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# Anterior Cerebral Artery Infarction as the Initial Presentation of Advanced HIV-Associated Cryptococcal Meningitis: A Case Report

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## Abstract

**Background:** Cryptococcal Meningitis (CM) remains a leading cause of mortality among individuals with advanced Human Immunodeficiency Virus Infection (HIV), particularly in sub-Saharan Africa. Cerebrovascular complications are increasingly recognized in CM; however, large-vessel territorial infarctions as the initial manifestation are rare. Infarction within the Anterior Cerebral Artery (ACA) distribution is particularly uncommon and may mimic primary ischemic stroke, creating diagnostic challenges.

**Case Report:** We report a 40-year-old Ugandan male with previously undiagnosed advanced HIV infection who presented with a three-week history of progressive headache, low-grade fever, weight loss, and cognitive decline, followed by acute onset right lower limb weakness and urinary incontinence. Neurological examination revealed abulia, reduced spontaneous speech, and right lower limb weakness (power 2/5) with upper motor neuron signs. HIV testing was positive with a CD4 count of 29 cells/μL. Cerebrospinal Fluid (CSF) analysis demonstrated encapsulated budding yeasts on India ink staining and positive cryptococcal antigen, confirming cryptococcal meningitis. Non-contrast brain CT revealed a hypodense lesion in the medial left frontal lobe consistent with an ACA territory infarction without hemorrhagic transformation. The patient received induction therapy with single-dose liposomal amphotericin B combined with flucytosine and high-dose fluconazole, in accordance with 2022 World Health Organization recommendations and evidence from the AMBITION-cm trial. Serial therapeutic lumbar punctures were performed for intracranial pressure control. Aspirin was initiated cautiously for secondary stroke prevention. Clinical improvement was observed, with partial neurological recovery at discharge.

**Conclusion:** This case illustrates a rare presentation of advanced HIV-associated cryptococcal meningitis manifesting initially as an ACA territory infarction. In high HIV-burden settings, acute focal neurological deficits in young patients without conventional vascular risk factors should prompt evaluation for opportunistic central nervous system infections. Early recognition and combined management of infectious and cerebrovascular pathology are critical to improving outcomes.

**Keywords: Cryptococcal meningitis; HIV infection; Cerebral infarction; Anterior cerebral artery; Opportunistic infections**

## Introduction

Cryptococcal Meningitis (CM) remains one of the most life-threatening opportunistic infections in individuals with advanced Human Immunodeficiency Virus (HIV) infection [1]. Despite the expansion of Antiretroviral Therapy (ART) programs globally, CM continues to contribute substantially to AIDS-related mortality, particularly in sub-Saharan Africa, where late HIV presentation remains common [2]. Recent estimates suggest that CM accounts for approximately 15% of AIDS-related deaths worldwide, predominantly among patients with CD4 counts below 100 cells/μL [2].

In response, the World Health Organization (WHO) recommends routine Cryptococcal Antigen (CrAg) screening in patients with advanced HIV disease, alongside prompt initiation of amphotericin B–based induction therapy followed by high-dose fluconazole for consolidation and maintenance to improve survival outcomes [3].

Clinically, HIV-associated CM typically presents insidiously over days to weeks, with persistent headache, fever, nausea, progressive cognitive impairment, and features of raised Intracranial Pressure (ICP) [4]. Elevated Cerebrospinal Fluid (CSF) opening pressure–often exceeding 25

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cmH2O – occurs in more than half of cases and is strongly associated with neurological deterioration and increased mortality if not managed with serial therapeutic lumbar punctures [4,5].

Although focal neurological deficits may occur, they are usually associated with advanced disease, hydrocephalus, cryptococcomas, or secondary complications rather than as an initial presentation [6]. Increasing evidence indicates that cerebrovascular complications in CM are underrecognized, with ischemic infarctions reported in 13% to 26% of cases, most commonly affecting small perforating vessels supplying the basal ganglia, thalami, and internal capsule [6,7].

Large-vessel territorial infarctions, however, are uncommon. In particular, involvement of the Anterior Cerebral Artery (ACA) territory is rarely reported in CM [6]. ACA infarctions typically manifest with contralateral lower limb weakness, abulia, behavioral changes, and executive dysfunction, often mimicking primary ischemic stroke [8].

HIV infection itself further increases the risk of ischemic stroke, especially in the setting of uncontrolled viremia and severe immunosuppression [9]. Most reported cases of CM-associated infarction occur during established infection or following ART initiation in the context of Immune Reconstitution Inflammatory Syndrome (IRIS) [10]. In contrast, cerebral infarction as the initial presentation of previously undiagnosed advanced HIV-associated CM is rare.

