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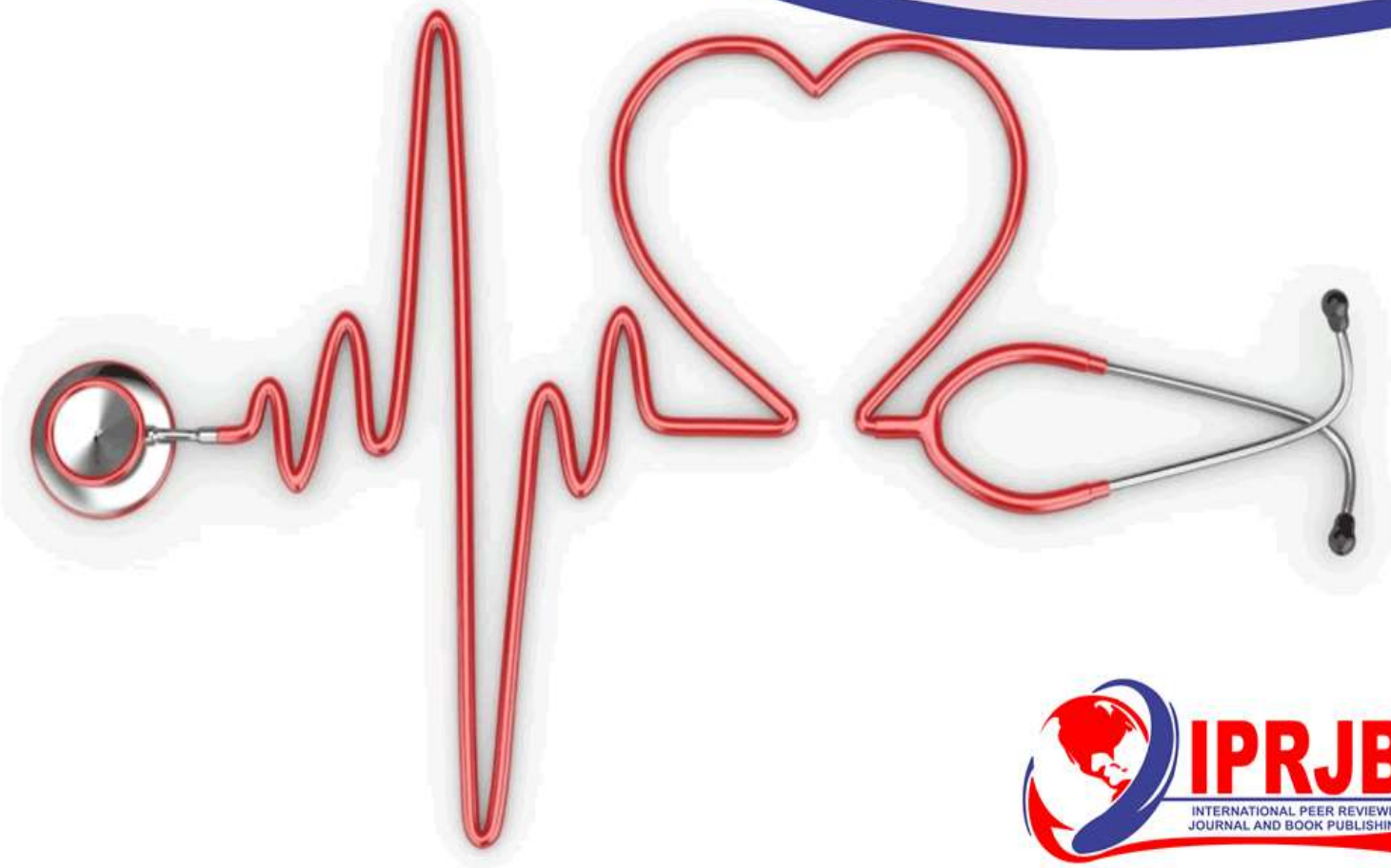

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CNS Cryptococcoma in an Immunocompetent Adult from a Low Resource Setting: An Illustrative Case Report

David Kitya FCS-ECSA[1*], Joseph M Ssembatya MBChB, Blessing M Taremwa FCS-ECSA[1], Herve M Lekuya FCS-ECSA[1], Josephine Najjuma MNS[1], Raymond Atwine MMed Pathology[2], Vallence Niyonzima MNS[3], Fuller T Anthony MScGH[4]

[1]Division of Neurosurgery, Mbarara University of Science and Technology, Mbarara, Uganda
[2]Department of Pathology, Mbarara University of Science and Technology, Mbarara, Uganda
[3]Department of Nursing, Mbarara University of Science and Technology, Mbarara, Uganda
[4]Division of Global Neurosurgery and Neurology, Duke University, Durham, NC, USA

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Abstract

Purpose: Cryptococcal infection in the Central Nervous System (CNS) is frequently seen in human immunodeficiency virus (HIV) patients and others with low immunity. CNS cryptococcoma in immunocompetent patients is rare. We present a case of CNS cryptococcoma in an immunocompetent patient and review literature.

