

Placental and pulmonary cryptococcosis associated with fungemia in patient with acquired immunodeficiency syndrome

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SUMMARY

Cryptococcosis is a systemic mycosis with a chronic or subacute progression caused by the inhalation of dehydrated yeasts or basidiospores. The causative agents are *C. gattii* and *C. neoformans*. The latter is more commonly associated with cellular immunodeficiency and is not rare in patients with Acquired Immunodeficiency Syndrome (AIDS). Cryptococcosis is common in pregnant women with AIDS; however, it

is uncommon for the placenta to be affected, with few reported cases in the literature. We present the case of a pregnant woman with AIDS who had placental and pulmonary cryptococcosis associated with fungemia, with a satisfactory clinical outcome obtained after therapy.

Keywords: placental cryptococcosis, *C. neoformans*.

INTRODUCTION

Cryptococcosis, also known as torulosis, European blastomycosis, and Busse-Buschke disease, is a systemic mycosis with a chronic or subacute progression caused by the inhalation of dehydrated yeasts or basidiospores. The causative agents are *Cryptococcus gattii* and *Cryptococcus neoformans*. The latter is more commonly associated with cellular immunodeficiency [1]. According to Mizra et al., 89% of infections by *Cryptococcus* occur in HIV-infected people [2].

In most cases, the infection manifests by affecting the central nervous system with severe meningoencephalitis that is sometimes fatal. Pulmonary involvement may occur with this infection. Some patients present with fungemia and may rarely

present with skin, bone, and adrenal gland complications [3].

Cryptococcosis is not uncommon, especially among immunocompromised patients. However, placental cryptococcosis is rare, with few reported cases in the literature [4-6].

CASE REPORT

A 19-year-old pregnant patient of African descent who was born in Goiania, Brazil, presented with a dry cough, dyspnea, and a 40-day history of persistent daily fever. She had been pregnant for 28 weeks and 6 days and had been recently diagnosed with HIV during a prenatal examination. The patient initially visited a health care service that prescribed treatment for *Pneumocystis jirovecii* pneumonia, obtaining partial clinical recovery. The patient was transferred to another health care service that would have been able to better monitor her pregnancy and to investigate her persistent fever.

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On admission, the patient was conscious, eupnoeic, pale, dehydrated and with an axillary temperature of 38.2°C. The patient presented a systolic murmur of 2+/6+ on cardiac examination. Her abdomen showed the presence of a single fetus, with movements and a heart rate of 140 beats per minute. On genital examination, polymorphic lesions were found, along with vesicular, warty, and ulcerated lesions on the labia majora and perianal region.

Laboratory tests revealed pancytopenia. Chest radiographs showed pulmonary infiltration in the right lung and a computed tomography chest scan showed bilateral consolidative opacities. The TCD4+ cell count was 59 cells/mL and the viral load was 2,000 copies (flow cytometry/FACSCalibur-Multitest).

A lumbar puncture was performed and the cerebrospinal fluid (CSF) analysis showed normal cellularity: leukocytes: zero; red blood cells: 2/mm³, proteins: 49 mg/dL, and glucose: 43 mg/dL. Direct bacterioscopy yielded a negative result, as did the scraping tests for fungi and mycobacteria. CSF cultures were also negative. The results of a transthoracic echocardiogram were normal. A biopsy of the patient's genital lesions yielded three different diagnoses: genital herpes, molluscum contagiosum, and human papillomavirus. The staining methods used were hematoxylin-eosin (HE), Periodic acid-Schiff - Fungi (PAS), and Grocott.

The patient gave birth prematurely at a gestational age of 29 weeks, 2 days following the detection of acute fetal distress on an obstetric doppler scan. A cesarean section was performed and a live male infant (1,155 g) was delivered.

Analysis of the placenta revealed accentuated chronic inflammation of the placental villi with

diffuse necrosis and without chorioamnionitis or funiculitis. Histiocytes filled with round structures were observed (7.0 microns). These cells tested positive for *Cryptococcus* spp using PAS-Fungi, Grocott, and mucicarmine staining (Figure 1).

