

Cerebral Cryptococcosis in an Immunocompetent Patient: Case Report and Literature Review



Hollman Armando Avila-Coy^{1*}, Maria Jose Lopez-Mora² and Oscar Bernal-Pacheco³

¹Neurology Resident Physician, Nueva Granada Military University, Colombia

²Infectology Physician, Infectology Specialist, Central Military Hospital, Colombia

³Neurologist, subspecialist in Abnormal Movements, Central Military Hospital, Colombia

Submission: June 26, 2021; Published: July 20, 2021

*Corresponding author: Hollman Armando Avila Coy, Neurology Resident Physician, Nueva Granada Military University, Bogotá, Colombia

Abstract

Cryptococcosis in the central nervous system is an infrequent infection in immunocompetent patients. The cryptococcus complex of which *Cryptococcus neoformans* and *Cryptococcus gattii* is a part, cause infection that starts in the lung and later causes infection in the central nervous system; being more frequent in immunocompetent patients *Cryptococcus gattii* and in immunocompromised patients *Cryptococcus neoformans*; having as a relevant clinical presentation headache due to increased intracranial pressure; This article reports a clinical case of a 46-year-old male, immunocompetent, who attends due to headache with warning signs, the warning signs being: first episode of headache with characteristics of increased intracranial pressure, which does not subside with analgesia, performing complementary studies, these being neuroimaging and lumbar puncture with identification with polymerase chain reaction in cerebrospinal fluid, in which infection in the central nervous system by *Cryptococcus gattii* is identified and during hospital stay a pulmonary nodule with cryptococcoma is identified, for which lobectomy was performed, and treatment with amphotericin B and fluconazole was ordered.

Keywords: Cerebral cryptococcosis; Neuroinfection; Immunocompetent; Central nervous system; *Cryptococcus Gattii*

Introduction

Cryptococcus neoformans and *Cryptococcus gattii*, is a yeast that contains a polysaccharide capsule, which metabolizes urea and catecholamines, and is generally transmitted by inhalation of bird droppings, mainly pigeons; Cryptococcosis is a fungal disease that is transmitted by inhalation and subsequent pulmonary infection, it can spread to the CNS and cause meningitis or meningoencephalitis [1-3]. Generally, the initial infection is pulmonary and from there it spreads to other organs with special preference for the central nervous system, where it causes meningoencephalitis and very rarely granulomatous focal lesions known as cryptococomas [4]. This infection mainly affects 2 sites: the lung and central nervous system (CNS), although it can affect other organs, such as the kidney, prostate and bones. Of the target sites, it mainly affects the CNS, which represents the site where 50% of cases are generated due to the tropism of the fungus [5]. Most cases occur in immunosuppressed hosts, including HIV / AIDS patients, patients receiving immunosuppressive drugs, and solid organ transplant recipients. However, cryptococcosis also occurs in immunocompetent individuals [2,6]. Cryptococcosis in the central nervous system is a rare infection in immunocompetent

patients; The presentation of cryptococcosis in the CNS can be in 2 ways:

- a. Cysts in the cerebral cortex with granulomatous meningeal reaction
- b. White matter granulomas called cryptococomas [1,6,7]

It has been reported that in immunocompetent patients there is a male: female ratio of 2: 1, while in immunocompromised patients there is a ratio of up to 11: 1 [8,9]. In most documented cases, treatment of CNS *C. gattii* infection requires aggressive management of elevated intracranial pressure in conjunction with standard antifungal therapy [10-12]. Treatment is divided into three phases as follows: Amphotericin B deoxycholate induction phase 0.7mg / kg / day intravenous (IV) or Liposomal amphotericin B 3-4 mg / kg / day + 5 fluocytosine 100mg / kg / day orally (PO) divided into 4 doses over 2 weeks (up to 6 weeks in the presence of cryptococcoma), followed by a consolidation phase for which a negative cerebrospinal fluid culture must be performed Fluconazole 400 - 800 mg orally every day for 8 weeks, and a final maintenance phase Fluconazole 200-400mg / day orally at least 12 months [13,14].

Methods

We describe a clinical case confirmed by performing a culture in cerebrospinal fluid of Cryptococcosis in the central nervous system by *Cryptococcus Gatti* in an immunocompetent patient, in the Neurology service of Hospital Militar Central

Bogotá (Colombia); Likewise, a review of the updated available literature about cryptococcosis in the central nervous system in immunocompetent patients is carried out; The information was taken from the Clinical History of the Central Military Hospital, prior approval by informed consent by the patient.