Methodology: A 62-year-old, HIV negative, immunocompetent female patient with no known chronic illness, presented with 5 months' history of a progressive headache, associated with on and off episodic generalized convulsions. She had been to several hospitals before referral to our center with a diagnosis of a brain tumor on CT scan imaging. Before this and despite a negative CSF analysis result, she had received treatment for bacterial meningitis with no success.

Findings: At Mbarara Regional Referral Hospital (MRRH), she had surgery with excision biopsy which showed features consistent with cryptococcosis on histology. The patient had a successful adjuvant treatment with antifungal drugs following surgery.

Unique Contribution to Theory, Practice and Policy: The diagnosis of a CNS cryptococcal infection in an immunocompetent patient and its successful treatment by including surgery, were both unusual. Fatal postsurgical outcomes have been reported by other authors who favor a totally conservative approach to the treatment of this lesion.

Keywords: *Cryptococcal Meningitis, Immunocompetent Patient, Uganda*

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INTRODUCTION

Disseminated cryptococcus infection, including cryptococcal meningitis (CM), is predominantly caused by cryptococcus neoformans or Gattii[1]. Over the years the incidence of CM has increased and 90% of those living with HIV are retroviral naïve[2]. CM diagnosis in an immunocompetent patient is exceedingly rare[2]. Generally, the diagnosis of this condition requires a high index of suspicion among health workers. In general, all reported cases of CM infection in the brain have a fatal outcome[3 4 5]. Reported predisposing factors for cryptococcal infection include HIV infection, diabetes mellitus, cancer, solid organ transplant, chemotherapeutic agents, corticosteroid therapy, hepatic failure, renal failure/dialysis, lung diseases, and haematological malignancies[2].

The clinical presentation of CM is nonspecific and usually runs in a chronic or subacute course. Depending on the location, it manifests with headache, fever, vomiting, altered consciousness, seizure, vision loss, behaviour changes, and cognitive impairment[6].

The identification of Cryptococcus in the cerebrospinal fluid (CSF) or cryptococcal antigen is sufficient for the diagnosis of this condition. Nevertheless, brain imaging is necessary in patients suspected of CM before carrying out lumbar puncture as this may cause herniation in those with increased intracranial pressure.

Brain magnetic resonance imaging (MRI) or computed tomography (CT) scanning help to differentiate CM from other infectious or parasitic diseases and neoplasms like glioma. The typical characteristics of neuroimaging alterations include dilated Virchow-Robin (V-R) spaces, pseudocyst, cryptococcomas, and leptomeningeal enhancement.

Cryptococcal meningeal disease is commonly found at the bases of the brain, though, it can also involve the choroid plexus, perivascular spaces and the parenchyma[7]. This infection is prevalent among the immunosuppressed where conservative management usually leads to a poor outcome.

At Mbarara Regional Referral Hospital (MRRH), we are presenting a rare and challenging case of an immunocompetent female patient who was successfully treated for a confirmed disease of cryptococcal meningitis. In this case report, we described the clinical presentation, investigations we carried out, treatment including surgery, as well as a brief review of the related literature of this rare medical condition.

PATIENT AND METHODS

Case Presentation

Patient Description

The patient was a 62-year-old female, fulltime housewife who participated in cattle rearing with no known chronic illnesses. She reported no relevant social, environmental, or family history. She did not smoke or drink alcohol. She has nine children. She presented to our hospital with a five-month history of a progressive headache which had no known relieving or exacerbating factors. This was associated with generalized convulsions and on-and-off episodes of vomiting for one month prior to admission. There was no reported blurring of vision. She had been receiving treatment against bacterial meningitis from a private facility, though CSF results were negative.

In the review of other systems, there was nothing remarkable; in particular, there was no history of fever, cough, chest pain, or difficulty in breathing.

On admission, the blood pressure (BP) was 138/68_ mmHg heart rate (HR) of_ 64 bpm and temperature_ 36.8ºC. She was not wasted, not pale, not jaundiced or dehydrated. She was fully conscious, had soft neck, and with no focal neurological deficits detected other than power of 4/5 in all limbs.