Such atypical presentations create significant diagnostic challenges, as management of acute ischemic stroke differs fundamentally from that of opportunistic central nervous system infections. Delayed recognition of an infectious etiology may lead to postponement of antifungal therapy, which remains the most critical determinant of survival [3,5].

We report a case of advanced HIV-associated cryptococcal meningitis presenting as an anterior cerebral artery territory infarction, highlighting the importance of maintaining a high index of suspicion for opportunistic CNS infections in immunocompromised patients presenting with acute focal neurological deficits, particularly in high HIV-burden settings.

## Case Presentation

A 40-year-old male was admitted to Bwera General Hospital in February 2026 with a three-week history of progressively worsening headaches. Initially, the headaches were intermittent, mild, and diffuse, but they gradually became persistent, dull, bifrontal, and moderate in intensity. They were partially relieved by simple analgesics early in the course but later became refractory. The pain was worse in the early morning and occasionally associated with nausea, without projectile vomiting. He had no prior history of chronic headaches or migraine.

During the same period, he developed low-grade intermittent fever, progressive fatigue, reduced appetite, and unintentional weight loss of approximately 4 kg to 5 kg. Family members also reported gradual behavioral changes, including apathy, reduced speech output, slowed responses, decreased social interaction, forgetfulness, and impaired attention. No seizures were reported.

Five days prior to admission, his headache worsened significantly and became continuous, accompanied by repeated episodes of non-projectile vomiting and increasing cognitive slowing. One day before presentation, he developed sudden-onset weakness predominantly affecting the right lower limb, which was maximal at onset and non-progressive. This resulted in inability to stand or walk without support. The weakness was associated with urinary incontinence and further reduction in spontaneous speech. The right upper limb was mildly weak but remained functional. There was no loss of consciousness, seizures, or head trauma.

His past medical history was unremarkable, with no known hypertension, diabetes, cardiovascular disease, or prior chronic illness. He had never been tested for HIV and was not on any regular medications. There was no history suggestive of tuberculosis, intravenous drug use, or immunosuppression. Family and social history were non-contributory.

On examination, he appeared ill with a Glasgow Coma Scale score of 12/15 (E3V4M5). His temperature was 37.9°C, blood pressure 118/74 mmHg, pulse 92 beats per minute, and oxygen saturation 97% on room air. Neurological examination revealed reduced spontaneous speech, abulia, mild disorientation to time, and impaired attention. Cranial nerves were intact. Motor examination showed right lower limb weakness (power 2/5) with increased tone, hyperreflexia, and an upgoing plantar reflex. The right upper limb had mild weakness (power 4/5), while the left side had normal strength. There was mild sensory reduction in the right lower limb. He was unable to ambulate. Mild neck stiffness was present, though Kernig's and Brudzinski's signs were negative. Other systemic examinations were unremarkable.

**Diagnostic assessment**

Initial laboratory investigations revealed leukocytosis (white blood cell count 20.78 × 109/L with neutrophilia (74.6%) and lymphopenia (16.5%). HIV testing was positive, with CD4 count of 29 cells/mm3, consistent with advanced HIV disease.

Lumbar puncture was performed. Cerebrospinal Fluid (CSF) was clear and normal glucose (2.7 mml/L). Indian ink staining: Encapsulated budding yeasts consistent with cryptococcus neoformans and cryptococcal antigen testing were positive, meningitis. TB LAM testing negative as shown in summary in Table 1.

Non-contrasted CT brain- shows hypodense lesion in the medial aspect of the left frontal lobe, distribution consistent with Anterior Cerebral Artery (ANCA) infarction, no hemorrhagic transformation as shown in Figure 1.

**Diagnosis**

Based on clinical presentation, neurological findings and CSF analysis and CT brain results, a diagnosis of anterior cerebral artery infarction as


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initial presentation of advanced HIV-associated cryptococcal meningitis was made.

**Management**

Patient was admitted to HDU-at Bwera general hospital, in accordance with the 2022 updated recommendations from the World Health Organization, and evidence from AMBITION-cm trial, single dose of IV-Liposomal Amphotericin B (L-AmB) 520 mg (10 mg/kg) on day 1, combined with orally flucytosine 1,300 mg QID for 14 days, and orally fluconazole 1,200 mg once a daily for 14 days. Therapeutic lumbar puncture was done daily for 3 days where 20 ml were removed every day. Adequate hydration and close monitoring of renal function and electrolyte were measured.

