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SCIENTIFIC ARTICLE - REVIEW ARTICLE

CONGENITAL NEUROTOXOPLASMOSIS IN A NEWBORN SON OF A MOTHER WITH REINFECTION BY TOXOPLASMA GONDII: A CASE REPORT

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ABSTRACT

The article describes a rare case of congenital neurotoxoplasmosis in a newborn born to an immunocompetent mother, an illicit drug user and exposed to syphilis, with reactivation of the disease during pregnancy.

Keywords: Congenital neurotoxoplasmosis, Reinfection, Congenital infections

INTRODUCTION

Congenital toxoplasmosis is an infection caused by the protozoan Toxoplasma gondii[1], which can be transmitted from mother to fetus during pregnancy. Although the infection is more commonly associated with mothers who have never had the disease before, meaning they do not have protective antibodies against the parasite, cases of congenital toxoplasmosis have also been reported in immunocompetent mothers who were previously infected with the protozoan.[2]

After primary maternal infection with T. gondii during pregnancy, the parasite has the ability to penetrate the fetus's bloodstream through the placenta. Placental transmission occurs less frequently when the infection is acquired before the tenth week of gestation and is extremely rare when the infection occurs even before conception. Without treatment, the incidence rate of fetal infection is approximately 10% to 15% if the infection occurs in the first trimester, 30% in the second trimester, and 60% in the third trimester.[3]

Early maternal infection (during the first and second trimesters) can result in severe congenital toxoplasmosis, including fetal death and miscarriage. On the other hand, late maternal infection (during the third trimester) usually results in subclinical toxoplasmosis in newborns. In these cases, the infection initially goes unnoticed, but these babies may develop chorioretinitis and other complications later in life.[1] Acute infection is followed by the formation of cysts in chronic infection and is associated with an

immune response that typically provides protection against reinfection. This chronic infection is characterized by stable levels of specific IgG. In immunocompetent mothers who were immunized against toxoplasmosis before conception, immune mechanisms prevent the transmission of infection to their fetuses.

Congenital toxoplasmosis that occurs due to the reactivation of a chronic infection in pregnant women with a competent immune system is considered rare. The reported cases associate a possible decrease in cellular response during pregnancy, which may affect the control of the parasites and the clinical development of the infection in the mother, thereby increasing the risk of vertical transmission[2], as well as a new infection by a different strain.[4,5]

The clinical characteristics of congenital toxoplasmosis in newborns of immunocompetent mothers can vary. In some cases, the infection may be asymptomatic in both the mother and the fetus. However, in other cases, the infection can lead to severe complications in the fetus, including intrauterine growth retardation, microcephaly, ocular lesions, cerebral calcifications, and neurological dysfunction.[6]

The objective of this article is to report a case of congenital toxoplasmosis resulting from reinfection in an immunocompetent mother diagnosed in a public hospital in Goiás, along with a literature review on the topic.

CASE REPORT

A.V.A. was born on March 17, 2023, via cesarean section due to oligohydramnios and intrauterine growth restriction (IUGR), with a gestational age of 37 weeks and 1 day calculated by first-trimester ultrasound.

The mother, 39 years old, had four previous pregnancies with no miscarriages (G4P4A0), completed high school, and was a homemaker. She had eight prenatal consultations. The patient reported being a user of illicit drugs (marijuana and crack), with the last use occurring 24 hours before delivery, and she was occasionally homeless. The following serologies were performed on September 15, 2022: Anti-HIV: non-reactive, Treponemal Syphilis: reactive, VDRL: reactive 1/2, and serology for Toxoplasmosis with IGM - non-reactive and IGG - reactive. Regarding syphilis, she stated that she had been treated in a previous pregnancy three years ago and had not received treatment during the current pregnancy. At the maternity ward, she presented VDRL - non-reactive, Rapid Test for Syphilis - reactive, and Rapid Test for HIV - non-reactive.

