

## Case Report

# Congenital toxoplasmosis: the challenge of early diagnosis of a complex and neglected disease

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### Abstract

The objective of this study was to report a case of congenital toxoplasmosis that illustrates the difficulties in diagnosing this disease. The case highlights the lack of prophylactic guidelines and shortcomings in the gestational screening process. It demonstrates the peculiarities of the non-specific clinical picture of the infection acquired during pregnancy and identifies the challenges of ophthalmological and high-sensitivity exams in newborns that are crucial for an early diagnosis. These factors contribute to a delay in early treatment of both the mother and the newborn. The lack of skill and expertise of clinical physicians to manage the disease is also addressed.

**Keywords:** Toxoplasmosis. Child. Vertical transmission.

### INTRODUCTION

Toxoplasmosis is a disease with particular clinical manifestations and symptoms. Children with congenital toxoplasmosis are asymptomatic at birth in over 70% of cases<sup>1</sup>. In Brazil, infections with highly virulent and polymorphic strains are causing ocular and neurological involvement in children<sup>2</sup>. In addition, toxoplasmosis is also the most common cause of acquired chorioretinitis in immunocompetent patients<sup>3</sup>.

The diagnosis of congenital toxoplasmosis is often challenging because it requires a combination of epidemiological, clinical, laboratory, and imaging analyses. Because toxoplasmosis is a neglected disease, there is no systematization and standardization of respective healthcare services and procedures. There are only a few reference centers that specifically attend to the mother-child binomials, which complicates case-by-case assessment and identification of children with sequelae because notification occurs only in these units<sup>4</sup>.

Fluctuating levels of acute serological markers in the child and immunotolerance due to pregnancy in the mother may also hinder early diagnosis of the newborn<sup>1,5</sup>. The present study

aimed to report an emblematic case of congenital toxoplasmosis due to difficulties in establishing an early diagnosis and an appropriate management of this disease.

### CASE REPORT

A 6-month-old female child was referred to the reference outpatient clinic for infectious diseases in Montes Claros, Northern Minas Gerais State, Brazil, with suspected toxoplasmosis based on fundoscopy examination and detection of various chorioretinitis lesions.

The mother of the child was 32 years old at delivery, had completed higher education, and had 2 previous pregnancies with 2 deliveries and hence no previous miscarriages or abortions. She chose to receive her prenatal care, which was started between 3 to 4 weeks of gestation, from the supplementary healthcare network. The initial serological analyses showed that she was susceptible to toxoplasmosis, and she was tested again in the second gestational trimester with negative results for toxoplasmosis IgG and IgM. She stated that she had not received prophylactic instructions regarding the risk of *T. gondii* contamination during her pregnancy. When questioned, she did not recall having contact with cats or consuming raw foods or undercooked meat. She reported having a "virus-like" condition around the sixth month of gestation, with low fever (not measured), headache, adynamia, and "ganglia" in the lateral cervical region of the neck. She consulted an obstetrician and was diagnosed with mumps for which she used symptomatic

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drugs that led to spontaneous improvement. No exam was requested at the time, either for toxoplasmosis or mumps.

The baby was delivered in a natural birth at a gestational age of 34 weeks. The weight of the newborn was 2,445 g, the height 44.5 cm, and the head circumference 31 cm. The Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score was 6 at minute 1 and 8 at minute 5 after birth. No obvious reason for the premature birth was identified. The newborn was hospitalized for 10 days to receive treatment with penicillin and gentamicin for presumed late sepsis with CNS involvement. She required supplementary oxygen therapy with continuous positive airway pressure (CPAP) for 4 days and with an oxygen hood after that, progressively weaning her from the oxygen supply. She was discharged on day 10 after birth in a good health condition and her mother was provided with general instructions for childcare.

The heel prick test was performed as part of neonatal screening when she was 11 days old. The blood was analyzed by enzyme-linked immunosorbent assay (ELISA) and was IgM negative for toxoplasmosis.

The mother first noticed that the child opened her right eye less wide than the left one at the age of 1 month and later observed symptoms indicating gradual strabismus and nystagmus. She also noticed that the child had difficulty following objects with her eyes. Four ophthalmological consultations were carried out by different physicians and chorioretinitis lesions were discovered at the age of 6 months, with the left eye showing an active peripheral lesion of the macula and the right eye showing multiple lesions in the final stage of scarring reaching the macula. The mother reported experiencing scotomas and discrete visual blurring in the right eye during pregnancy, and ophthalmological examination 6 months after delivery showed the presence of active peripheral chorioretinitis in her right eye.

The child was subjected to cranial computed tomography at 5 months of age that identified microcephaly with a head circumference of 35 cm and cortical hemispheric calcifications with diffuse distribution (**Figure 1**).

Fundoscopy performed at 18 months of age revealed chorioretinitis scars of the right eye throughout the posterior pole and upper chorioretinitis scars of the left eye straining the retina with fibrosis causing mild macular ectopy.