The concomitant ischemic ACA infarction was managed conservatively alongside antifungal therapy. Aspirin 75 mg od was started after careful assessment of bleeding risk in the context of repeated lumber punctures. Blood pressure was optimized to maintain adequate cerebral perfusion without increasing the risk of hemorrhagic transformation. Mechanical thromboprophylaxis, swallowing assessment and early physiotherapy were instituted to prevent complications of immobility and support neurological recovery.

From a neurological perspective, there was partial recovery of deficits after 10 days in the ward his GCS become 15/15 with improvement in motor strength compared to admission. Residual limb weakness persisted, but he was able to mobilize with minimal assistance. There was no new focal neurological deficits, seizures, or evidence of hemorrhagic transformation of follow-up clinical assessment.

Patients were discharged after 14 days and given consolidation therapy with fluconazole 800 mg orally once a daily for 8 weeks followed by maintenance therapy with fluconazole 200 mg once daily for 1year or when CD4 >200 cell/L reached. Also, low dose aspirin for secondary stroke prevention and a structure physiotherapy plan. And ART initiated after 4 weeks after initiation of ant-fungal therapy.

## Discussion

Cryptococcal Meningitis (CM) remains a major cause of morbidity and mortality among individuals with advanced HIV infection, particularly those with CD4 counts below 100 cells/μL [1,2]. In this case, a 40-year-old man with previously undiagnosed HIV infection presented with acute right lower limb weakness, with subsequent evaluation revealing severe immunosuppression (CD4 29 cells/μL), positive serum and Cerebrospinal Fluid (CSF) cryptococcal antigen, and Anterior Cerebral Artery (ACA) territory infarction. This represents a rare presentation in which a cerebrovascular event served as the initial manifestation of CM.

The patient's preceding three-week history of progressive headache, low-grade fever, malaise, and cognitive slowing is characteristic of CM and likely reflects evolving meningeal inflammation and raised Intracranial Pressure (ICP) [4]. Headache occurs in up to 90% of CM cases and frequently precedes focal neurological deficits [4]. Behavioral changes such as abulia and reduced spontaneous speech in this patient are consistent with medial frontal lobe dysfunction, supporting involvement of the ACA territory [8].

Cerebrovascular complications in CM are increasingly recognized but remain underdiagnosed. Most reported infarctions involve small perforating vessels supplying deep brain structures such as the basal ganglia and thalami [6,7]. In contrast, large-vessel infarctions, particularly involving the ACA territory, are rare. Similar cases described in the literature suggest that stroke may occur either during established CM or, less commonly, as an initial presentation, especially in patients with advanced immunosuppression [10,11].

Several pathophysiological mechanisms may explain ischemic stroke in CM. These include:

(1) Inflammatory vasculitis, characterized by direct fungal invasion of vessel walls leading to inflammation and luminal narrowing; (2) Non-inflammatory vasculopathy, involving endothelial dysfunction and vascular injury without overt inflammation; (3) Thrombotic occlusion, driven by cytokine-mediated hypercoagulability and HIV-associated prothrombotic states; and (4) ICP-related vascular compromise, where markedly elevated intracranial pressure reduces cerebral perfusion or causes mechanical compression of cerebral vessels [6,7,9,12,13].

In this patient, the subacute meningeal symptoms, severe immunosuppression, and absence of traditional vascular risk factors suggest that infectious vasculopathy possibly compounded by raised ICP was the most likely mechanism.

Important differential diagnoses were considered. Primary ischemic stroke due to atherosclerotic disease was unlikely given the patient's age and absence of conventional risk factors. HIV-associated vasculopathy remains a possibility; however, the presence of confirmed cryptococcal infection with compatible clinical features favors a secondary infectious mechanism [9]. Cardioembolic stroke was considered less likely due to the absence of cardiac symptoms, normal cardiovascular examination, and lack of known arrhythmia. Other central nervous system infections, particularly tuberculous meningitis, were also considered; however, negative TB Lipoarabinomannan (LAM) testing and positive cryptococcal antigen in CSF supported CM as the primary diagnosis.

Neuroimaging demonstrated a hypodense lesion in the medial left frontal lobe consistent with ACA territory infarction, without hemorrhagic transformation. However, advanced imaging such as Magnetic Resonance Imaging (MRI), Computed Tomography Angiography (CTA), or Magnetic Resonance Angiography (MRA) was not available. As a result, direct visualization of vascular pathology (e.g., vessel narrowing, vasculitis, or thrombosis) could not be performed. This limitation restricts definitive characterization of the underlying stroke mechanism and should be considered when interpreting this case [4].