Examination of all other systems showed normal findings. There were no suspicious lesions for primary tumors found.

RESULTS

Investigations Done before Presentation and Findings

Laboratory tests showed white blood cell count (WBC) of $10.56x10^9$/L (differential counts were normal, no eosinophilia), hemoglobin concentration (HGB) of 13.9gms/dl, and platelets of $210x10^9$/L. CSF results: macroscopy: slightly xanthochromia, glucose: 16.7mg/dl (40.0-75.0), Proteins: 1.10g/dl (1.5-4.5), Gram stain: no gram organisms seen, Zn: No AFB seen, India ink: Negative. The following tests were negative: liver function tests (LFTs), Typhoid fever antibody titers, TPHA, HIV serology (CD4 count: 468 U/L), Gene expert for tuberculosis (TB), and Toxoplasmosis Gondii antibody titers. We did not have any repeat CSF analysis in our center.

A non-contrasted brain CT scan, Figure 1 showed a cystic lesion in the left temporal lobe with a hyperdense lesion in its medial wall. A cranial MRI study from a facility in Kampala, which is a 5-hour drive by road from our hospital, showed a left temporal cystic dilatation with similar intensity to CSF on all sequences surrounded by perilesional oedema in the temporal lobe. There was leptomeningeal enhancement, also affecting the ependyma and the choroid plexus. It also showed a fibrous connection with the atrium of the left lateral ventricle, which could be the glomus of the choroid plexus, Figures 2-4.

The differential diagnosis at this stage were: cerebral abscess with features of meningoencephalitis, cerebral metastases, astrocytoma, glioblastoma multiforme, or any parasitic cyst. In view of this, we decided to perform an excision biopsy.

Approach for Surgery, Findings and Definitive treatment

Under general anesthesia, we performed a left craniotomy and opened the dura. Through a left middle temporal gyrus, we approached the lesion and drained the cyst. Then we carefully excised the included firm mass which had a consistency of small inspissated granular aggregations, a gross total resection was achieved as shown in the follow up CT scan images, Figure 5 A, B and C. The craniotomy wound was closed in the usual way. The patient spent one night in ICU. The immediate post-operative period was uneventful, her normal speech and vision were preserved, and she was ambulating without support before discharge. She continued with Phenytoin _300mg per day.

Histology results from two separate laboratories showed features consistent with cryptococcal infection, Figure 6 A, B and C. She requested for discharge on day eleven post-surgery because she wanted to continue with adjuvant treatment near her home. The antifungal treatment she received included intravenous (IV) Flucytosine 100mg/kg once daily for 7 days, IV Amphotericin B 50mg once daily for 5 days, and supportive treatment.

About nine months after surgery, she is well at home, living an independent life, though she still gets occasional short attacks of headache.

Discussion

Intracranial cryptococcal infection is a rare situation in immunocompetent patients. The incidence of intracranial cryptococcoma that is characterized by accumulation of cryptococcus and inflammatory cells is even much less common[8]. CNS cryptococcosis produces a wide variety of MRI features that may vary depending on the immunological status of the patient. Chronic granulomatous reactions caused by C. neoformans are more common in immunocompetent hosts than in those with immunosuppression[9]. Major symptoms and signs can be attributed to intracranial hypertension and compression of adjacent structures and blurred by the non-specific location of the lesion. This is worsened by absence of an immunosuppressed history and other clinical findings in HIV positive patients. Without that guidance, the diagnosis of CNS cryptococcoma can be quite challenging for neurosurgeons[8].

In our case the diagnosis of CNS cryptococcoma was missed before surgery. There was no specific clinical picture, and all imaging studies showed a cystic lesion in the left temporal lobe simulating a primary or secondary tumour. The diagnosis was only settled on histology following resection of the swelling. Though, probably we could have made the same diagnosis if we repeated CSF examination and found it positive. This would have rendered the operation redundant. There was no clinical suspicion because the patient was thought to be immunocompetent (CD4 count=468). Nevertheless, several investigators reported a fatal outcome following conservative treatment for this condition. We had only one patient, not confounded by immunosuppression, she had surgery followed by adjuvant antifungal treatment. She survived, well and she is non-dependent at home.

Conclusion

The diagnosis of cryptococcal CNS infection in this patient was unexpected. The clinical picture was different from that seen in immunocompromised patients. Imaging characteristics were similar to those for neoplasms (primary or secondary) or other pyogenic infections. A diagnosis of cryptococcoma was made on histology after surgery, though CSF analysis could help in some cases. The patient did well on surgery and adjuvant antifungal treatment.

