Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

Francisco Arreola Banda¹, Diego Aguilar Romero¹, Guillermo García Maldonado¹, Norma Lizeth Alvarado Franco², Carlos Salvador Alcázar Quiñones¹

¹Instituto Mexicano del Seguro Social – General Hospital of Zone No. 33. Department of Internal Medicine. Monterrey, Nuevo León, México.
²Instituto Mexicano del Seguro Social – General Hospital of Zone No. 33. Department of neurology. Monterrey, Nuevo León, México.

ABSTRACT

Introduction: Human immunodeficiency virus (HIV) is a neurotrophic, neuroinvasive, and neurovirulent pathogen, which can cause direct infection of the central nervous system (CNS) but also predisposes to a variety of other neuroinfections through impaired T-cell mediated immunity. Among the imaging findings in HIV patient with CNS infection, the presence of ring-enhancing intracranial lesions are considered not rare but quite puzzling diagnostic dilemma. The differential diagnosis for these lesions commonly includes metastasis, abscess, glioblastoma, infarct, contusion, demyelinating disease, radiation necrosis, resolving hematoma or infections. Many features need to be considered altogether to help narrow the differential.

Case description: Male, 32 years old, with history of chronic smoking, pets: one cat dewormed and vaccinated, and positive diagnosis of HIV infection with a CD4 T lymphocyte count of 24 cells/mm3, without antiretroviral treatment. His main symptom was headache, associated with fever, nausea, and vomiting. Therefore, he was hospitalized for his diagnostic approach. Complete laboratory work was done, head CT, lumbar puncture, and MRI, finding rounded intra-axial lesions with well-defined and hyperintense edges in the parietal and occipital region with annular enhancement after the administration of contrast. After symptomatic treatment and anthelmintic therapy, a follow-up imaging study evidenced involution of these lesions. The patient met diagnostic criteria for definitive diagnosis of neurocysticercosis.

Conclusion: Even though, Neurocysticercosis is not a rare disease, our group decided to publish this case report because its association with an HIV positive patient, in which has not been yet linked to, in behalf of the lack of evidence and studies, considering the ethical issue of performing rutinary head CT scans in asymptomatic individuals.

KEYWORDS: HIV; Acquired Immunodeficiency Syndrome; Neurocysticercosis.

INTRODUCTION

Human immunodeficiency virus (HIV) is a neurotrophic, neuroinvasive, and neurovirulent pathogen, which can cause direct infection of the central nervous system (CNS) but also predisposes to a variety of opportunistic CNS infections through impaired T-cell mediated immunity. The neurological clinical findings depend on the stage of infection, degree of immunosuppression, the pathogenic agent and on whether the patient is on antiretroviral therapy.¹ ² UNAIDS data 2023 estimated that there are 39.0 million people living with HIV (PLH) in 2022 and there were 1.3 million new infections.³ About 70% of PLH develop neurological disease and is the first manifestation of HIV infection in approximately 10–20% of PLH.²

The diagnostic approach to patients with suspected infection of CNS should include imaging techniques like computed tomography (CT) or magnetic resonance imaging (MRI). Among the findings in these imaging studies, the presence of ring-enhancing intracranial lesions are considered not rare
Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

but quite puzzling diagnostic dilemma. These lesions are characterized by a contrast enhancing halo with a non-enhancing center and they may present solitary or multiple on a brain MRI.\textsuperscript{4-5}

The differential diagnosis for these lesions commonly includes metastasis, abscess, glioblastoma, infarct, contusion, demyelinating disease, radiation necrosis, resolving hematoma or infections.\textsuperscript{6} Many features of the lesion, as well as the clinical presentation and the patient’s demographics, need to be considered altogether in order to narrow the diagnostic possibilities.\textsuperscript{6}

Within the microorganisms that cause cerebral ring lesions, neurocysticercosis (NCC) is considered an endemic infection in many regions such as Latin America, Africa, and Asia and results from the localization of the larvae of Taenia solium in the CNS.\textsuperscript{7} It is estimated a prevalence of approximately 50 million people worldwide, and it has been attributed with about 50,000 deaths each year. The most frequent clinical manifestations are seizures, intracranial hypertension, neurological deficits, and sometimes psychiatric manifestation. It is responsible for more than 50\% of the cases of late-onset epilepsy in developing countries.\textsuperscript{8}

We present a case report of a male patient with brain ring-enhancing lesions with recent diagnosis of HIV, which meets diagnostic criteria for NCC. Also, we will review the current literature with the intention to raise awareness in the medical staff, in order to achieve an early diagnosis and treatment.