Clinical Case

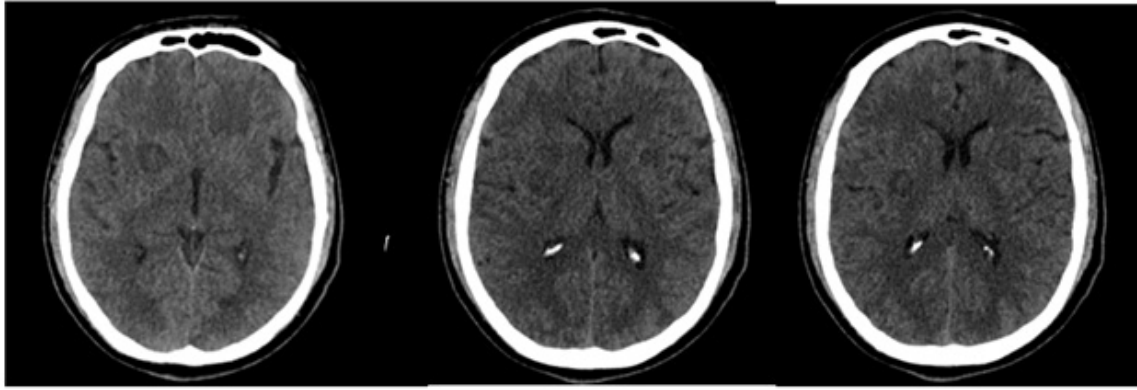


Figure 1: Multiple hypodense focal lesions located in the nucleo-basal regions, probably of infectious-inflammatory etiology.

46-year-old male patient, right-handed, whose profession is an aircraft structures technician, who is admitted with a 5-day headache, holocranial, with progressive onset, stabbing type, reaches maximum intensity 8/10, without photo or phonophobia, without nausea or emesis, which increases with changes in position and valsalva maneuvers, which temporarily subsides

with acetaminophen and diclofenac, makes it possible to fall asleep, sometimes the headache wakes up, without a history of importance for the current disease; To the physical and neurological examination within normal limits, neuroimaging studies are taken as part of comprehensive care, finding the following in Cranial Tomography (Figures 1 & 2):

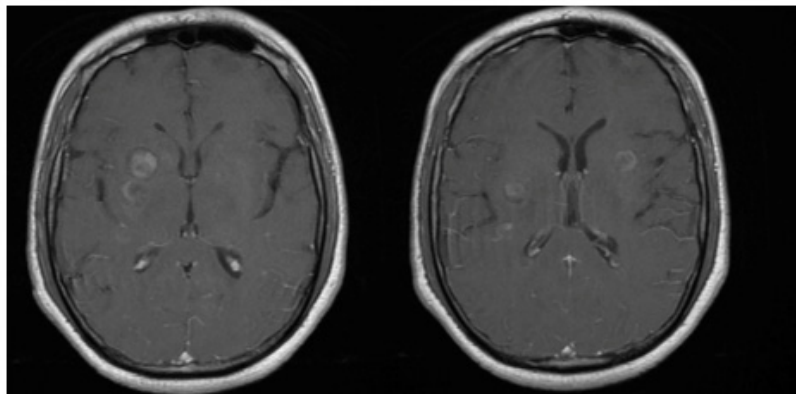


Figure 2: Rounded, well-defined, bilateral nucleo-basal focal lesions with low signal intensity in T1 sequences, high signal in fluid-sensitive sequences, some of them presenting slight perilesional edema and irregular thick central enhancement after administration of associated intravenous contrast to leptomeningeal enhancement.

And given the findings likely to be related to increased intracranial pressure, a lumbar puncture was performed, finding the following results:

- a. P.A.: 40 cmH₂O P.C.: 12 cmH₂O
- b. Cloudy appearance
- c. Gram negative for microorganisms
- d. Total proteins 117.4
- e. CSF Glucose 4.17 Serum 93 IG 0.04
- f. Leukocytes 150, 27 Segmented 20 lymphocytes, 3

monocytes

- g. Hematies 48 hatched 10
- h. VDRL Non-reactive

- i. Cryptococcus neoformans / gattii positive film array
- j. Gene Xpert Negative TBC
- k. Positive Chinese ink for encapsulated yeast (Figure 3)

Result Summary	
Bacteria	
Not Detected	<i>Escherichia coli</i> K1
Not Detected	<i>Haemophilus influenzae</i>
Not Detected	<i>Listeria monocytogenes</i>
Not Detected	<i>Neisseria meningitidis</i>
Not Detected	<i>Streptococcus agalactiae</i>
Not Detected	<i>Streptococcus pneumoniae</i>
Viruses	
Not Detected	Cytomegalovirus
Not Detected	Enterovirus
Not Detected	Herpes simplex virus 1
Not Detected	Herpes simplex virus 2
Not Detected	Human herpesvirus 6
Not Detected	Human parechovirus
Not Detected	Varicella zoster virus
Yeast	
✓ Detected	<i>Cryptococcus neoformans/gattii</i>

Figure 3: FILM ARRAY.

