Rapidly progressive dementia with an atypical presentation of rigid-akinetic syndrome caused by Cryptococcus Gattii: A case report

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Case Report

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Abstract

Background

Meningoencephalitis by Cryptococcus gattii (C. gattii) can be responsible for unspecific neurological clinical features, and its lesions in the brain can be diffuse with a preference for basal ganglia.

Case presentation

Here we describe the case of a 72- year-old woman who developed dementia and akinetic rigid syndrome with bilateral hand myoclonus in six-month period. Brain magnetic resonance imaging revealed striking leptomeningeal compromise and lesions in the midbrain. Film array and culture for C. gattii in cerebrospinal fluid were positive and she was diagnosed with meningoencephalitis by C. gattii. Antifungal management with amphotericin B plus flucytosine was started, and induction therapy was proposed for 4 to 6 weeks.

Conclusions

Our case showed that meningoencephalitis by C. gattii associated with rapidly progressive dementia, gait disturbance and a pseudo-parinaud syndrome could be an atypical clinical presentation of meningoencephalitis by cryptococcus.

Background

Rapidly progressive dementia (RPD) refers to a group of etiologies that cause neurocognitive decline in a period of months to days, being a diagnostic challenge and of great importance due to the underlying functional impairment (1). Regarding the common etiologies of RPD, early detection or exclusion of treatable conditions such as infections, metabolic alterations, autoimmune or toxic etiologies, is a priority as it allows the potential recovery of cognitive functions (2).

Among the infectious causes related to RPD, human immunodeficiency virus (HIV), syphilis and Lyme disease (3) are the most common causes. However, entities such as fungi are scarce in the literature, as is the case of cryptococcus. Of the 30 species of cryptococcus spp., C. neoformans and C. gattii are the most pathogenic in the general population, but evidence has shown that those infected are frequently immunosuppressed.

Neurological manifestations of C. gattii include meningitis, encephalitis, or meningoencephalitis (4). In older adults, cryptococcal meningitis increases morbidity and mortality due to its atypical presentation and physiological changes related to aging, where the notorious manifestations are fever, headache, or focal neurological signs; with RPD or parkinsonism being atypical presentations (5).

This case report highlights the neuroanatomic role of the dorsal structures in the midbrain such as superior colliculus (SC) and cerebellum causing a rapidly progressive dementia, associated with gait disturbances due to subcortical involvement, and a pseudo-parinaud syndrome, caused by C. gattii.

Case Presentation

A 72- year- old woman with a history of seropositive rheumatoid arthritis (anti-CCP > 1200) and osteoporosis, managed with methotrexate 20 mg once a week, previously fully functional and independent (Barthel index 100/100), progressed over a six-month period to complete dependence for basic personal and instrumental activities of daily living (Barthel index 0/100). Main cognitive findings were characterized by language compromise, mainly presenting anomia and proper name anomia, progressing to an inability to complete a conversation with her peers, using increasingly less complex language, reaching automatic language only using monosyllables.

With the same time of evolution, the patient presented difficulty eating due to orolingual and upper limb apraxia (using the knife and fork), followed by liquid dysphagia. Other symptoms evident for her family members were bilateral hand myoclonus, disorientation in time and place, and a rapidly progressive inability for walking, requiring external aids a month after the onset of symptoms, and wheelchair at four months.

On examination, she was alert with hypomimic facies, did not emit autonomous language, and only followed simple orders such as closing her eyes. She had bilateral ptosis, and presented saccadic intrusions during sight fixation. She presented limitation for voluntary eye movements in the vertical plane, mainly for eye supraversion; and involuntary movements were compromised during the vertical phase of doll's eye reflex. Voluntary and involuntary horizontal eye movements were preserved. She had upper limb paresis with strength of 4/5, and 3/5 in lower limbs. The limbs were hypotrophic, presented generalized akinesia with a score of 4 according to the Unified Parkinson's Disease Scale (UPDRS-III) and axial rigidity (UPDRS-III score 4), with neck stiffness; symmetrical appendicular rigidity was also found (UPDRS-III score 3). She had frontal release signs (bilateral palmomental reflex), generalized hyperreflexia (+++/++++), left Babinski, and bilateral upper limb myoclonus.