The newborn had a birth weight of 1830 grams, a length of 45 cm, and a head circumference of 29 cm. After birth, he developed respiratory distress and was transferred to the Care Room, requiring ventilatory support with Hood at 30% for about 17 hours. At 41 hours of life, he was transferred to the Rooming-In facility, on an oral diet via bottle, as the mother refused to breastfeed. On the third day of life, due to changes in the blood count (leukopenia and thrombocytopenia), associated with refractory hypoglycemia and untreated maternal urinary tract infection at the time of delivery, empirical treatment for neonatal sepsis with ampicillin and gentamicin was initiated.

An echocardiogram was also performed, revealing an interatrial septum and a patent foramen ovale, with a slight left-to-right shunt; conclusion: patent foramen ovale. An ultrasound of the kidneys and urinary tract showed no abnormalities, and a transfontanelle ultrasound revealed a hyperechoic image

with slight acoustic attenuation measuring 0.3 cm, indicating intraparenchymal calcification. Following this finding on the transfontanelle ultrasound, an investigation of congenital infections was initiated, and serologies for the mother/newborn pair were requested.

On the fourth day of life, the newborn was hypochromic, developing petechiae and cyanosis in the upper limbs and perioral area. He was transferred back to the Care Room for monitoring and then moved to the Intermediate Care Unit (ICU).

The serological tests for the mother/newborn pair confirmed the infection by T. gondii. The mother had reactive anti-Toxoplasma IgM (9.727) and reactive anti-Toxoplasma IgG (422.31) through the chemiluminescence technique, while the newborn had reactive anti-Toxoplasma IgM (29.998) and reactive anti-Toxoplasma IgG (1582.55). The fundoscopic examination revealed an active ocular lesion in the macula/optic nerve region. A cerebrospinal fluid (CSF) collection was performed on March 22, 2023, showing low cellularity, so a differential count was not conducted; glucose: 32 mg/dL, protein: 321 mg/dL.

In light of the situation, treatment was initiated on the fifth day of life with pyrimethamine 1 mg/kg/day once daily, sulfadiazine 100 mg/kg/day every 12 hours, folinic acid 10 mg three times a week, and prednisolone 1 mg/kg/day due to ocular involvement.

A cranial tomography was also performed, which showed hypodensity without mass effect in the symmetric and bilateral cortical/subcortical frontal/parietal/temporal regions, with intermixed granulomatous calcifications. There were also ependymal calcifications as shown in Figures 1 and 2.

