

## Cryptococcal Meningitis in An Immunocompetent Child

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### Introduction

Cryptococcosis is a serious fungal infection that enters the body through the respiratory tract. It has multi-systemic localization; however, this yeast has a marked tropism for the central nervous system, causing meningoencephalitis. It occurs preferentially in patients with a profound immune deficiency, in particular patients infected with the human immunodeficiency virus (HIV), for which it is one of the first opportunistic infections. Its occurrence is rare outside this context, but remains fatal in the absence of treatment [1,2]. We report here a case of cryptococcal meningoencephalitis in a 12-year-old child with no obvious immunosuppressive factors.

### Case report

Faiçal, a 13-year-old boy, from a non-consanguineous marriage, with a history of good psychomotor development with a prolonged contact and no recent tuberculosis infection, He was admitted to the pediatric department 1 for a febrile meningeal syndrome evolving one month before his admission, with helmet headache and projectile vomiting, associated with cervical pain in a context of fever of 40° and deterioration in general condition with weight loss of 5 kg in one month. On admission clinic exam, the child was conscious, hemodynamically and respiratorily stable, normocardial at 86 HR, eupneic at 19 b/min, and febrile at 38.5°. For neurological examination, there was meningeal neck stiffness with positive Kernig and Brudzinski signs, without tonus disorder or sensory-motor deficits, nor impairment of the cranial pairs.

Biologically, there was a lymphopenia of 780/mm<sup>3</sup>, a negative CRP of 2.7 mg/l, the cytobacteriological examination of the CSF revealed: WBC of 240 e/mm<sup>3</sup> (PNN: 40%, Lyc:60%), RBCs at 140 e/mm<sup>3</sup>, direct examination was negative, however, the culture showed *Cryptococcus Neoformans*, the search for circulating cryptococcal antigen in the CSF was positive at a title of 1/80, multiplex PCR in the CSF confirmed the presence of *Cryptococcus Neoformans*. On the other hand, the search for *Mycobacterium Tuberculosis* was negative.

An immune workup was performed as part of the etiological workup: the child's and mother's HIV serology were negative, the immunoglobulin weight assay was normal, the lymphocyte subpopulation count revealed global lymphopenia involving CD3 (700/mm<sup>3</sup>), CD4 (369/mm<sup>3</sup>), CD8 (275/mm<sup>3</sup>), and CD16 (25/mm<sup>3</sup>), and HLA DR expression was normal. Brain CT showed an extra-axial cystic formation related to an arachnoid cyst which was confirmed on MRI.

Therapeutically, the patient was put on an antibacillary treatment, Fluconazole, and intravenous corticotherapy, once the diagnosis of *cryptococcus neoformans* meningitis was confirmed; the child received Amphotericin B liposomal IV for two weeks then relayed per os by fluconazole 400 mg/d for 4 weeks then 200mg/d for 6 months. The clinical evolution was marked by a clear improvement of the meningeal syndrome and a defervescence at D7 of the antifungal treatment. The child then presented an IH syndrome at day 40 of treatment; therefore, benefiting from a LP discharge.

### Discussion

Cryptococcal meningitis is an opportunistic infection of the central nervous system (CNS) caused by *Cryptococcus neoformans*, a saprophytic yeast of the external environment whose reservoirs are mainly pigeon or other bird feces [2]. Contamination occurs by inhalation of spores (latent primary pulmonary infection), much more rarely by skin inoculation. It often occurs in immunocompromised individuals, particularly adults with HIV aged 20-50 years, while in children the incidence is less than 1% with a mean age of 12 years and a male predominance [1,8,9,10]. Recently, there has been an increasing number of reports of cryptococcal meningitis in immunocompetent children [5,6]. Several reports have been published describing the development of cryptococcosis in patients after exposure to birds or avian feces. (e.g., pigeons, chickens, parrots, sparrows, starlings, turtle doves, canaries and skylarks), suggesting that human infection may result from this source. Through the use of molecular techniques, it has been

possible to demonstrate that isolates obtained from bird feces on the one hand and patient isolates on the other hand are closely related.