We recommend a high index of suspicion among clinicians especially those who work in endemic regions for CNS Cryptococcal meningitis infection. Surgery may lead to a good outcome in some selected patients with this condition.

Figure Legends

Figure 1

Non-contrasted CT Scan images (Axial views) taken. Images show a cystic lesion with similar density to CSF in the left temporal lobe with a hyper dense /calcifying component in its medial wall, probably thickened choroid plexus (the glomus). There was mild perilesional oedema.

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Axial Views

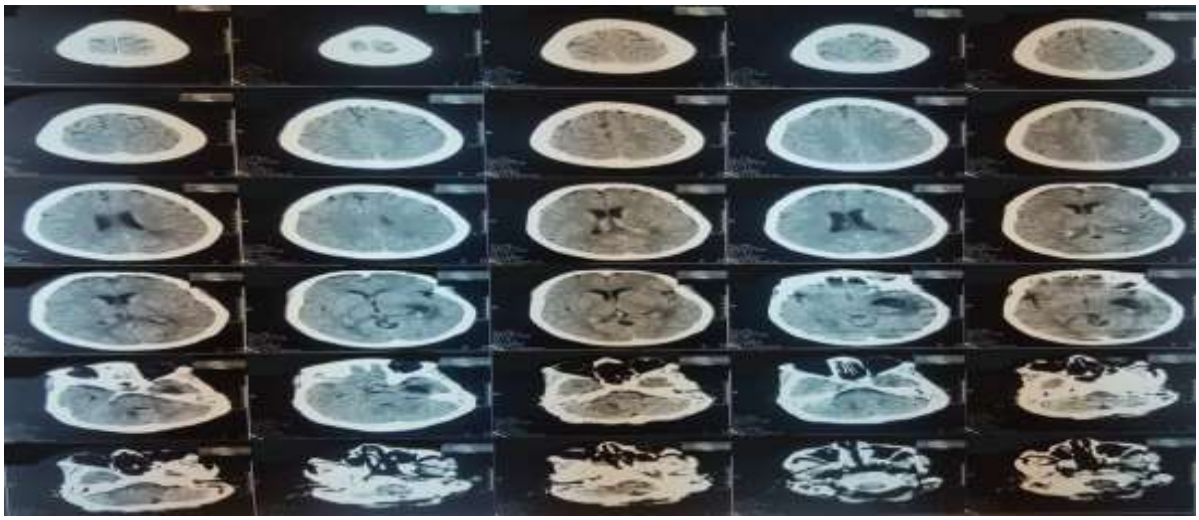

Figure 1: Axial Views

Figures 2 shows MRI images with left temporal cystic lesions of similar intensity to CSF surrounded by perilesional oedema. There is fibrous connection with the antrum of the left ventricle. This could be thickened glomus.

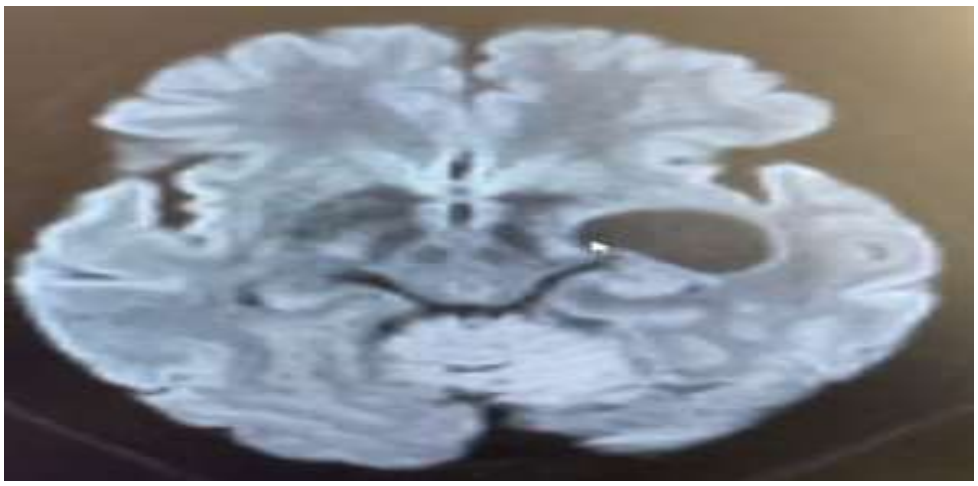

Figure 2a: Axial T1 MRI Image

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Figure 2b: Coronal T2 MRI Image