METHODOLOGY

A review of the related literature was carried out in databases such as Pubmed, Google Scholar, SciELO and Elsevier, analyzing the most relevant data regarding epidemiology, impact, approach, timely diagnosis and treatment. The final review of the case was performed by a specialist in neurology and internal medicine.

Legal authorization was consented for the patient's review of the medical history.

CASE REPORT

Male, 32 years old, resident of Nuevo León, Mexico, warehouseman in a company. History of chronic smoking (1.2 packs/year), alcoholism and other drug addictions denied, pets: one cat dewormed and vaccinated. He reported a diagnosis of HIV infection with a CD4 T lymphocyte count of 24 cells/mm\textsuperscript{3} in August 2022 and denied an initial antiretroviral treatment. The rest of the questionnaire without relevant background.

His condition began in September 2022 referring oppressive, bifrontal headache radiating to the rest of the skull, reaching high intensity within hours, without a time predominance, aggravated when lying supine, attenuated with the use of NSAIDs accompanied by nausea, vomiting and unquantified fever. He attended an outpatient infectious disease clinic that indicated urgent hospitalization as a suspected diagnosis of an opportunistic infection located in central nervous system, at the beginning of October 2022.

During his initial evaluation, he was awake, oriented with bradypsychia, bradylalia, mild dysarthria and dysphonia, intact cranial nerves, strength in four extremities 5/5 MRC, normal deep tendon reflex, indifferent plantar response, without sensitive symptoms, cerebellum without alterations, and negative meningeal signs. Rest of physical examination with no relevant findings.

Laboratory: Leukocytes 5,600/\mu L, Neutrophils 2,800/\mu L, Hemoglobin 11.6 g/dL, Platelets 251,000/\mu L, Serum glucose 80 mg/dL, Urea 18 mg/dL, Creatinine 0.72 mg/dL, Lactic dehydrogenase 162 IU/L HIV viral load 13,738 cp/ml CD4 count 30 cells/mm\textsuperscript{3} (3.2%).

Simple brain CT (Figure 1), where hypodense and poorly defined areas are identified at the level of the basal ganglia and in the right parieto-temporal region.

Additionally, a lumbar puncture was performed with the following results: Cerebrospinal fluid (CSF) cytology: Transparent, colorless, Glucose 51 mg/dL, Lactic dehydrogenase 11 IU/L, Leukocytes 0 cells/mm\textsuperscript{3} and Total proteins: 492 mg/dL. CSF stains: Ziehl Nielsen negative, KOH negative, India ink negative. Negative CSF GeneXpert MTB/RIF.

Due to inconclusive findings, a contrast-enhanced MRI of the brain was requested (Figure 2), identifying multiple supra- and infratentorial lesions with annular enhancement after the application of contrast medium, as well as positive TORCH IgG. Serology for CMV, rubella, and Toxoplasma gondii. HBV and HCV serology negative, VDRL negative. CSF culture results were collected without bacterial growth.

Figure 1: Head CT An axial within the ventricular level, we can find an hypodense lesion with poorly defined borders, located in the right parietal and temporal region.

Corresponding Author: Francisco Arreola Banda
Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

Figure 2: Contrast-enhanced MRI of brain: An axial section is observed at the supratentorial level in FLAIR sequence (Image A), identifying rounded intra-axial lesions with well-defined and hyperintense edges in the parietal and occipital region with annular enhancement after the administration of contrast (Image B). Additionally, multiple contrast-enhancing lesions are observed in the coronal section, the largest being 10 mm associated with vasogenic edema (Image C).

Due to the distribution and characteristics of the lesions, it presented a picture compatible with NCC; however, due to IgG (+) for T. gondii, cerebral toxoplasmosis was not ruled out. Therefore, since there was no laboratory study to distinguish between both entities, empirical treatment with TMP/SMZ and Albendazole with dexamethasone was given to cover both microorganisms.

During his hospital stay, management with levetiracetam was started due to an episode of clonus in the right thoracic limb. He followed an antiparasitic regimen for 21 days, achieving cessation of headache along with fever spikes. A post-treatment control MRI was performed on November 2, 2022. A mayor decrease in size and number of lesions was observed in contrast with previous MRI. Thus, antiretroviral treatment and prophylaxis was prescribed upon his discharge.