Cryptococcosis preferentially affects the central nervous system and presents as meningoencephalitis in 69% of HIV-negative subjects and 90% of HIV-positive subjects [1,3]. It is usually misdiagnosed as tuberculosis or other diseases and therefore Delay in diagnosis and treatment leads to high morbidity and mortality rate [4,7]. The initial manifestation may be pauci- or asymptomatic (asthenia, weight loss, memory disorders), sometimes frustrated and chronic, leading to diagnostic delays with a high mortality rate, especially in patients without identified risk factors [4,5]. Its classical clinical presentation associate's headache in the foreground followed by moderate fever, nausea/vomiting as well as neurological signs in half of the cases such as memory disorders, personality disorders and at a later stage, convulsions. Signs of meningeal irritation are uncommon and focal signs are rarer. The existence of consciousness disturbance usually secondary to acute hydrocephalus is a poor prognostic factor [1,3,6].

The brain scan is normal in 50% of cases. Magnetic resonance imaging identifies specific lesions in 90% of cases (pseudocysts, Virchow-Robin space dilatations) [7]. Serum biology is not very helpful.

Lumbar puncture is very useful for the initial diagnosis. As in our patient's case, CSF analysis shows low cellularity (less than ten elements), hyperproteinorachia and moderate, even inconstant hypoglycorachia [11]. Such a CSF cytochemistry classically leads to the search for and emergency treatment of Herpes simplex virus and *Listeria monocytogenes* infection. In case of immunosuppression or unfavorable evolution without germ on direct examination, a Koch's bacillus or a cryptococcal yeast must be rapidly looked for and treated. Ziehl-Neelsen staining reveals acid-fast bacilli, suggestive of tuberculosis. Direct examination with Indian ink reveals encapsulated yeasts of the genus *Cryptococcus* [15,16]. This test is positive in 80% of cases in HIV patients and in 30-50% of cases in HIV-negative patients. Culture ensures a diagnosis within 48 to 72 hours, and the diagnosis is then confirmed by an Elisa® test for cryptococcal capsular antigens in blood and CSF. The antigen titre, reflecting the fungal load, correlates with the degree of severity of the infection [11,15].

The treatment is composed of three phases (induction, consolidation and maintenance), and classically includes amphotericin B (Fungizone®) (0.7 to 1 mg/Kg/d) in slow intravenous infusion or better Ambisome® (3-6mg/kg/d) and 5 fluorocytosine (5 FC) (Ancotil®) (100 to 150 mg/Kg/d) [11] at least for 2 weeks (induction treatment). If the evolution is good: The relay is then taken by fluconazole (Triflucan®) at 400 mg/d for 8 to 10 weeks (consolidation treatment) then 200 mg/d as secondary prophylaxis (maintenance treatment). In case of intracranial hypertension, lumbar evacuation punctures are also performed [11,12,17]. [11,12,17]. They should be performed 2 to 3 times a week if the CSF pressure is higher than 25 cmH<sub>2</sub>O. The control of IH is a major element of the prognosis [19].

Clinical improvement is usually slow, lasting one to two weeks, and remission is achieved only after at least 6 weeks of loading therapy [13,14]. [13,14]. It is judged on the regression of symptoms, stabilization of intracranial pressure after 3 to 5 days, sterilization of mycological cultures and not on the negativation of direct examination, decrease of antigenic titers in CSF and serum. The absence of a decrease or an increase is frequently correlated with severity of infection, therapeutic failure or extrameningeal dissemination. Monitoring is performed at the beginning of treatment, at the 2nd, 4th and 10th week of treatment. Nevertheless, the repetition of LPs for mycological sterilization are not recommended in patients with a good clinical course. Sequelae may persist after cure if a cranial nerve has been affected (deafness, blindness) [13].