Isolating in culture of cerebrospinal fluid: *Cryptococcus gattii*, sensitive to amphotericin and fluconazole.

Given its clinical picture and microbiological isolation, it was decided to start treatment with liposomal amphotericin B and fluconazole, in the induction phase for 6 weeks of treatment (cryptococcal context); During hospitalization, immunity studies are carried out, being: HIV (NEGATIVE) on three occasions, and primary immunity studies within normal limits.

With negative control cultures in cerebrospinal fluid, and with adequate clinical evolution, due to the absence of headache, for which he was discharged from hospital in the consolidation phase with fluconazole 400 mg every day. However, the patient is reconsidered a month after discharge due to a new headache with the same characteristics, for which new neuroimaging is taken. Isolating in culture of cerebrospinal fluid: *Cryptococcus gattii*, sensitive to amphotericin and fluconazole. Given its clinical picture and microbiological isolation, it was decided to start treatment with liposomal amphotericin B and fluconazole, in the induction phase for 6 weeks of treatment (cryptococcal context); During hospitalization, immunity studies are carried out, being: HIV (NEGATIVE) on three occasions, and primary immunity studies within normal limits. With negative control cultures in cerebrospinal fluid, and with adequate clinical evolution, due to the absence of headache, for which he was discharged from hospital in the consolidation phase with fluconazole 400 mg every day. However, the patient is reconsidered a month after discharge due to a new headache with the same characteristics, for which new neuroimaging is taken.

Lumbar puncture:

- a. Opening pressure: 32
- b. Closing pressure: 18
- c. Gram negative
- d. Negative Chinese ink
- e. Glucose index 0.48
- f. VDRL: Non-reactive
- g. Proteins: 79
- h. Leukocytes: 2 (Lymphocytes)
- i. Negative film array

And it was decided to hospitalize for extension studies, these being a high-resolution chest tomography showing a pulmonary nodule located in the upper segment of the lower left lobe with diameters of 29x17mm, for which a biopsy was performed showing: Cryptococcoma left lower lobe and performed Left lower lobectomy with findings from pathology studies: pulmonary parenchyma with extensive chronic granulomatous inflammation with the presence of *Cryptococcus Gattii*-type microorganisms, this being the primary source of infection; Therefore, the multidisciplinary board decided to restart induction therapy with amphotericin B and flucytosine for 6 weeks, and again culture of cerebrospinal fluid at the end of said phase, this culture being negative for which treatment with fluconazole was continued in the consolidation phase. and maintenance, with clinical and paraclinical improvement of the patient followed by the outpatient clinic, with a good course of evolution (Figure 4).

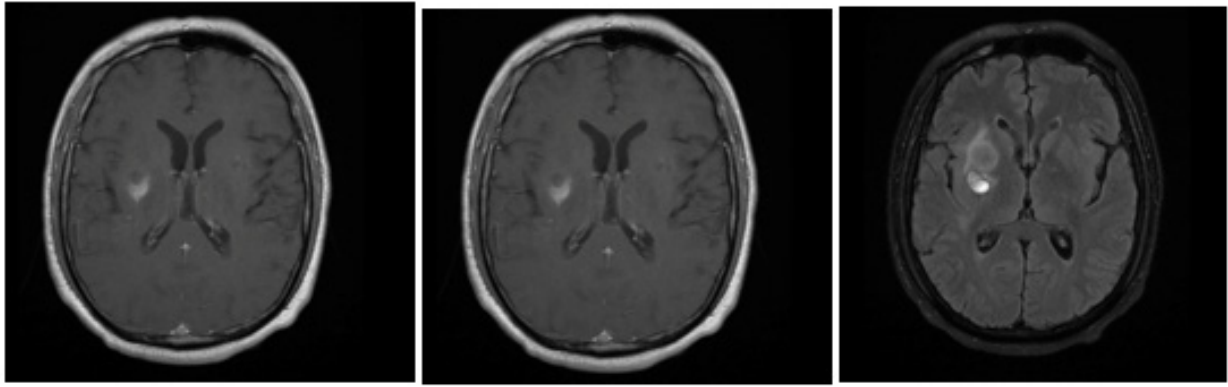


Figure 4: MRI: Significant imaging improvement compatible with response to established treatments persisting smaller with reduction of the vasogenic edema reaction.