Figure 3: Contrast-enhanced MRI of the skull: An axial section is observed at the supratentorial level in FLAIR sequence (Image A), identifying a decrease in size of the previously observed hyperintense lesions. The same pattern is observed in the coronal section (Image B).

In September 2023, he attended a follow-up appointment with a new skull CT scan (Figure 4) without evidence of active lesions, electroencephalogram without epileptic
Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

activity and undetectable viral load with CD4 T lymphocytes 137.43 cells/µL. No alterations were documented in the physical examination and reported asymptomatic. It was decided to continue antiepileptic treatment.

Figure 4: Follow up head CT: An axial cut, at the ventricular level with no lesions at the level of the basal ganglia, parietal and occipital lobe.

DISCUSSION

Acquired Immunodeficiency Syndrome (AIDS) is the most severe stage of VIH, in which the diagnosis is certain when opportunistic infections present or when their CD4 cell count drops below 200 cells per milliliter of blood even in asymptomatic patient. Furthermore, opportunistic infections of the CNS in AIDS are one of the main causes of severe morbidity and mortality in this group of immunocompromised patients. The most frequent opportunistic infections of the CNS are toxoplasmosis, cryptococcosis, and tuberculosis.

The initial approach to suspected CNS infection is usually guided by clinical symptoms, detailed neurological examination, blood studies, imaging studies, and CSF profile. These findings may point toward a specific microorganism, such as bacterial, viral, fungal, neoplastic or even autoimmune. Nonetheless, in our patient, CSF analysis was normal. Therefore, due to the non-specific findings in the brain CT, it required an MRI in which, multiple ring-enhancing brain lesions were exposed.

The differential diagnosis in multiple ring-enhancing brain lesions can be neoplastic, inflammatory, sarcoidosis, Behcet disease, radiation encephalopathy, and some vasculitic disorder or infectious. Infective causes may include tuberculosis, cysticercosis, demyelinating disorders, pyogenic abscess, toxoplasmosis or fungal infections.

Due to the distribution of the lesions, clinical findings and our epidemiology, NCC infection was considered the main diagnostic possibility in our patient. This infection is likely the most common parasitic disease involving the CNS worldwide and remains a substantial burden in terms of morbidity and mortality. Seroprevalence studies report that about 12% of the Mexican population has anticisticercic antibodies and it is responsible for 20% to 25% of craniectomies performed in specialized institutions.

NCC is an heterogeneous disease due to differences in number, location, size and stage of the parasites, as well as the degree of response/host inflammatory conditions. Most symptomatic patients present between 15-40 years of age, without predilection for sex. The most common clinical findings include seizure (70%), headache, intracranial hypertension, encephalitis, and meningitis. Throughout the infection, they have been described four main pathological stages: First, the vesicular phase, which is characterized by viable parasite with intact membrane and therefore no host reaction; Second, the colloidal vesicular phase, where parasite dies within 4-5 years if untreated, or earlier with treatment and the cyst fluid becomes turbid. As the membrane becomes edema surrounding the cyst. This is the most symptomatic stage; In third place, granular nodular phase, which is marked by the diminished edema and the cyst retracts further and the enhancement persists. Finally, nodular calcified phase, end-stage quiescent calcified cyst remnant without edema nor enhancement.

Additionally, according to the location of the parasite the infection can either be intraparenchymal (in the brain and medulla tissues) or extraparenchymal. Intraparenchymal lesions are more common and are generally associated with seizures, headaches, visual or cognitive changes and focal neurologic deficits. Although intraparenchymal NCC has a more favorable outcome compared to extraparenchymal lesions, the outcome is dependent on the number of cysts and degree of inflammatory response, which may lead to an epilepsy related death. Extraparenchymal lesions have a more scattered distribution, affecting the ventricles, subarachnoid space, spine, and the eyes, therefer more diverse signs and symptoms. These are typically associated with a larger parasite burden. Due to this process, these lesions are largely correlated with a worse prognosis, mortality most commonly a result of obstructive hydrocephalus, and the effects of elevated intracranial hypertension. Consequently, the combination of lesion location and evolutionary stage of lesions results in a wide array of clinical presentations. In Table 1 we show nonexclusive categorization of these lesions.
Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

