the intensive care unit (ICU) in regular general condition, drowsy, without ocular opening on call, with reactive pupils, response to painful stimulus, hydrated, afebrile, with normal oxygen saturation and without respiratory distress. Cerebrospinal fluid examination was not suggestive of infection; cytochemistry showed no evidence of inflammation and the FilmArray test was negative for herpes simplex 1 and 2 and zoster. He was administered trimethoprim-sulfamethoxazole until MRI results were obtained. Among the diagnoses compatible with the imaging and clinical findings were progressive multifocal leukoencephalopathy due to JC virus and encephalopathy due to HIV or cytomegalovirus. Antiretroviral treatment was not started at the time, due to the high risk of immune reconstitution syndrome; he remained in ICU with high risk of morbidity and mortality.

MRI revealed in the FLAIR sequence with T2 information multiple bilateral hyperintense nodular lesions and in the gangliobasal region, in the juxtacortical and periventricular white matter of left predominance, without relevant findings after contrast medium injection (Figures 3 and 4). These findings were compatible with opportunistic lymphoproliferative and infectious processes and do not rule out an acute disseminated encephalomyelitis.

Infectious disease follow-up diagnosed HIV infection AIDS stage (CD4+/mm3 29), viral load of 1,800,000 copies/mL, esophageal candidiasis, bacterial acute diarrheal disease with positive FilmArray for Shigella, enteroinvasive E coli and Campylobacter, positive viral load for Epstein Barr virus and positive CSF PCR for Toxoplasma Gondii. The results allowed the diagnosis of neurotoxoplasmosis and other opportunistic diseases. Management was continued with trimethoprim-sulfamethoxazole, metronidazole and fluconazole, ciprofloxacin+azithromycin and antiretrovirals were added to the pharmacological treatment, and tracheostomy and gastrostomy were performed.

Weeks later, pseudoanalgesia was progressively discontinued. The patient remained alert, hydrated, afebrile, without signs of respiratory distress or systemic inflammatory response syndrome (SIRS), but with constant diarrheal stools. The antibiotic, antiparasitic and antiretroviral management regimen was maintained with clinical improvement and without wasting syndrome. The patient remained in the ICU under observation, and paraclinical tests and MRI with contrast medium under sedation were requested to complement the follow-up.

Imaging

When opportunistic neuroinfection is suspected, the imaging technique of first choice is CT. Its sensitivity is not as high in comparison with MRI, but it allows showing multiple low density foci with mass effect that appear more frequently in the areas of the basal nuclei, thalamus and corticomedullary junction (5, 6). These findings may be typical or atypical; typical lesions are found in approximately 80% (2, 5) of patients with cerebral toxoplasmosis. On CT they consist of contrast-enhancing lesions with a ring-shaped pattern characterized by low density centers and higher density rim with perilesional edema. Atypical findings, as in the present case, appear in less than 20% of patients and are characterized by low density lesions with mass effect without annular enhancement, lesions not visible in CT, but visible in MRI or in diffuse encephalitis without visible focal lesions. The imaging finding most suggestive of neurotoxoplasmosis is the "eccentric target sign", which shows a high density nodule in the wall of the ring lesion (2).

MRI is a more sensitive technique for detecting lesions, especially in the posterior fossa. The lesions also present with annular enhancement and enhance with contrast medium. The most frequent patterns are found in contrast-enhanced T1-weighted images (71%) and in T2/FLAIR sequences with the target sign; there are few cases with no enhancement or no sign (29%). Typical lesions in images with T1 information are observed as two-signal lesions or ring pattern with high peripheral signal and lower central signal, while in T2 these signals are inverted (7).

Among the differential diagnoses that should be taken into account for this disease are primary lymphomas of the central nervous system, metastases, demyelinating lesions due to multiple sclerosis, abscesses, tuberculosis and ischemic cerebral infarcts (6). The imaging differentiation between lymphoma and toxoplasma lesion is complex due to their great similarity; however, the presentation of the lesions can guide the suspicion. Neurotoxoplasmosis usually presents in a multinodular, bilateral and ganglionbasal predominant form, while lymphoma presents in a solitary and periventricular or subependymal form (6, 7).