Literature Review and Discussion

Cryptococcus infection in the central nervous system in immunocompetent patients is rare, with *Cryptococcus gattii* having a higher incidence in this type of patient, causing greater morbidity due to the presentation of cryptococci, and longer treatment time; The clinical diagnosis is difficult to establish due to the subacute onset of symptoms and the unspecific manifestation in immunocompetent patients, most of the cases, it presents as a subacute or chronic meningitis characterized by headache, nausea, vomiting, fever, altered consciousness, signs of intracranial hypertension and meningeal signs and in more complex cases cryptococomas occur; the diagnosis is by means of a lumbar puncture and the Chinese ink the tool that will give the definitive diagnosis; yeast will be found in approximately 75% of patients with HIV and 50% of immunocompetent patients, and the culture allows us to know the type of cryptococcus causing the infection; In the case of our patient, a cryptococoma in the lower lobe of the left lung was found as the primary focus of the infection; and of special interest the presence of cryptococomas in brain parenchyma in immunocompetent patients, which leads to a longer treatment time [7,13,15].

Funding

For the realization of this article, no financial support was required, as it was a description of a clinical case.

References

1. Franco Paredes, Tanea Womack, Teri Bohlmeier, Brenda Sellers, Allison Hays, et al. (2015) Management of *Cryptococcus gattii* meningoencephalitis. *Lancet Infect Dis* 15(3): 348-55.
2. JA Galnares Olalde, S Loza Jalil (2014) Cryptococcal meningitis in an immunocompetent patient: Case report and literature review. *Revista Médica del Hospital General de México* páginas 137-141.
3. Z Tay, R Lara, C Velasco, A Gutiérrez (2002) *Parasitología médica*. 6 Méndez (Eds).
4. AQ Rana, U Saeed, AN Rana (2014) Role of environmental factors in cryptococcal meningitis in immunocompetent individuals. *Acta Neurol Belg* 114 (1): 75-76.
5. Eileen K Maziarz, John R Perfect (2016) Cryptococcosis. *Infect Dis Clin North Am* 30(1): 179-206.
6. Sharon CA Chen, Wieland Meyer, Tania C Sorrell, (2014) *Cryptococcus gattii* infections. *Clin Microbiol Rev* 27(4): 980-1024.
7. José Felix Pérez-Veitia, (2017) Cryptococcal meningoencephalitis: a case report, *Revista Mexicana de Neurociencia*, Julio-Agosto, 18(4):80-85.
8. Jeremy N Day, Tran TH Chau, Marcel Wolbers, Pham P Mai, Nguyen T Dung, et al. Combination Antifungal Therapy for Cryptococcal Meningitis. *N Engl J Med* 368(14):1291-1302.
9. Jarrín Maisincho K, Cordovez Navas M, Vera Pérez E (2012) Criptocomas Cerebrales en un Paciente Inmunocompetente: Reporte de un Caso. *MedPre* 2(1): 23-33.
10. Martin-Blondel G, Ysebaert L (2014) Disseminated Cryptococcosis. *N Engl J Med* 370: 1741.
11. Marco barquero argüello, meningitis por *Cryptococcus neoformans*, *revista medica de costa rica y centroamerica* 619: 205 - 208.
12. Jorge Cortés, Alejandro Kral y Gonzalo Wilson (2018) Cryptococcosis in Hospital Carlos Van Buren, Valparaiso: a clinical serie. *Rev Chilena Infectol* 35(4): 420-423.
13. A Wilfredo TE, Alejandro RI, Swany AR, Carlos G-Mejía, Renato VC (2016) *Cryptococcus neoformans* meningoencephalitis in a malnourished teenager. *Acta Med Peru* 33(3): 232-235.
14. Fernando A Messina, Elena Maiolo (2015) Therapeutic alternatives meningeal cryptococcosis. *buenos aires junio* 23(88): 25-32.
15. Glubis W Gomez Pelaez (2019) Risk factors of Cryptococcosis in patients with HIV in the hospital of infectology Dr. José Daniel Rodríguez Maridueña in the period (2015-2016). *Dom Cien* 5(1) pp. 736-750.



This work is licensed under Creative Commons Attribution 4.0 License
DOI: 10.19080/OAJNN.2021.15.555920

**Your next submission with Juniper Publishers
will reach you the below assets**

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats
(Pdf, E-pub, Full Text, Audio)
- Unceasing customer service

Track the below URL for one-step submission

<https://juniperpublishers.com/online-submission.php>