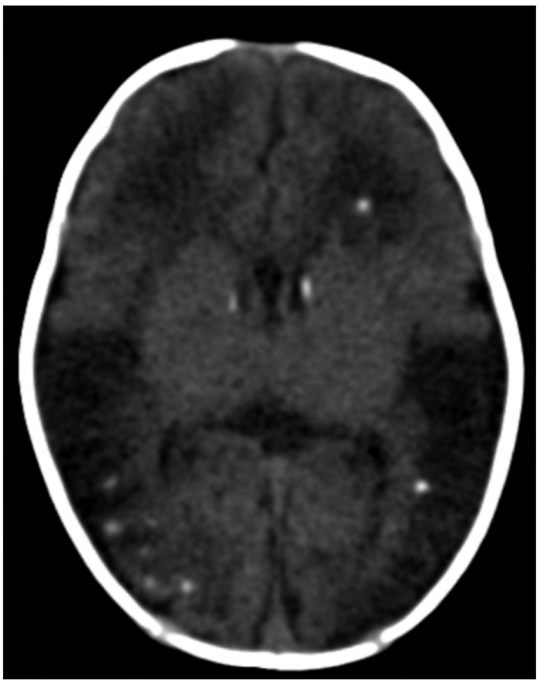

Figure 1

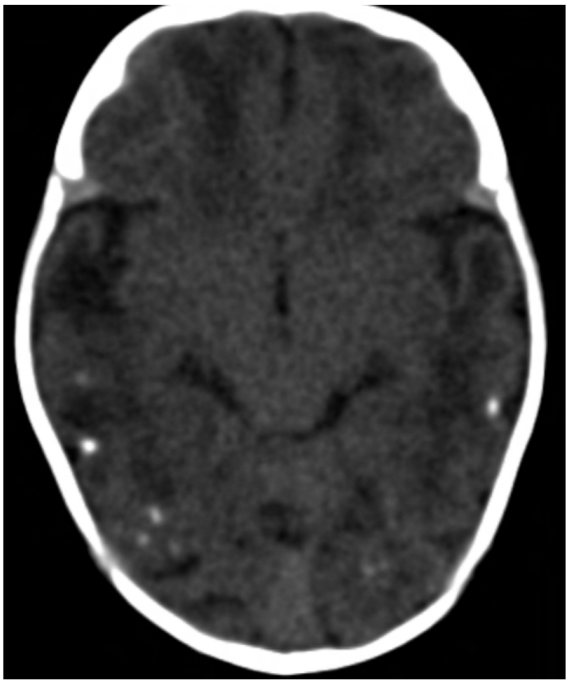

Figure 2

The patient continues to be monitored on an outpatient basis with a team of pediatrics, ophthalmology, and pediatric infectious diseases. She is experiencing significant delays in growth and neuropsychomotor development

Table with Description of Fundoscopy Findings in the Child During Treatment:

Date	Result
03/21/2023	Active lesion (ocular/in macula/nerve)
04/17/2023	OD: macular and mid-peripheral chorioretinitis, ROP, and Zone II OS: optic neuritis, macular and mid-peripheral chorioretinitis, hemorrhage, ROP, and Zone II.
04/27/2023.	OD: macular and mid-peripheral chorioretinitis, ROP, and Zone II OS: worsening optic neuritis, active significant hemorrhagic macular chorioretinitis, mid-peripheral chorioretinitis, hemorrhage, ROP, and Zone II.
05/02/2023	OD: ROP with Zone III avascular, chorioretinitis healing with macular involvement, OD with adequate coloration. OS: ROP with Zone III avascular, inferior nasal ORVCR with subretinal hemorrhage in the macular retinitis area and slight improvement in optic neuritis.
05/09/2023	OD: maintained retinitis OS: improvement of ORCVR in the inferior quadrants and improvement in optic neuritis.
05/16/2023	OD: retinitis healing OS: improvement of retinal vascular occlusion: sequelae of ORVCR in the inferior quadrants and improvement in optic neuritis.
05/30/2023	OD: retinitis healing, physiological, extensive macular scar OS: improvement of ORCVR in the inferior quadrants and improvement in optic neuritis, however, pallor of OD and slight blurring still at the temporal border.
06/13/2023	OD: healed retinitis, physiological, extensive macular scar OS: improvement of ORCVR in the inferior quadrants and improvement in optic neuritis, however, pallor of OD with resolution of the temporal border blurring.

Table 1: Source Authors

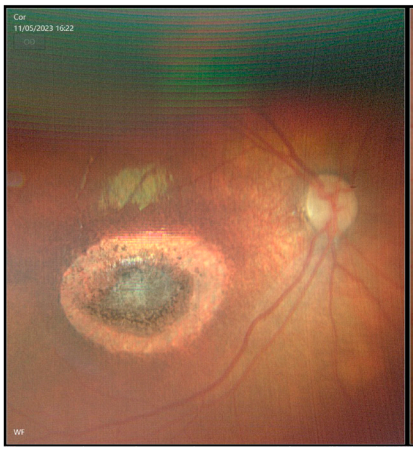

Figure 1: Right eye fundus examination showing chorioretinitis scar in the posterior pole in the paramacular area.