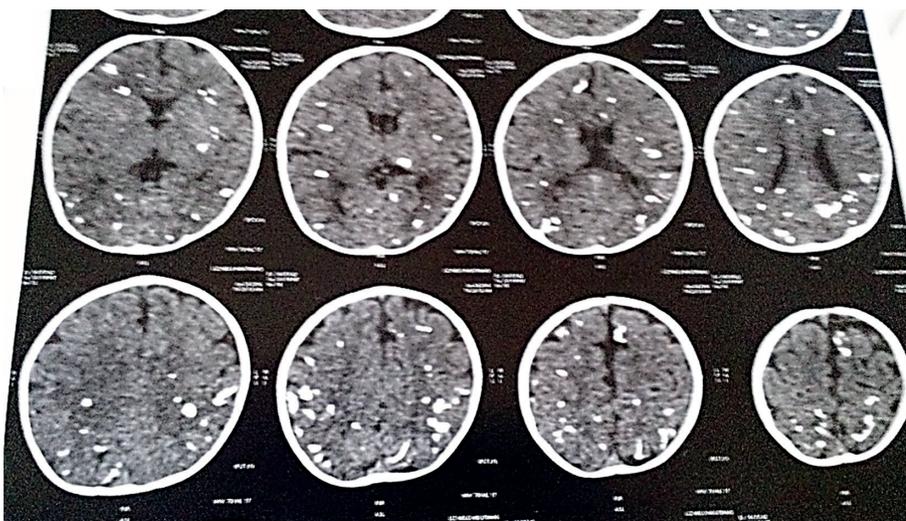
The results of serological tests for toxoplasmosis were as follows: 133.6 IU/mL IgG and 0.29 IU/mL IgM (measured by chemiluminescent microparticle immunoassay/CMIA) at 11 months of age and >650.0 IU/mL IgG (measured by electrochemiluminescence immunoassay/ECLIA) at 15 months of age.

The serological analysis of the mother's blood showed a toxoplasmosis IgG level of >200 IU/mL and an IgM level of 2.3 IU/mL (measured by CMIA) 6 months after delivery.

The child was treated with a regimen of sulfadiazine (100 mg/kg/day), pyrimethamine (1 mg/kg/day), folic acid (10 mg/day, 3×/week for 7 months), and prednisolone (1 mg/kg/day for 2 months until the ocular lesions were scarred). Blood tests were performed every 15 days in the first 2 months to monitor any adverse effects of the medications and in monthly intervals afterwards until 1 month after the end of the treatment. No adverse reactions were observed. The child is currently 26 months old and still has sub-normal vision, but has good socialization skills, does not exhibit any behavioral changes, and attends a regular school. She is undergoing ocular physiotherapy with ophthalmological, neurological, and pediatric follow-ups on a regular basis.

## DISCUSSION

This case illustrates the current situation of prenatal care with respect to congenital toxoplasmosis in both public and supplementary healthcare networks in Brazil. Because the acquired form of toxoplasmosis may be asymptomatic, the clinical diagnosis is frequently confused with other viral pathologies and may go unnoticed by the patient. In the case presented here, the patient did experience symptoms of toxoplasmosis but it was not even considered was still not



**FIGURE 1:** Cranial computed tomography scan showing diffuse calcifications and microcephaly.

diagnosed, which limited further examination of the mother and delayed diagnosis in the child. The disease may present as an infectious mononucleosis-like syndrome and there are studies associating maternal chorioretinitis with congenital toxoplasmosis<sup>6</sup>. Because toxoplasmosis is still a neglected disease and the appropriate management remains controversial, the attending physician is often not familiar with the disease and has difficulty diagnosing, monitoring, and treating the patient. In addition, basic prophylactic interventions may not be carried out that could prevent fetal contamination in up to 70% of susceptible pregnant women<sup>7</sup>.

Serological screening at delivery followed by monthly or at least quarterly postpartum screening intervals in susceptible women should be part of the monitoring routine. In the case described herein, serological screening was performed only twice during pregnancy.

Early diagnosis in the newborn is difficult because about 70% of infected children are asymptomatic at birth. Even sensitive serological tests may only provide transient results and not detect immunoglobulins early<sup>1,5,8</sup>. It should be emphasized that the neonatal heel prick test generally shows a high sensitivity and was performed at the right time in the present case, but specific IgM was not detected, pointing to the limitations of laboratory tests for an accurate diagnosis.

Even though the child presented microcephaly at birth and required antibiotics, there were no further imaging exams or analysis of the cerebrospinal fluid (CSF), which could have supported an earlier diagnosis and justified the use of corticosteroids against the active disease<sup>1</sup>. Ophthalmological diagnosis proved difficult in this case, illustrating the failure of the involved physicians to accurately evaluate the results of the exam in the newborn.

The lack of protocols and consensus on the mother-child binomial approach and the unavailability of specific reference centers further complicate a timely management of the disease<sup>4,8,9</sup>.

Although treating the pregnant mother or the newborn does not guarantee cure of the disease or absence of lesions, it is the most effective way to prevent relapses and even more serious sequelae in the longterm<sup>1,10,11</sup>. Based on our observations, strategies for the appropriate management of congenital toxoplasmosis are urgently needed.

**Conflict of Interest:** The authors declare that there is no conflict of interest.

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