She was admitted to the neurology department under the possible diagnosis of rapidly progressive dementia, with a wide possibility of differential diagnosis concerning etiologies such as infections, prion disease, autoimmune encephalitis, vitamin deficiencies, metabolic or toxic disturbances, etc. Blood examination demonstrated a white blood cell count of 9000/mm3, erythrocyte sedimentation rate of 10mm/h, the thyroid-stimulating hormone of 0.65mIU/L, vitamin B12 of 1241pg/mL (slightly elevated), folic acid of 16ng/mL, non-treponemal test negative, creatinine of 0.59mg/dL, and electrolyte levels were normal. Additionally, urinalysis was suggestive of infection, thus management with intravenous cefazolin was initiated. Thoracic, abdominal, and pelvic computed tomography (CT) scan with contrast ruled out malignancy.

Magnetic resonance imaging (MRI) findings are shown in Figs. 1 and 2. Cerebrospinal fluid (CSF) examinations showed lymphocytic pleocytosis (12/mm3), elevated protein levels (732mg/dL) and low glucose level (< 20mg/dl with central glucose of 127mg/dL). Indian ink, KOH, and cryptococcal antigen were negative in CFS, however film array detected cryptococcus in CSF. CSF culture was positive for C. gattii. CSF cytology showed no malignancy.

Based on the patient's symptoms, images, and CSF results we diagnosed a C. gattii meningoencephalitis and ventriculitis with noncommunicating hydrocephalus, associated with a rapidly progressive dementia with parkinsonism and a supranuclear palsy syndrome (PSP), leading to gait disturbance. Antifungal management was started with amphotericin B plus flucytosine. It was proposed to take induction therapy up to 4 to 6 weeks and to perform a new lumbar puncture 14 days after the initiation of antifungal therapy. In the follow-up of the case the patient presented improvement in her neurological symptoms such as neck stiffness and upper limbs rigidity (UPDRS-III 3/4 to 2/4); she also started communicating with her family members. However, before a second lumbar puncture was performed, the patient was diagnosed with SarsCov2 pneumonia and died of respiratory distress.

Discussion

We identified a patient with RPD caused by meningoencephalitis by C. gattii who presented with symptoms of cognitive impairment characterized by compromise of the semantic content of language, orolingual and upper limb apraxia, and symmetrical akinetic rigid syndrome, supra nuclear palsy, with a rapid progression from gait disturbances to the need of a wheelchair.

Even though the leptomeningeal compromise is common in patients with cryptococcal meningoencephalitis (9), in our case the extensive involvement of the subarachnoid space is striking, including the bilateral engagement of the cerebellum. Also, the left midbrain and superior colliculus showed an atypical enhancement in the MRI and a subacute infarct in the right cerebellum was found, as shown in Figs. 1 and 2. Parkinson patients with akinetic rigidity variant have shown significantly decreased functional connectivity between basal ganglia and posterior cerebellum lobule (10), which has an important role in fine motor coordination; this is not a typical neurological finding in patients with cerebelar infarcts, however it may have a correlation with the rigid akinetic syndrome.

The mesencephalic locomotor region, which is also affected in our patient, has been proven to be affected in patients with freezing of gait (11), due to reduced neuronal activity. Our patient initially presented difficulties in walking that progressed in four months from freezing gait to a wheelchair, explained by the mesencephalic compromise. Additionally, Parkinson's disease patients have been reported to have impaired active avoidance (12), due to affected pathways involving the superior colliculus. In our patient the affected left superior colliculus could have affected her active avoidance, however, it was not evaluated due to the limitations in her neurological exam due to her cognitive impairment.

