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Cryptoccocal Neuromeningitis in Immunocompetent Infant in Bonassama District Hospital, Douala: A Case Report

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Abstract

Cryptococcosis is rare in children. We report a case of cryptococcal meningitis in an infant whose mother works as a poultry farmer (chicken farm). The infant was received in the context of fever with convulsions. We performed a lumbar puncture and started antibiotic treatment. Cerebrospinal fluid (CSF) analysis was performed including Indian ink staining. CSF results showed the presence of yeast and we replaced antibiotics with fluconazol-based treatment. After the loss of sight and the appearance of a motor deficit, a brain scan was performed showing cerebral edema. Several lumbar punctures were performed for 02 weeks until partial recovery of visual acuity and motor deficit. This case highlights the importance of taking into account the patient's history when making the diagnosis. In our case, the working conditions and the employment of the mother guided the realization of the Indian ink coloring of the CSF. Treatment with fluconazol continued for 22 weeks with a completely regained visual acuity and gradual improvement in motor deficit despite limited resources.

Keywords

Cryptococcis, Meningitis, Immunocompetent, Infant

1. Introduction

Neuromeningeal cryptococcosis is an inflammation of the brain caused by an

encapsulated neurotropic yeast, *Cryptococcus neoformans*, the most common clinical presentation of which is meningoencephalitis [1]. It is a common infection in immunocompromised patients, and its incidence increased with the onset of HIV infection [2] but other causes are possible [3]. Observational studies conducted in South Africa and America, have reported cryptococcosis in children with an incidence from 2% to 2.6% [4] [5] [6].

Although a large number of studies have been conducted in the adult population with co-infection with HIV or cytomegalovirus (CM), very few studies have been devoted to the presentation, the progression and management of cryptococcal meningitis in children due to small sample sizes [5] [6].

In Senegal, Ndiaye *et al.* described 3 cases including 2 HIV-positive patients and an immunocompetent patient at the Fann University Hospital in Dakar over a period of 5 years [7]. In Cameroon, a study conducted among children under 15 by Nguefack *et al.* in 2018 found a prevalence of 3.6%, all patients were immunocompromised to HIV [8]. We report an observation in an infant immunocompetent to HIV who was diagnosed cryptococcal meningitis with good evolution after treatment.

2. Patient

18-month-old female infant, admitted on March 4, 2020 to the pediatric service at the Bonassama district hospital in Douala, presenting with convulsions associated with fever. The appearance of symptoms date back to 5 days was marked by the onset of an unmeasured, intermittent fever, without other signs prompting the use of paracetamol and other unspecified medication. With this treatment, the status of the child was marked by the persistence of the fever and the occurrence of an episode of tonic convulsions of unknown duration with sphincter relaxation, which motivated a consultation in a health center. Antimalarial treatment was administered with worsening of the neurological condition and persistence of convulsions, hence the referral to our department.

The medical history found a poorly followed-up pregnancy due to migration in a context of political instability, an eutocic delivery with a good adaptation to the extrauterine life. Only the first vaccine of expanded immunization program was received by the infant. She has had good height and weight growth (z-score weight for age = 0) and good psychomotor development for her age. The mother is an artisanal poultry farmer (chicken farm) and regularly goes to work with her infant where she set up a rest area for the infant inside the henhouse.

3. Clinical Results

On admission, she was in a superficial stage 2 coma with the systemic inflammatory syndrome (temperature 38.5˚C, tachycardia, tachypnea without respiratory distress). She presented with a stiff neck without a motor deficit. The diagnosis of bacterial meningitis was suggested and treatment with 3rd generation cephalosporin at a meningeal dose, phenobarbital and injectable paracetamol

was administered after sampling of Full Blood Count (FCB: WBC 8×10^3/µl, Hb 7.1 g/dl), Cerebrospinal fluid CSF (2 cells/fields, no leukocytes and presence of yeasts after staining with Indian ink, proteinorachia 2.34 and glycorachia 0.79) as well as a concomitant glycemia of 1.4 g/dl. The HIV serology was negative. The requested serum electrolyte test found values within the normal limits (Na + 136.2K + 4.77Cl − 108.4Ca^2 + 100Mg^2 + 19.5).

With the presence of yeast in the CSF, after the use of India ink, the diagnosis of meningeal cryptococcosis was made and the antibiotics stopped. Identification of the exact pathogen could not be made due to the family's financial limitations. Fluconazol was started at 12 mg/kg/day by nasogastric tube. After initiation of treatment and faced with the persistence of convulsions on D3, clonazepam was added, in combination with phenobarbital.

The persistence of the fever and the lack of improvement in consciousness as well as the appearance of a motor deficit in the left half of the body on D4 prompted the request for a brain CT scan which was not done. Faced with mucocutaneous palor and respiratory distress on D5, an urgent FBC requested returned with Hb at 5.1 g/dl prompting a blood transfusion. The course was marked by the persistence of fever and coma until D10 when the patient regained consciousness with apyrexia with the persistent motor deficit. The visual assessment on D11 found a loss of sight which motivated the parents to perform a brain CT scan which found cerebral edema associated with partial filling of the maxillary sinuses (**Figure 1**).

