

## Case Report

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# Cryptococcal Meningitis in Pregnancy, the Neglected Diagnosis: A Case Report

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## ABSTRACT

**Introduction:** Cryptococcal meningitis is an opportunistic infection of human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) that can cause maternal and fetal mortality and morbidity. This case report aims to help clinicians to consider it as a differential diagnosis in HIV-seropositive pregnant women presenting with vague symptoms. This is particularly important as HIV/AIDS is now a global pandemic. There is a test available for disease surveillance.

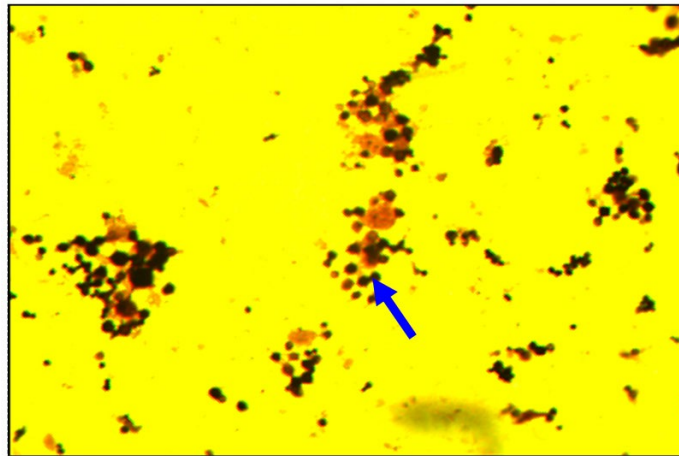
**Case Report:** A 31-year-old P3 G4 HIV seropositive patient on antiretroviral therapy/cotrimoxazole presented at 29 weeks gestation by dates complaining of draining clear fluid per vagina for 24 hours, slight frontal headache and vomiting. On admission, she was ill-looking but was afebrile with a body temperature of 36.2 °C. A sterile speculum examination confirmed ruptured membranes with a pool of liquor in the posterior vaginal fornix. She was treated as a case of preterm pre-labour rupture of membranes. Therapy consisted of erythromycin and dexamethasone. She complained of increasing frontal headaches and vomiting and on detailed examination was found to be now having neck stiffness. A lumbar puncture was performed and microscopy showed *Cryptococcus neoformans*. She was managed by a multidisciplinary team involving physicians and was treated with antifungals. She delivered prematurely by normal vaginal delivery a baby boy weighing 2100 g with Apgar 7 and 9 scores at 1 and 5 minutes respectively. Post-partum she continued to fit for a day but subsequently the convulsions stopped and the patient began to improve clinically.

**Conclusion:** There is need to raise awareness amongst clinicians about serious opportunistic infections in HIV infected pregnant mothers for early diagnosis and treatment. Antifungal therapy can be life-saving and prevent maternal deaths.

**KEYWORDS:** Cryptococcal meningitis; Pregnancy; Amphotericin B; Maternal death; Perinatal outcomes.

## INTRODUCTION

The first cases of Cryptococcal neoformans meningitis in pregnancy in the literature were described in 1962<sup>1</sup> and 1972.<sup>2</sup> It is an opportunistic fungal infection that presents with an insidious onset. Fungal spores like those in Figure 1 can be found in the cerebrospinal fluid in the brain causing significant maternal morbidity and mortality. There is currently sparse information on this subject in the literature. Cryptococcal meningitis is a serious disease that can cause adverse maternal and fetal outcomes especially in HIV/AIDS infected patients. Furthermore, pregnancy is immunosuppressive hence the combination with HIV can be catastrophic with maternal death. The disease can occur in HIV sero-negative and sero-positive patients.<sup>3,4</sup> The HIV/AIDS pandemic has assumed global status and the cases that occur need to be reported to raise clinical awareness. Awareness among clinicians is vital to help with early diagnosis, treatment and reduce morbidity and mortality.



The arrow shows cryptococcus neoformans organisms.

**Figure 1:** A slide showing *Cryptococcus neoformans* in a CSF sample.

## CASE REPORT

A 31-year-old P3 G4 HIV seropositive patient on antiretroviral therapy/cotrimoxazole presented at 29 weeks gestation by dates complaining of draining clear fluid per vagina for 24 hours. She also complained of a slight frontal headache and vomiting. She had been feeling dizzy and having generalised body weakness for the past 2 months.