Table 1: Types of neurocysticercosis.\textsuperscript{16}

<table>
<thead>
<tr>
<th>Location</th>
<th>Stage</th>
<th>Perilesional Inflammation/edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenchymal (single or multiple)</td>
<td>Viable</td>
<td>Variable</td>
</tr>
<tr>
<td></td>
<td>Degenerating</td>
<td>Usually present and marked</td>
</tr>
<tr>
<td></td>
<td>Calcified</td>
<td>May be present (associated with symptoms)</td>
</tr>
<tr>
<td>Extra parenchymal, intraventricular</td>
<td>Viable or in degeneration, rarely calcified</td>
<td>No</td>
</tr>
<tr>
<td>Extra parenchymal, subarachnoid</td>
<td>Viable or in degeneration, rarely calcified</td>
<td>Arachnoiditis or pachymeningitis, occasionally without a defined parasitic lesion</td>
</tr>
</tbody>
</table>

The diagnosis of NCC should be suspected in any patient with neurological symptoms who lives in endemic areas or patients with travel history to endemic areas, staying prolonged periods of time.\textsuperscript{13} Moreover, the diagnosis is based on the sum of epidemiological, clinical, radiological and immunological data (detection tests for antiticisticercus antibodies in blood and CSF).\textsuperscript{14}

There are multiple tests intended to identify antiticisticercus antibodies in blood, saliva and CSF, among which stand out: the complement fixation reaction, the antigen-detection enzyme-linked immunosorbent assay (ELISA) and the immunoblot. These tests are useful, but should never be used in isolation to confirm or rule out the diagnosis of neurocysticercosis, due to the high percentage of false-positives and false-negatives.\textsuperscript{13}

Neuroimaging techniques, such as CT and MRI, have been efficient for the diagnosis of neurocysticercosis, by providing objective evidence of the number and location of the lesions, their stage, and degree of host inflammation.\textsuperscript{13} In general terms, MRI is more sensitive than CT in detecting parenchymal and extraparenchymal disease, although its sensitivity to detect calcified lesions, particularly small ones, is quite limited.\textsuperscript{16}

Parenchymatous presentation it is distinctive by its nodular calcifications <20 mm in diameter (often 1 to 5 mm) with or without surrounding edema and/or contrast enhancement, cystic or nodular enhancing lesion <2 cm in size and in brain/medullar tisse, vesicular lesions often with evidence of associated contrast enhancement and/or surrounding edema. The scolex is often visible on high-definition imaging.\textsuperscript{17}

By contrast, in the extra parenchymatous form there are three main sites of affection: Intraventricular where you can see the parasite within the ventricles, obstructive hydrocephalus or loculated hydrocephalus with disproportionate dilatation of the ventricles (suggestive of a cysticercus). Subarachnoid form where the cysticerci can be seen in the Sylvian fissure, in the basilar cisterns, or interhemispheric spaces as well as strokes or meningitis without discrete cysts. Finally, spinal form where you can see cysticerci within the spinal subarachnoid space with or without evidence of inflammation/diffuse spinal arachnoiditis as well as intramedullary cysticerci within the spinal cord.\textsuperscript{17}

As a resut, diagnosing NCC can be complicated due to clinical manifestations are nonspecific, most neuroimaging findings are not pathognomonic, and some serologic tests have low sensitivity and specificity.\textsuperscript{14} This is why, a unified set of criteria for NCC has helped to standardize its diagnosis in different settings (Table 2)\textsuperscript{18} as could be observed in our patient, who met neuroimaging criteria as enhancing lesions and cystic lesions without a discernible scolex that resolved after cytocidal drug therapy in addition to clinical manifestations suggestive of NCC.

Table 2: Diagnostic criteria and degrees of diagnostic certainty for neurocysticercosis.\textsuperscript{18}

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absolute criteria:</strong></td>
</tr>
<tr>
<td>• Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion.</td>
</tr>
<tr>
<td>• Visualization of subretinal cysticercus.</td>
</tr>
<tr>
<td>• Conclusive demonstration of a scolex within a cystic lesion on neuroimaging studies.</td>
</tr>
<tr>
<td><strong>Neuroimaging criteria:</strong></td>
</tr>
<tr>
<td>Major neuroimaging criteria:</td>
</tr>
<tr>
<td>• Cystic lesions without a discernible scolex.</td>
</tr>
<tr>
<td>• Enhancing lesions.</td>
</tr>
<tr>
<td>• Multilobulated cystic lesions in the subarachnoid space.</td>
</tr>
<tr>
<td>• Typical parenchymal brain calcifications.</td>
</tr>
<tr>
<td>Confirmative neuroimaging criteria:</td>
</tr>
<tr>
<td>• Resolution of cystic lesions after cysticidal drug therapy.</td>
</tr>
</tbody>
</table>
Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

- Spontaneous resolution of single small enhancing lesions.
- Migration of ventricular cysts documented on sequential neuroimaging studies.
  