On the other hand, the reports of vasculitis caused by C. gattii are limited, with lacunar infarcts being more common (13) in basal ganglia, thalamus, and cerebral lobes. In a retrospective observational study, the incidence was 13%. Hence, our patient presented a non-lacunar infarct in an unlikely territory (cerebelar hemisphere), however it is not discarded that the etiology of this infarct was due to vasculitis by C. Gattii.

The patient's main clinical course was a rapidly progressive dementia, involving all cognitive domains and therefore could not be categorized as a clinical cognitive syndrome of PSP based on the 2017 Movement Disorder Society criteria for PSP (14). She presented parkinsonism given the global akinesia associated with the gait disturbance, the rigidity, and a supranuclear gaze palsy due to pseudo-parinaud syndrome. All these findings could be explained by the noncommunicating hydrocephalus with involvement of the rostral midbrain and mesencephalic structures such as the superior colliculi. Given the rapidly progressive nature of the disease and that the syndromic diagnosis was RPD, PSP was discarded.

Additionally, the isolation of in our case shows again how C. gattii is an important pathogen throughout the tropics including South America (15), and how it can affect immunocompetent hosts with risk factors such as autoimmune diseases due to the use of immunosuppressive therapy, such as our patient; she also made steam inhalation with eucalyptus, which is a probable cause of exposure to the pathogen in our case. In Colombia the annual incidence of C. gattii is estimated to be 0.7 cases per million, which makes this case a rare occurrence (16). Considering that in our case C. gattii was isolated in a non-HIV patient, the induction therapy established with amphotericin B plus flucytosine for four to six weeks was the correct approach. This case highlights the importance of considering cryptococcal meningoencephalitis by C. gattii in patients with rapidly progressive dementia and parkinsonism.

Abbreviations

- C. Gattii: Cryptococcus Gattii
- CSF: cerebrospinal fluid
- RPD: rapid progressive dementia
- HIV: human immunodeficiency virus
- PSP: progressive supranuclear palsy
- SC: superior colliculus
- Anti-CCP: anti-cyclic citrullinated peptide
- UPDRS: Unified Parkinson's Disease Rating Scale
- CT: computed tomography
- MRI: magnetic resonance imaging

Declarations

Ethics approval and consent to participate

This case report was approved by the Research and Institutional Ethics Committee of the Faculty of Medicine of the Pontificia Universidad Javeriana and the San Ignacio University Hospital.

Consent for publication

Written informed consent for publication of medical records, including images was obtained from the patient's son.

Availability of data

The data used for this article are not publicly available due to them containing information that could compromise the patient's privacy and anonymization. All data used were taken from the private and confidential medical history of the patient.

In case someone needs to request the data from this study, the corresponding author of this paper should be contacted: Elkin García-Cifuentes MD at elkingarciaci@gmail.com

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

LAFG and EGC recollected and synthetized the patient's data, also contributed to the background investigation and writing the manuscript, CGA and CCC supervised, revised, and approved the final version of the manuscript. AMG synthetized patient's information and help with the construction of the discussion along with EGC. IM an MFA contributed in writing the manuscript and revising the final version. All authors read and approved the final manuscript.