On admission, she was ill-looking but was afebrile with a body temperature of 36.2 °C. Her blood pressure (BP) recording was 122/76 mmHg. The fetal heart was normal on Pinard auscultation. A sterile speculum examination confirmed ruptured membranes with a pool of liquor in the posterior vaginal fornix. A high vaginal swab was taken.

The differential diagnosis was that of preterm pre-labour rupture of membranes and urinary tract infection. A full blood count showed a normocytic normochromic anaemia of 9.8 g/dl, white blood cell (WBC) count of  $10.63 \times 10^9/L$ , a platelet count of  $297 \times 10^9/L$ . The CD4 count was 379 cells/mm<sup>3</sup>. Urinalysis showed no glucosuria and a trace of protein and a sample was sent for microscopy and culture. An ultrasound scan showed a fetus of 30 weeks gestation and adequate liquor volume. Therapy consisted of Erythromycin 250 mg 6 hourly per os to prevent infections and dexamethasone 6 mg intramuscularly twice per day for 2 days for fetal lung maturation. The high vaginal swab and urine samples did not grow any organisms on culture.

After 3 days of admission, she complained of increasing frontal headaches and vomiting. The blood pressures remained within normal ranges. On detailed examination she was found to be now having neck stiffness. A lumbar puncture was done. The cerebrospinal fluid (CSF) was clear but under pressure. CSF glucose and proteins were normal. Microscopic examination showed *Cryptococcus neoformans*. The culture also grew *Cryptococcus neoformans*. The serum cryptococcal antigen (CrAg) test was positive.

A team of physicians was consulted and reviewed the

patient. The patient was commenced on Amphotericin B 50 mg intravenously once daily plus Fluconazole 800 mg once daily per os. She received dexamethasone 10 mg intravenously 8 hourly.

After 3 weeks of therapy she started having convulsions. The patient went into preterm labour and delivered by normal vaginal delivery a baby boy weighing 2100 g with Apgar scores 7 and 9 at 1 and 5 minutes respectively. Post-partum she continued to fit for a day but subsequently the convulsions stopped and the patient began to improve clinically. A fortnight after delivery she was completely fit free and asymptomatic and able to sit up and feed properly. The neonate was well, needing no further treatments.

## DISCUSSION

This case report is important in that it raises awareness about an important condition that may cause considerable morbidity and mortality in pregnant patients. Other studies and case reports have reported similar clinical scenarios. This case report therefore adds more knowledge about this condition. Increased awareness can help reduce poor perinatal outcomes.

The differential diagnosis in this patient included pre-eclampsia/eclampsia but there was no clinical or laboratory evidence to support this diagnosis as the patient had no proteinuria or elevated blood pressures. The other diagnosis to consider was tuberculous meningitis (TBM) but the lumbar puncture results were conclusive for cryptococcal meningitis (CM). HIV/AIDS presentation can present with abnormal ways such as opportunistic infections like cryptococcal meningitis.

The prevention of cryptococcal meningitis in subclinical cases in HIV infected patients with CD4 cell counts of  $<100$  cells/mm<sup>3</sup> is possible. The diagnostic use of cryptococcal capsular polysaccharide antigen (CrAg) in serum is advisable<sup>5</sup> this allows life-saving antifungal therapy to be initiated. In low resource settings, this test is not readily available due to cost implications. In the presented case there was delay in diagnosis as

there were vague clinical symptoms pointing to a serious condition such as meningitis.

The management of the patient should be multidisciplinary involving physicians. Antifungal chemotherapeutic drugs used include Amphotericin B alone or in combination with flucytosine.<sup>6</sup> Fetal teratogenic effects of these drugs have not been reported, in fact both good maternal and fetal outcomes have been reported.<sup>7-11</sup> Another antifungal drug that can be used is fluconazole or itraconazole with good outcomes.<sup>12</sup> Cryptococcal placental infection without neonatal infection has been reported in the literature.<sup>13</sup> Only one case of mother-to-child transmission of cryptococcosis has been described in the literature.<sup>14</sup> In this case report, the baby did not seem any signs of being affected hence did not need any further treatments. Patients followed up to 8 months post-infection have shown no signs of infection.<sup>15</sup>

## CONCLUSION

There is need to raise awareness amongst clinicians about serious opportunistic infections in HIV infected pregnant mothers for early diagnosis and treatment. The widespread use of CrAg as a screening tool can help early disease detection hence allowing the commencement of antifungal therapy that can be life-saving and prevent maternal deaths.

## CONSENT

The authors obtained written informed consent from the patient for submission of this manuscript for publication.

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