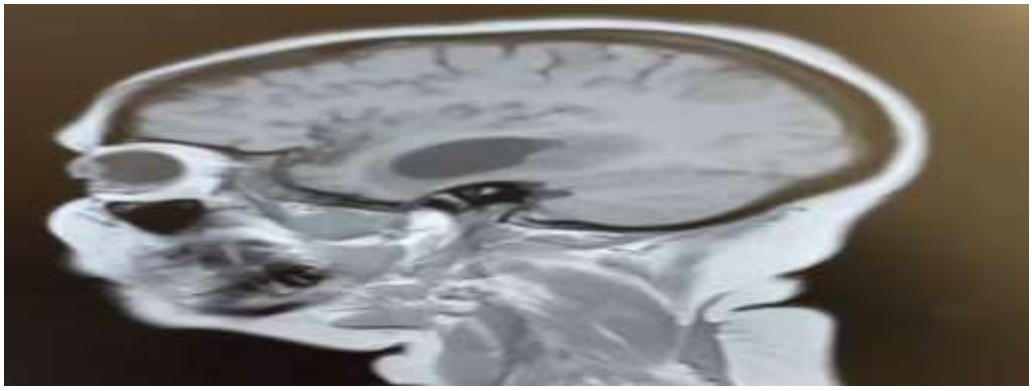


Figure 2c: Sagittal MRI with a Flare

Fig_5A-5C show post-operative non contrasted cranial CT scans images, axial views, showing that gross total resection was achieved, and the brain was relaxed.

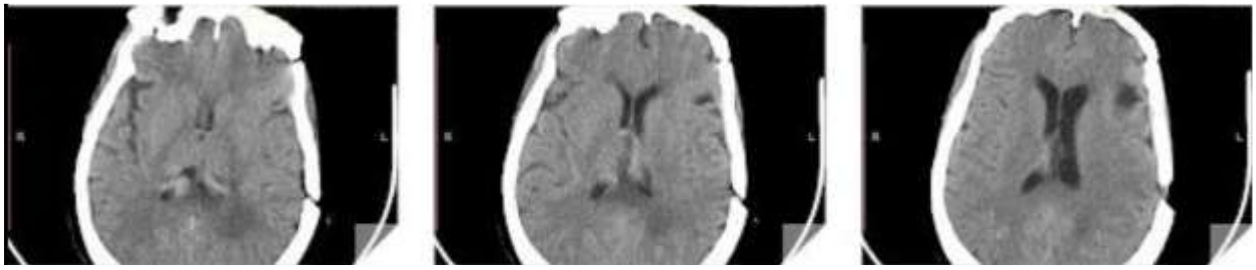
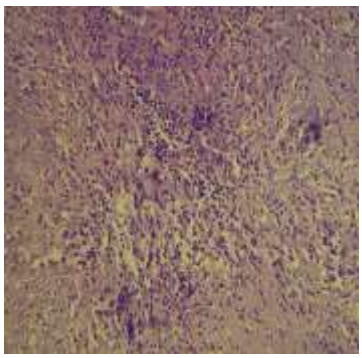
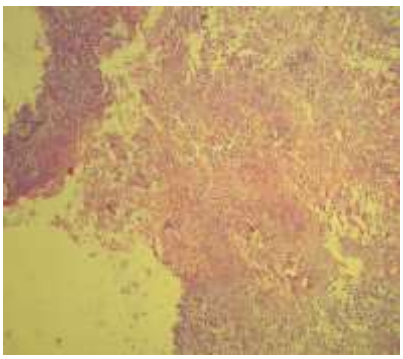
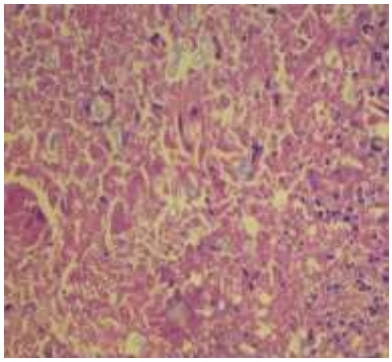


Fig_5A 5B 5C

Histology results. Figure 6A-6C

Histology results from two laboratories (one based at the hospital and the other a private laboratory outside the hospital) showed necrotizing granulomatous inflammation with encapsulated fungal organism, consistent with cryptococcal infection. The results were received 10 days after the operation.

6A: Inflammatory soup 6B: Necrosis and giant cells 6C: Yeast- thick mucoid capsule

Magnification: X20 X10 X40

Stains Used: Hematoxylin and Eosin

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