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Figures

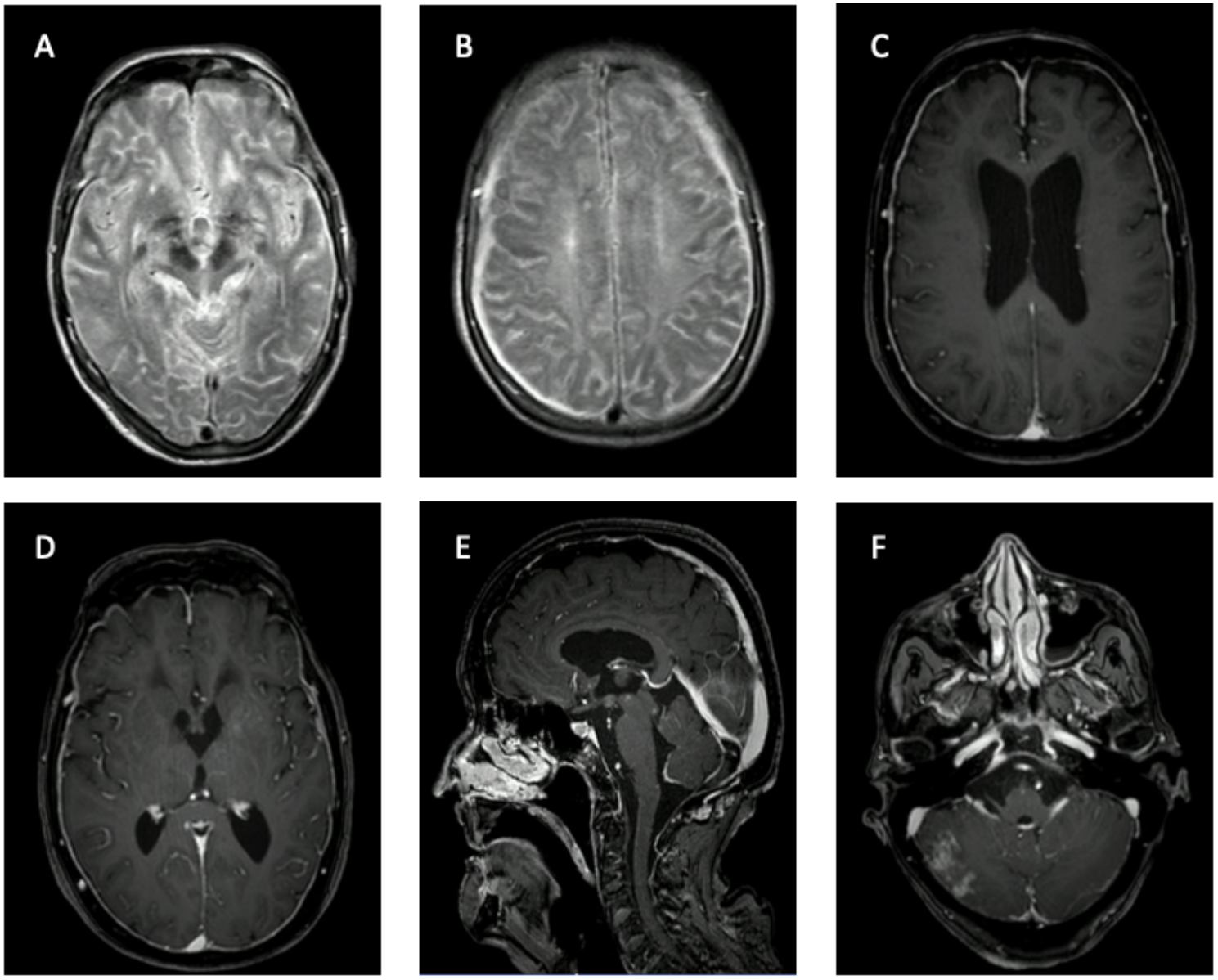

Figure 1

Magnetic Resonance Imaging of the Patient.

(A, B) Brain fluid attenuation inversion recovery (FLAIR) showed diffuse alteration in the signal intensity of the subarachnoid space. (C, D) Magnetic resonance imaging (MRI) enhanced with gadolinium showed leptomeningeal and dural enhancement. (E) MRI enhanced with gadolinium showed two enhancing lesions in the midbrain, one in the inferior colliculus and the other ventral in the midbrain. (F) MRI enhanced with gadolinium showed a right cerebellar heterogeneous enhancing lesion that was compatible with a subacute ischemic injury in the diffusion-weighted image and the apparent diffusion coefficient.