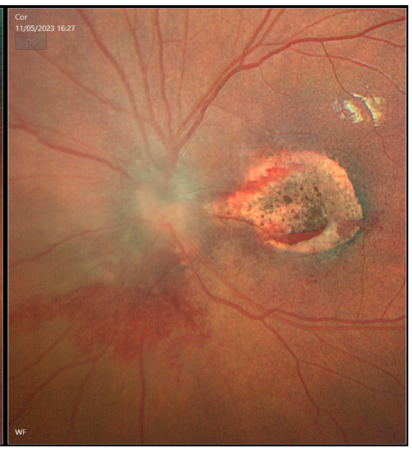

Figure 2: Left eye retinography: evidence of retinal venous occlusion due to papilledema and active chorioretinitis lesion in the macular region.

DISCUSSION

It was believed that primary maternal infection with T. gondii protected against reinfection; however, several cases of reinfection have been reported in previously infected mothers. The described cases suggest a possible association with a decrease in cellular response during pregnancy, which can affect parasite control and the clinical development of the infection in the mother, thus increasing the risk of vertical transmission.[2,7]

In addition, cases resulting from a new infection have been described, in which IgM and, especially, IgA antibodies were detected due to the immune response of the gastrointestinal tract to the ingestion of T. gondii oocysts. [8,9,10] Reinfection is accompanied by an intense immune response, often characterized by increased levels of IgG and the presence of IgM antibodies. In an immunocompetent pregnant woman with a serological history indicative of latent infection (absence of IgM and IgA, and low levels of IgG), the detection of serological markers of acute toxoplasmosis (presence of IgM and/or IgA and elevated levels of IgG) suggests the occurrence of reinfection, which may result in transmission to the fetus.[11]

The hypothesis of reinfection is supported by experimental studies conducted with chronically infected animals, which observed that they can produce offspring with congenital infection when reinfected with different strains of the parasite.[4] Another study by Gaballah et al. simulated the impact of reinfection in mice experimentally infected with a lethal strain of T. gondii after primary infection with a non-virulent genotype. The results highlighted that mice with chronic toxoplasmosis developed acute disease when reintroduced to another virulent strain. Therefore, it suggests that chronic infection with T. gondii does not prevent reinfection nor does it preclude the colonization of the brain with tissue cysts after superinfection by virulent strains. This explains the possibility of congenital toxoplasmosis in immunocompetent pregnant women when reinfected with a virulent strain of T. gondii.[5]

Recently, naturally mixed infections in humans have been observed, resulting from simultaneous or sequential exposure to parasites of different genotypes. However, it is still unclear whether the protection conferred by primary infection is genotype-specific.[12]

Gavinet et al. reported a case of congenital infection in an immunocompetent mother, in which the serological investigation conducted early during pregnancy indicated a chronic infection by T. gondii. Sequential serological tests showed the emergence of IgM and IgA antibodies, as well as an increase in IgG antibody titers, suggesting the possibility of reinfection.[11]

Hennequin et al. and Kodjikian et al. described cases of toxoplasmosis in which chronically infected mothers transmitted the infection to their children, with the diagnosis being made early in the neonatal period. Upon retrospectively analyzing maternal blood samples, an increase in IgG antibody levels and the emergence of IgA antibodies were observed in both cases. There was no compromise of the mothers' immune systems in either case, and no evidence of reactivation during pregnancy was found, suggesting that reinfection was the most likely explanation.[10,13]

Silveira et al. describe a case of congenital toxoplasmosis diagnosis through routine screening in a mother who was already infected 20 years before pregnancy. In this case, the possibility of reinfection by the same strain or by a different strain of the parasite was raised. According to the literature, reinfection may be associated with exposure to a large number of parasites, a more virulent strain, or a parasite of a different genotype.[2]

Lebas et al. describe a severe case of congenital toxoplasmosis in a woman who was infected before pregnancy, suggesting that she may have been infected by a different strain of the parasite, corroborating the hypothesis of Silveira et al. regarding the possibility of reinfection.[8]