The patient underwent bronchoscopy and the bronchoalveolar lavage showed round structures with a clear outer halo on the inside of the cells and tested positive for *Cryptococcus* spp by PAS-Fungi, Grocott, and mucicarmine staining. A Nankin ink test showed these yeast-like structures again, producing an image that resembled a starrynight sky. The blood culture showed the presence of *Cryptococcus neoformans*.

Cryptococcal antigen test was not used in our investigation because the assay was unavailable in our institution.

Treatment with amphotericin B deoxycholate was administered (50 mg per day for 3 days) and later changed to liposomal amphotericin (3 mg/kg/day for 3 weeks) combined with fluconazole (800 mg per day) due to worsening kidney function. Such a change resulted in significant symptom improvement and the patient was discharged from the hospital, with instructions to continue treatment through daily hospital visits.

The newborn presented with neonatal sepsis and was treated with ampicillin and amikacin in an intensive care unit. As he progressed poorly and due to the severity of symptoms, the decision was made to start antifungal therapy with amphotericin B deoxycholate, despite the lack of confirmation through laboratory testing that he too had *C. neoformans*. The newborn progressed well from this point forward and was discharged from the intensive care unit. The fungus was therefore not isolated from cultured samples taken from the newborn.

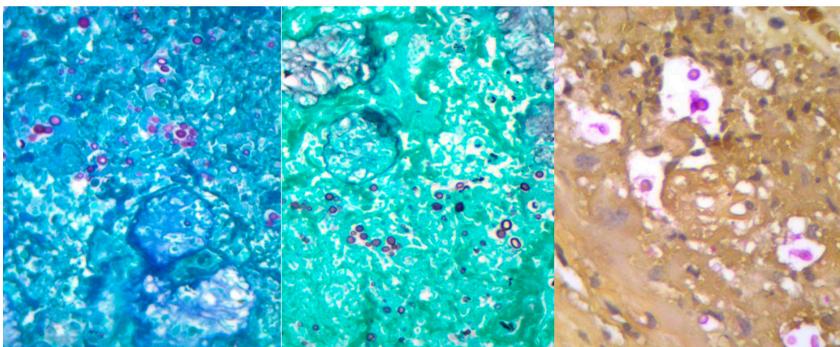


Figure 1 - Placenta. Staining method using PAS-Fungi, Grocott, and Mucicarmine. Maximum magnification: positive yeast-like structures, identifying *Cryptococcus* spp.

DISCUSSION

Although several cases of cryptococcosis in pregnant, immunocompromised women have been reported, placental infection is uncommon, and its mechanism has not been well established [7-10]. Vertical transmission is also rare [9, 11]. In the present case, the patient presented with pulmonary impairment and associated fungemia. It is likely that this patient's extremely compromised cellular immunity allowed the hematogenous dissemination of the infection that had its focus in the lungs. While the newborn presented with signs and symptoms that could suggest fungal infection, it was not confirmed by laboratory testing. However, the newborn showed significant clinical improvement after treatment with amphotericin B, strongly suggesting a neonatal fungal infection. Some authors have described the placenta as a barrier through which transmission of *Cryptococcus* spp would be hampered [9]. Nonetheless, the early presentation of cryptococcosis in neonates, the association with intracranial calcifications in some cases and the histopathological evidence of chorionic villi invasion suggest transmission through the placenta may occur [4, 11, 12].

In the case we report, the baby was delivered through cesarean section because there were signs of fetal distress, also because of the HIV viral load and the presence of lesions in the mother's genital area. However, the baby was probably compromised. The late diagnosis of both HIV infection and the systemic fungal disease contributed to the placental compromise and point to fungal infection vertical transmission. Taking all the findings into consideration, it is important to consider mother and child when managing cryptococcosis during pregnancy.

Conflict of interest

The authors do not have any conflict of interest.

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