

(CASE REPORT)



Neuromeningeal cryptococcosis (CNM) in an immunocompromised child

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Abstract

Background: Cryptococcal meningitis is one of the most common opportunistic infections in immunocompromised patients. Mostly it manifests as subacute/chronic meningitis, although pathological findings suggest extensive tissue invasion of the brain parenchyma and meninges. This disease has a very high mortality rate, even with the administration of an antifungal combination.

Keywords: Cryptococcus neoformans; Meningoencephalitis; Human immunodeficiency virus; Immunocompromised child

1. Introduction

Cryptococcal meningitis is a systemic mycotic infection caused by the yeast *Cryptococcus* [1]. This yeast has a marked tropism for the central nervous system, causing meningoencephalitis. The pathogen *Cryptococcus neoformans* (*C. neoformans*) is predominately seen in immunosuppressed patients with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) [2]. However, Cryptococcal meningitis (CNM) is rare in children. Common symptoms include headache, nausea, vomiting, and malaise [5].

2. Case report

8-year-old girl, presented with a 11-day history of persistent global headaches with neck pain and stiffness, photophobia and vomiting. On examination, she was febrile on admission with a normal blood pressure of 110/65 mmHg. The physical examination showed frank meningeal syndrome with neck stiffness. Examination of the other systems was normal. A lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis appearance was clear and colourless, The CSF cell count was 1×10^6 cells/L without red blood cells, glucose level 4.38 g/L and protein level 0.56 g/L. Examination in the fresh state had shown yeasts, India ink preparation of CSF showed round, narrow and encapsulated budding yeast cells of size of 4-6 μ m in diameter with wide clear halo around these cells suggestive of *Cryptococcus* spp. Culture on enriched media after 8 days of incubation had given rise to rounded colonies, shiny at first whitish then ochre. Strain identification was performed by VITEK2: *Cryptococcus neoformans*. Immunocompromised patient, HIV serology was positive with a viral load of 1,240,000 c/ml. A chest CT-scan was carried out in view of the suspicion of pneumocystosis. The brain ct scan had revealed hydrocephalus. The patient had presented skin lesions during her hospitalization. The

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patient was put under: Amphotericin B for 2 weeks then relay by Fluconazole. The evolution is unfavorable with respiratory distress and relapse of the neurological picture requiring hospitalization in the neurosurgery department