## Conclusion

Cryptococcal meningitis is an uncommon condition in children, as opposed to adults, as evidenced by the paucity of publications. Rare cases of cryptococcal meningitis in immunocompetent patients have been reported, but most of them have been related to frequent exposure to avian feces. This infection has a high mortality rate despite the introduction of an effective antifungal treatment. In view of the seriousness of the disease, the lack of specificity of the clinical signs and the frequent normality of the CSF should prompt a systematic search for *Cryptococcus neoformans* in the presence of any acute or subacute meningoencephalitis that is not proven.

## References

1. Lizarazo J, Escandón P, Agudelo CI, Castañeda E. Cryptococcosis in Colombian children and literature review. *Mem Inst Oswaldo Cruz*. 2014; 109(6):797-804.
2. YUANJIE, Zhu, JIANGHAN, Chen, NAN, Xu, et al. Cryptococcal meningitis in immunocompetent children. *Mycoses*, 2012, vol. 55, no 2, p. 168-171.
3. Guo LY, Liu LL, Liu Y, et al. Characteristics and outcomes of cryptococcal meningitis in HIV seronegative children in Beijing, China, 2002-2013. *BMC Infect Dis*. 2016; 16:635
4. Lui G, Lee N, Ip M, Choi KW, Tso YK, Lam E, et al. Cryptococcosis in apparently immunocompetent patients. *QJM*. 2006; 99:143-51.
5. Chen YY, Lai CH. Nationwide population-based epidemiologic study of cryptococcal meningitis in Taiwan. *Neuroepidemiology*. 2011; 36:79-84.
6. Bandalizadeh Z, Shokohi T, Badali H, et al. Molecular epidemiology and antifungal susceptibility profiles of clinical *Cryptococcus neoformans*/*Cryptococcus gattii* species complex. *J Med Microbiol*. 2019. <https://doi.org/10.1099/jmm.0.001101>.
7. Huang KY, Huang YC, Hung IJ, Lin TY: Cryptococcosis in nonhuman immunodeficiency virus-infected children. *Pediatr Neurol* 2010, 42(4):267-270.
8. Joshi NS, Fisher BT, Prasad PA, Zaoutis TE: Epidemiology of cryptococcal infection in hospitalized children. *Pediatr Infect Dis J* 2010, 29(12): e91-e95.

9. GUO, Jianhua, ZHOU, Jikun, ZHANG, Shiyong, et al. A case-control study of risk factors for HIV-negative children with cryptococcal meningitis in Shi Jiazhuang, China. *BMC Infectious Diseases*, 2012, vol. 12, no 1, p. 376.
10. Renelleau, B., Girerd, R., Verdière, C.H. et al. *Cryptococcus neoformans* meningoencephalitis in an a priori immunocompetent patient. *Ann. Fr. Med. Emergency* 5, 334-336 (2015).
11. NDIAYE, M., DIAGNE, NR, SECK, LB *et al* *meningeal cryptococcosis in children: about 3 cases. Tropical medicine*, 2011, vol. 71, n° 2, p. 176-178.
12. French Association of Teachers of Parasitology and Mycology (ANOFEL) *Cryptococcosis* 2014.
13. NDIAYE, M., HAGERIMANA, R., DIAGNE, N. S., *et al*. Neuromeningeal cryptococcosis in an immunocompetent child: about an observation. *Archives of Pediatrics*, 2010, vol. 17, no 7, p. 1069-1071.
14. Shoai Tehrani M, Charlier-Woerther C, Lortholary O (2014) *Cryptococcosis*. EMC-Maladies Infectieuses Ed. Elsevier Masson, Paris 11:1-12.
15. College of Academics of Infectious and Tropical Diseases (2012) *Cryptococcosis*. E-pilly TROP, Tropical Infectious Diseases Ed. Alinéas Plus, Paris, p 866-8.
16. Institut Pasteur. *Cryptococcosis*, fact sheet. <http://www.pasteur.fr/en/institutpasteur/press/fact-sheets/cryptococcosis>.