The clinical characteristics of congenital toxoplasmosis in immunocompetent mothers can vary. In some cases, the infection may be asymptomatic in both the mother and the fetus. However, in other cases, the infection can lead to severe complications in the fetus, including intrauterine growth retardation, microcephaly, ocular lesions, cerebral calcifications, and neurological dysfunction. Additionally, congenital toxoplasmosis in immunocompetent mothers may present an increased risk of recurrence in subsequent pregnancies.[6]

The diagnosis of congenital toxoplasmosis in immunocompetent mothers is based on a combination of methods. Serology is an important method, as the detection of specific IgM and IgG antibodies for Toxoplasma gondii can indicate a recent or past infection. Additionally, amniotic fluid samples can be collected to detect the parasite's DNA using the Polymerase Chain Reaction (PCR) technique. Obstetric ultrasound also plays a significant role in detecting fetal anomalies.[1,14]

The treatment of congenital toxoplasmosis in immunocompetent mothers generally involves the administration of antiparasitic medications, such as spiramycin, during pregnancy. The aim of spiramycin is to reduce the risk of parasite transmission to the fetus. However, the efficacy of treatment in immunocompetent mothers is debated, as spiramycin does not cross the placenta in adequate amounts to treat fetal infection. In more severe cases, where fetal infection is confirmed, the use of more potent medications, such as pyrimethamine and sulfadiazine, may be necessary, in conjunction with spiramycin.[1,15]

The clinical outcome of congenital toxoplasmosis in immunocompetent mothers can vary widely. Some newborns may have permanent sequelae, such as neurological, visual, and auditory problems. Others may have a more favorable clinical course, with little or no evident clinical manifestation. The prognosis may also depend on the timing of the infection during pregnancy and the promptness of diagnosis and treatment.[16]

CONCLUSION

In conclusion, this case report of congenital toxoplasmosis in an immunocompetent mother highlights the possibility of reinfection with Toxoplasma gondii during pregnancy and the clinical challenges associated with this condition. The reviewed literature also reveals the existence of similar cases where previously immune mothers develop a new infection, resulting in the vertical transmission of the parasite to the fetus.

The diagnosis of congenital toxoplasmosis cannot be dismissed solely based on a previous maternal infection, and the means to document this diagnosis should be promptly employed in the presence of clinical features of fetopathy, considering the urgency of specific treatment.

Congenital toxoplasmosis can vary in severity and present a wide range of clinical manifestations, from asymptomatic cases to severe complications such as intrauterine growth retardation, microcephaly, ocular lesions, cerebral calcifications, and neurological dysfunction. Maternal infection occurring early, especially during the first and second trimesters, tends to be more severe and is associated with higher rates of fetal morbidity, including fetal death and miscarriage.

The proper detection of congenital toxoplasmosis requires a multidisciplinary approach, involving maternal and neonatal serological tests, imaging studies such as ultrasound and cranial tomography, as well as careful ophthalmological evaluation of the newborn. Early treatment with antiparasitic medications, such as pyrimethamine and sulfadiazine, is essential to control the infection and prevent future complications.

It is important to emphasize that congenital toxoplasmosis in immunocompetent mothers is considered a rare condition, but it warrants clinical attention and greater awareness regarding prevention methods. Conducting appropriate serological tests during prenatal care, especially in endemic areas, can identify pregnant women susceptible to infection and enable appropriate preventive interventions, such as avoiding the consumption of raw or undercooked meat and promoting proper hygiene measures to reduce exposure to the parasite.

In summary, congenital toxoplasmosis in immunocompetent mothers represents a significant clinical challenge. Understanding the mechanisms of reinfection, as well as implementing appropriate prevention and treatment strategies, are crucial for minimizing the adverse effects of this disease and improving clinical outcomes for affected newborns. The dissemination of knowledge about this condition through case studies and literature reviews is essential to provide up-to-date information to healthcare professionals and promote public awareness of congenital toxoplasmosis.

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