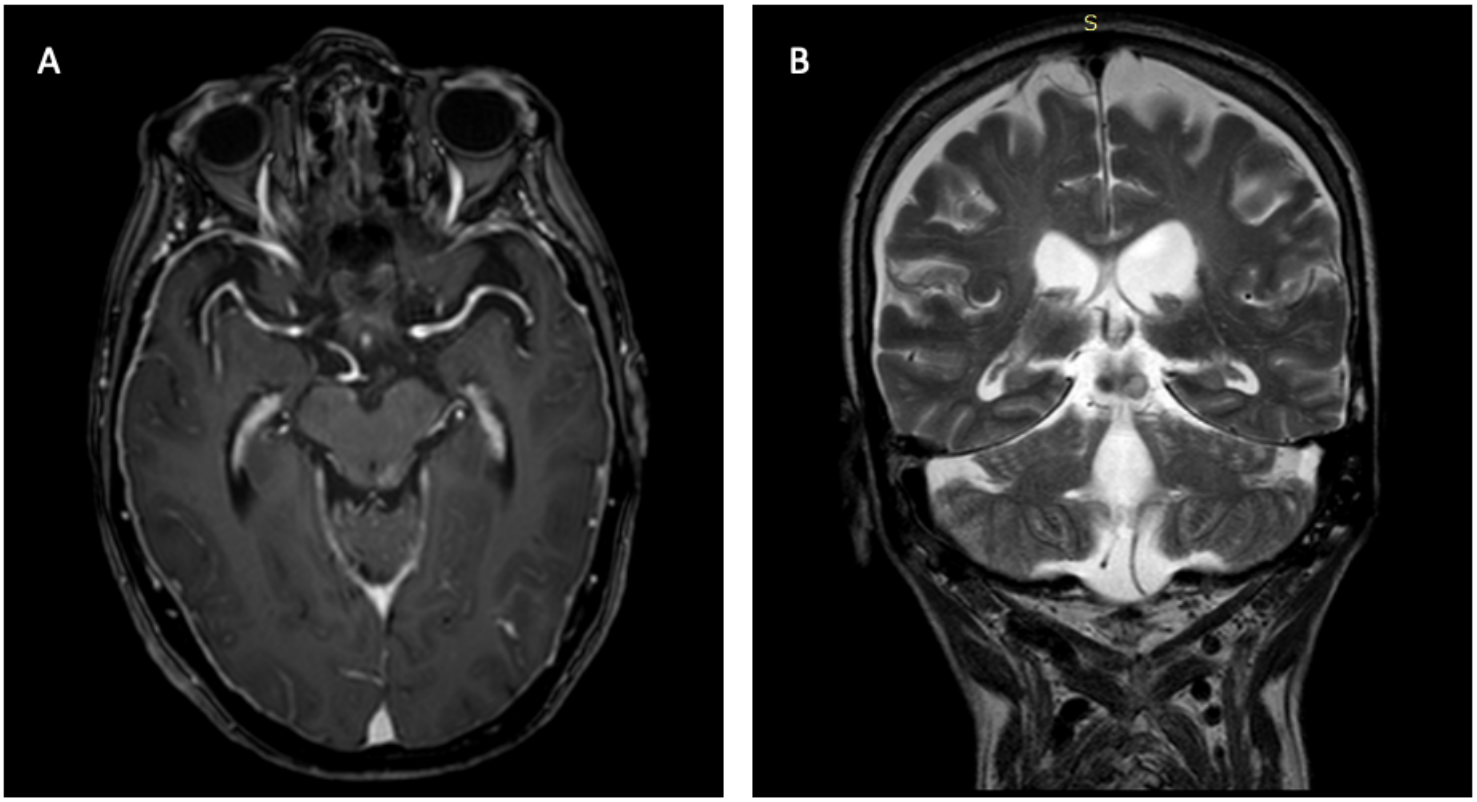

Figure 2

Magnetic Resonance Imaging of the Patient.

(A) Magnetic resonance imaging (MRI) enhanced with gadolinium showed an enhancing lesion in the left midbrain at the level of the superior colliculus. (B) Brain fluid attenuation inversion recovery (FLAIR) showed a hyperintense lesion at the level of the left red nucleus.