Treatment and prognosis

Currently there are no drugs capable of destroying the toxoplasma cysts, so the treatment of toxoplasmosis is focused on eliminating the tachyzoites and is only indicated in acute or reactivation cases. First-line pharmacological management includes pyrimethamine (200 mg orally, then 50-75 mg/day) with sulfadiazine (1.0-1.5 g/6 hours orally) or clindamycin (600 mg/6 hours intravenously) and folinic acid (10-50 mg/day), the latter decreasing marrow suppression and hematologic toxicity caused by pyrimethamine. The second line of management contemplates trimethoprim/sulfamethoxazole (80 mg/400 mg) (6, 7) and is used in cases in which there is no access to primary management. The prognosis of patients depends to a great extent on the immunological profile and the rapid initiation of treatment, since it reduces the severity of the symptoms and with efficient treatment, up to 50% of patients recover in cases of severe neurotoxoplasmosis. Patients show neurological improvement within weeks of starting treatment and up to 20% recover completely. Even so, mortality in patients admitted to the ICU is 24% and 100% in untreated cases (6). It is recommended to evaluate the progression of the disease by means of imaging studies.

Discussion

The most frequent cause of cerebral toxoplasmosis is the reactivation of cysts with the consequent parasitic replication in patients who begin a significant immunosuppression, among these the most affected are HIV-AIDS patients (5). Toxoplasma activity generates an inflammatory reaction that is frequently multifocal and affects both hemispheres and can rapidly progress to diffuse necrotizing encephalitis if not treated promptly (2). The lesions recognizable by CT or MRI and their clinical manifestations vary according to the degree of immunosuppression and brain parenchymal involvement. The most common symptoms are headache (79%), fever (55.68%), lethargy (55%), motor

deficits (44.31%) - such as ataxia (15-25%) - and consciousness disorders (29.54%), and even chorioretinitis and other visual disorders (8-15%) which can lead to loss of vision in patients (1, 2, 8). Given the involvement of the central nervous system and the high risk of mortality, early diagnosis and timely treatment are essential to improve the prognosis of patients. The definitive diagnosis of the disease is biological and is made with the identification of the tachyzoite in the cerebrospinal fluid. Its immediate approach depends on clinical semiology, serology, and radiology. The latter is very useful for the diagnosis of neurotoxoplasmosis due to the imaging patterns presented, which in conjunction with clinical findings are highly suggestive of neuroinfection (2, 4).

Despite the fact that primary prophylaxis and antiretroviral treatment decrease the probability of reactivation of the infection, neurotoxoplasmosis continues to be a public health problem in Colombia and one of the main causes of deterioration and death in patients with severe immunosuppression on a global scale. Due to the above, once the patient is admitted, presumptive diagnosis and immediate initiation of empirical treatment are essential to reduce complications, morbidity and mortality. The presentation of this case highlights the importance of clinical and radiological knowledge of the most common opportunistic diseases in our environment, such as neurotoxoplasmosis, as well as its semiology and imaging presentations, both typical and atypical, which allows a timely approach and a more complete diagnostic approach, thus reducing unnecessary treatment, sequelae with reduced quality of life and fatal outcomes such as death.

References

1. Delatorre Cifuentes LA, Faciolince LA, López de Mesa C. Toxoplasmosis ocular en Colombia: 10 años de aportes investigativos. Rev Soc Colomb Oftalmol. 2018;51(1):11-22.
2. Pereira-Chioccola VL, Vidal JE, Su C. Toxoplasma gondii infection and cerebral toxoplasmosis in HIV-infected patients. Future Microbiol. 2009;4(10):1363-79.
3. Gómez Marín JE. Toxoplasmosis: Un problema de salud pública en Colombia. Rev. Salud Pública [Internet]. 2002 [citado: 2022 jun 03];4(Suppl 1):7-10. Disponible en: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0124-00642002000400003&lng=en.
4. Schlüter D, Barragán A. Advances and challenges in understanding cerebral toxoplasmosis. Front Immunol. 2019;10. https://doi.org/10.3389/fimmu.2019.00242
5. Suzuki Y. Immunopathogenesis of cerebral toxoplasmosis. J Infect Dis. 2002;186(s2):S234-40.
6. Pantoja Ruiz C, Martínez A, Ferreirós A, Millán S, Coral J. Toxoplasmosis en sistema nervioso central: revisión sobre la patología, abordaje diagnóstico y tratamiento. Acta Neurol Colomb. 2021;37(1 supl. 1):141-7.
7. Masamed R, Meleis A, Lee EW, Hathout GM. Cerebral toxoplasmosis: case review and description of a new imaging sign. Clinical Radiology. 2009;64(5):560-3.
8. Hernández-González E, Zamora-Pérez F, Barnés-Domínguez J, Bender-del Busto JE, Rodríguez-Delgado F, Millán-Marcelo JC. Manifestaciones clínicas de la toxoplasmosis cerebral en pacientes cubanos con Sida. Rev Neurol. 2002;34(07):618-21.

Correspondence

Estephania Sáenz Sandoval
Calle 60C # 16F-23
Bucaramanga, Colombia
esaenz575@unab.edu.co

Recibido para evaluación: 10 de diciembre de 2021
Aceptado para publicación: 15 de febrero de 2022