Repeated lumbar punctures draining 3cc every 48 hours were started during hospitalization. The patient was discharged on D16 with fluconazol and CSF drainage punctures for 02 weeks until partial recovery of the motor deficit and visual acuity. The requested physiotherapy sessions were never done.

Full visual acuity returned after 06 weeks of treatment. A control CSF analysis was performed after 14 weeks, due to limited finances, and showed an absence of yeasts.

The treatment was carried out over 22 weeks with complete visual recovery

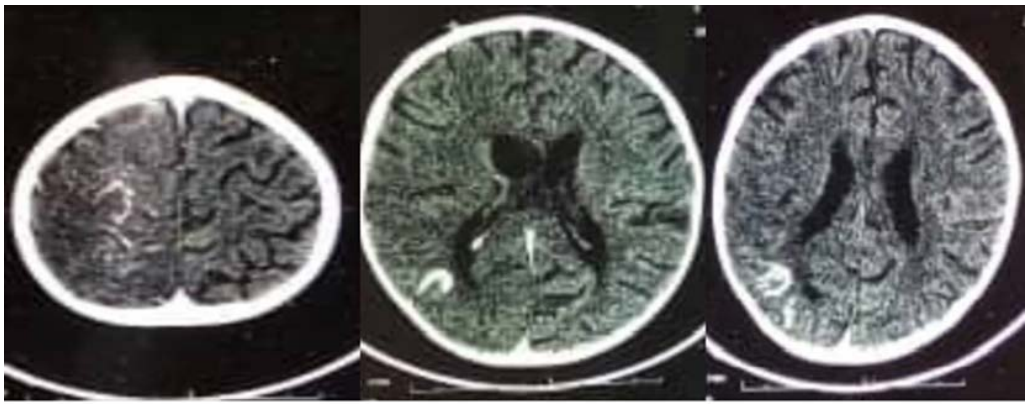

Figure 1. Cerebral CT scan. Gyriform contrast uptake in the right parietal lobe medial hypodensity/Left median shift of 02 mm/Undifferentiated sulcei in the right hemisphere/Hypodensity in the maxillary sinuses/Normal posterior cerebral fossa/No hydrocephaly nor suspicion of brain lesions.

and persistence of the motor deficit in the left upper limbs evaluated at 3/5.

Vaccination catch-up was started and parents were counselled on the importance of physiotherapy for full motor recovery.

4. Discussion

Cryptococcal meningitis is a common central nervous system (CNS) fungal infection with high morbidity and mortality. Globally, approximately 957,900 cases of cryptococcal meningitis occur each year, resulting in 624,700 deaths within 3 months of infection in adults and children with HIV [9].

However, in the pediatric population, the majority of patients are immunocompetent for HIV but present with other immune pathologies with non-neurological damage in cryptococcosis [10]. Cryptococcal meningitis mainly occurs in low-income countries, where health care and resources are limited.

The incidence of cryptococcosis in children remains low, varying between 1% - 2% depending on the studies and remains low even in children immunocompromised to HIV [6] [11] [12]. Cryptococcal infection in the immunocompetent is usually attributed to *Cryptococcus gattii* while that in the immunocompromised is predominantly by *C. neoformans* [13] [14].

The diagnosis is made mainly by India ink stain, which is less sensitive than the test for cryptococcal agglutination in the CSF. The accessibility of testing for cryptococcal antigens in CSF could have accelerated the diagnosis [15]. In our case, we were not able to obtain a culture due to a lack of financial means. Diagnosing primary immunodeficiency in our environment was not possible given the capabilities of our laboratory.

In this case, poorly conducted vaccination, exposure to chicken feces and the lack of clinical improvement despite properly conducted antibiotic therapy at a meningeal dose in the presence of signs of meningeal irritation made us suspect meningeal cryptococcosis [16].

This case highlights the importance of thinking about cryptococcal meningitis in the differential diagnoses of an immunocompetent child with signs of meningeal irritation. In addition to challenges in diagnosis, this case demonstrates the challenges of providing care in resource-constrained settings like Cameroon where there is limited availability of standard pharmacological agents, and where the standard treatment for cryptococcal meningitis, injectable fluconazole remains financially not very affordable.

The best treatment for cryptococcal meningitis in resource-limited settings is combination therapy with fluconazole and injectable amphotericin B [17].

In conclusion, meningeal cryptococcosis remains rare in the pediatric population. The diagnosis and treatment of cryptococcal infection in low-resource countries continues to be a challenge and the environmental context must be taken into account in the diagnostic discussion. The financial limitations of family delay diagnosis and hamper the progress and follow-up of patients according to standards. There is an urgent need to advocate for the availability of more

sensitive diagnostic tools and the wide availability of standard and effective fungicide treatment to reduce the morbidity associated with cryptococcal meningitis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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