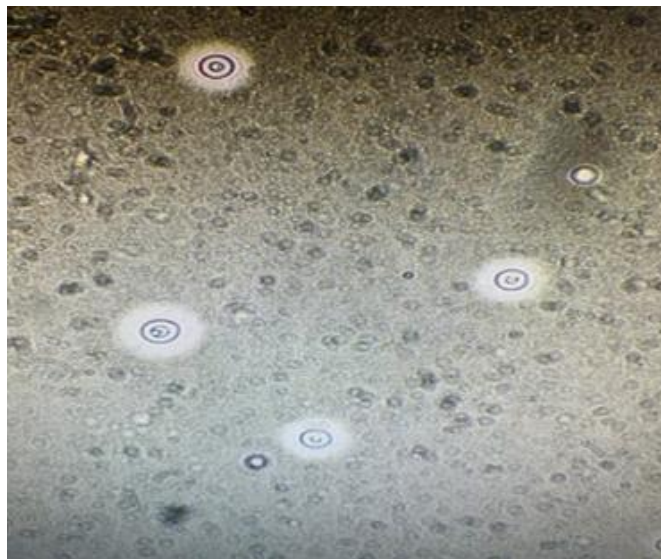


Figure 1 Round, narrow and encapsulated budding yeast in India ink preparation

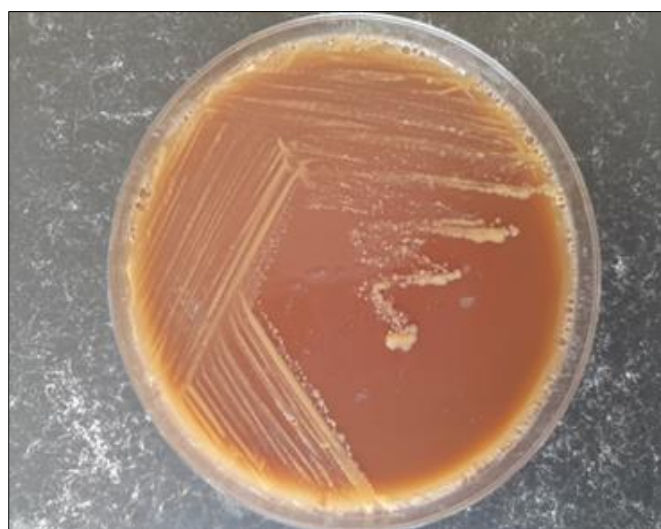


Figure 2 Rounded and ocher colonies on enriched media

3. Discussion

Neuromeningeal cryptococcosis (CNM) is a severe mycosis of the central nervous system, caused by the *Cryptococcus neoformans* / *Cryptococcus gattii* complex [1, 2]. In Morocco, the first case was described in 1978 in a seven-year-old boy at the children's hospital in Rabat [3]. It is an opportunistic mycosis which preferentially affects immunocompromised subjects and primarily HIV-positive patients, whose epidemiology has evolved in recent years. In the early 1980s, cryptococcosis increased during the AIDS pandemic, but the incidence of this mycosis decreased with the improvement of antiretroviral therapy in 1996. It is indicative of HIV infection in 29% cases, in our context, the CNM was revealing of HIV infection in our patient. In a Thai series of 16 CNM out of a total of 21 HIV-seropositive children, the most common signs found in children with neuromeningeal cryptococcosis were fever (81%), headache (81%), nausea and vomiting (75%). Signs of meningeal irritation were present in 63% of patients [4]. The 3 patients observed in Malawi did not present frank meningeal syndrome and were not febrile [5]. Cryptococcosis is a medical and therapeutic emergency. It requires a very rapid biological diagnosis, because its prognosis depends on the speed of the start of an appropriate treatment and only the isolation of *Cryptococcus* can confirm the diagnosis. The symptomatology of cryptococcosis being polymorphic and aspecific, laboratory methods are essential for diagnosis. Diagnosis of CNM is

based on direct examination of the CSF after staining with India ink. Cytochemical examination of the CSF almost always shows moderately high cellularity with lymphocyte predominance, hypoglycorrhachia and hyperproteinorrhachia [6,7] which is consistent with our results. Nevertheless; Cytological and biochemical abnormalities of cerebrospinal fluid may be minimal or even absent [8], making diagnosis difficult. In two cohorts of children co-infected with *Cryptococcus neoformans* and HIV, cytological and biochemical abnormalities were absent in more than half of the cases [9,4]. India ink staining is a simple technique, inexpensive and specific, to be performed in case of suspicion even if the CSF has normal cellularity and biochemistry. The lack of specificity of the clinical signs and the frequent normality of the CSF should encourage systematic search for *Cryptococcus neoformans* in the face of any picture of acute or subacute meningoencephalitis that does not prove its worth. The standard treatment for neuromeningeal cryptococcosis includes dual therapy combining amphotericin B and fluconazole. This therapeutic protocol has been adopted in our context. Amphotericin B should remain the treatment of first choice, fluconazole being used only as consolidation and maintenance treatment. Mortality with fluconazole used alone is heavy. In children, treatment is less codified, resulting in more delicate management [10]. The clinical evolution of our patient was fatal in a context of respiratory distress and neurological complication. This complication does not seem uncommon, especially since the observation reported by Ruggieri et al. [11] had the same evolution despite appropriate treatment.

4. Conclusion

Neuromeningeal cryptococcosis (CNM) is a deep opportunistic mycosis that preferentially affects the central nervous system responsible for serious damage. It occurs during the advanced stages of immunosuppression by HIV, but also in patients who are seronegative to this virus. A clinical-biological collaboration is necessary for a rapid diagnosis allowing the adaptation of an appropriate treatment.

Compliance with ethical standards

Disclosure of conflict of interest

Disclosure of conflict of interest There is no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study by signing the Free and Informed Consent Form

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