Management required a dual approach targeting both infection and cerebrovascular complications. Induction antifungal therapy with liposomal Amphotericin B, flucytosine, and high-dose fluconazole was initiated in accordance with World Health Organization (WHO) recommendations and supported by the AMBITION-cm trial, which demonstrated improved survival with single-dose liposomal Amphotericin B–based regimens


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[3,14]. Serial therapeutic lumbar punctures were performed to manage elevated ICP, a key determinant of survival in CM [5].

The use of antiplatelet therapy in CM-associated stroke is not well established. In this case, low-dose aspirin was initiated after careful assessment of bleeding risk in the context of repeated lumbar punctures. The decision was based on the presumed ischemic mechanism and absence of contraindications, although evidence guiding this practice remains limited.

Antiretroviral Therapy (ART) was initiated four weeks after antifungal treatment, consistent with current recommendations to delay ART in CM to reduce the risk of Immune Reconstitution Inflammatory Syndrome (IRIS), which may worsen intracranial inflammation and clinical outcomes [3,10]. This timing reflects a balance between controlling opportunistic infection and restoring immune function.

CM complicated by stroke is associated with increased mortality and poorer functional outcomes [6]. Early recognition and prompt antifungal therapy in this patient likely contributed to neurological improvement, although residual deficits highlight the need for ongoing rehabilitation.

## Limitations

This case report has several limitations. It represents a single patient, limiting generalizability. Advanced neuroimaging, including MRI and vascular imaging (CTA/MRA), was not available, preventing detailed assessment of vascular pathology and definitive differentiation between vasculitis, vasculopathy, and thrombosis. In addition, a comprehensive stroke workup—including cardiac evaluation and extended vascular risk assessment—was not performed. CSF opening pressure was not documented, limiting assessment of the contribution of raised intracranial pressure. Finally, the short follow-up period precludes evaluation of long-term neurological and functional outcomes. These limitations restrict causal inference and highlight the need for further studies.

## Conclusion

This case demonstrates that cryptococcal meningitis may rarely present as a large-vessel ischemic stroke, particularly in individuals with advanced HIV infection. In high HIV-burden settings, acute focal neurological deficits in patients without traditional vascular risk factors should prompt evaluation for opportunistic central nervous system infections. Early recognition, appropriate antifungal therapy, and careful integration of stroke management are essential to improving outcomes in this complex clinical scenario.

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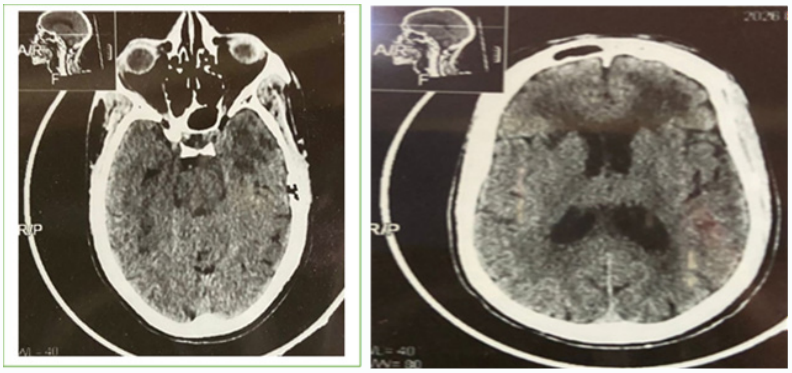

**Figure 1:** Image shows ischemia of anterior left side anterior part of the brain, and dilated ventricles.

**Table 1:** Summary of key laboratory and CSF findings.

| Test Name | Result | Normal Range | Interpretation |
|---|---|---|---|
| WBC | $9.81 \times 10^9$/L | 4.00–11.00 | Normal |
| Neutrophils (%) | 79.6% | 40–70% | high |
| Lymphocytes (%) | 16.5% | 20–40% | low |
| Hemoglobin (Hb) | 15.5 g/dL | 12–16 | Normal |
| RBC | $4.81 \times 10^{12}$/L | 3.8–6.0 | Normal |
| Platelets (PLT) | $260 \times 10^9$/L | 150–450 | Normal |
| CSF Protein | 1.8 g/L | 0.15–0.4 | High |
| CSF Glucose | 2.47 mmol/L | 2.5–4.0 | Low |
| CSF Cell Count | $0.0 \times 10^6$/L | Up to 5 | Low |
| India Ink | Positive | Negative | Positive for encapsulated yeast |
| Serum/CSF CRAG | Positive | Negative | Positive |
| CD4 Count | 29 cells/$mm^3$ | >200 | Severely immunocompromised |



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