  Minor neuroimaging criteria:
  - Obstructive hydrocephalus (symmetric or asymmetric) or abnormal enhancement of basal leptomeninges.

<table>
<thead>
<tr>
<th>Clinical/exposure criteria:</th>
</tr>
</thead>
</table>

- Major clinical/exposure:
  - Detection of specific anticysterceral antibodies or cysticercal antigens by well-standardized immunodiagnostic tests.
  - Cysticercosis outside the central nervous system.
  - Evidence of a household contact with T. solium infection.

- Minor clinical/exposure:
  - Clinical manifestations suggestive of neurocysticercosis.
  - Individuals coming from or living in an area where cysticercosis is endemic.

### Degrees of diagnostic certainty

#### Definitive diagnosis:
- One absolute criterion.
- Two major neuroimaging criteria plus any clinical/exposure criteria.
- One major and one confirmative neuroimaging criteria plus any clinical/exposure criteria.
- One major neuroimaging criteria plus two clinical/exposure criteria (including at least one major clinical/exposure criterion), together with the exclusion of other pathologies producing similar neuroimaging findings.

#### Probable diagnosis:
- One major neuroimaging criteria plus any two clinical/exposure criteria.
- One minor neuroimaging criteria plus at least one major clinical/exposure criterion.

An important differential diagnosis to consider in our patient was cerebral toxoplasmosis, which is a parasitic disease resulting, in most cases, from a reactivation of a latent cyst with *Toxoplasma gondii* caused by immunosuppression, and a definitive disease for AIDS. Cats and other felines are the definitive hosts of *Toxoplasma gondii* and symptoms are usually subacute and develop over a few days. The most typical ones include headaches, disorientation, and fever. The diagnosis of this entity is established with a combination of ancillary tests (presence of antibodies, imaging methods, low CD4 lymphocyte count – below 100 ml/l), as well as the clinical picture consistent with the disease. The typical MRI findings are an eccentric target sign on post-contrast T1-weighted sequences (which has 95% specificity and less than 30% sensitivity) and a concentric target sign on T2-weighted imaging. The patient had risk factors, such as exposure to cats and immunosuppression, although he met the immunological criteria for toxoplasma, the distribution of the images was not totally compatible for this condition. Despite so, it was decided to provide treatment with trimethoprim sulfamethoxazole, as a therapeutic and prophylactic measure, considering his CD4 range.

Treatment of NC should be individualized and symptomatic treatment, anthelmintic drugs (AHDs), and surgery should be considered depending on location and parasite viability and clinical manifestations. Symptomatic medication, including analgesics, antiepileptic drugs, mannitol, and steroids, should be individualized depending on the patient’s requirements. Implementing antiparasitic therapy is never urgent and should only be a consideration after initial symptomatic therapy. In patients with 1-2 enhancing lesions is recommended albendazole monotherapy dosed at 15 mg/kg/d (recommend a maximum dose of 1200 mg) in 2 daily doses for 10–14 days. In contrast, for patients with >2 viable parenchymal cysticerci is recommend albendazole (15 mg/kg/day) combined with praziquantel (50 mg/kg/day) for 10–14 days. Corticosteroids have been used to suppress the inflammatory response as cysts degenerate by antiparasitic therapy, as a result is recommending adjunctive corticosteroid therapy begun prior to antiparasitic drugs in all patients treated with antiparasitic therapy.

**CONCLUSION**

Even though Neurocysticercosis is not a rare disease, our group decided to publish this case report because its association with an HIV positive patient, in which has not been yet linked to, in behalf of the lack of evidence and studies, considering the ethical issue of performing routine head CT scans in asymptomatic individuals. However, ring enhancing lesions have several differential diagnosis in which the medical team has to individualize each patient and his medical history such as his clinical presentation. In this case, we can conclude, based on the diagnostic criteria, that our patient with AIDS confirmed and ring enhanced lesions, had 2 major imaging criteria plus an exposure/clínical criteria, therewise it is a definitive diagnosis with a favourable clinical result after symptomatic and antiparasitic treatment.
Neurocysticercosis with Classic Ring Enhancing Lesions in a Patient with AIDS: Case Report, Diagnostic Approach and Literature Review

INTEREST CONFLICT
The authors declare that they have no conflict of interest regarding this publication.

REFERENCES


