0021-7557/10/86-01/85
Jornal de Pediatria

Congenital toxoplasmosis from a chronically infected woman with reactivation of retinochoroiditis during pregnancy

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Abstract

Objective: To report a rare case of congenital toxoplasmosis from an immunocompetent mother with chronic infection who had reactivation of ocular disease during pregnancy.

Description: The newborn was asymptomatic at birth and identified by neonatal screening (IgM anti-*Toxoplasma gondii* in dried blood) among other 190 infants with congenital toxoplasmosis during a 7-month period. His mother had had a non-treated episode of reactivation of toxoplasmic retinochoroiditis during pregnancy, with stable IgG titers and negative IgM results. Results of IgM and IgG in the newborn's serum, as well as IgG immunoblotting were positive and active retinochoroidal lesions were detected in his peripheral retina. The neonate was treated with sulfadiazine, pyrimethamine and folinic acid. At 14 months of life, the child remained asymptomatic, with regression of retinochoroidal lesions and persistence of IgG.

Comments: It is possible that systematic neonatal screening in areas with high prevalence of infection may identify these cases.

J Pediatr (Rio J). 2010;86(1):85-88: Congenital toxoplasmosis, vertical transmission, neonatal screening, chorioretinitis, pregnancy.

Introduction

Congenital toxoplasmosis resulting from the reactivation of chronic infection in immunocompetent pregnant women is considered a rare event. Reported cases have been linked to a possible decreased cellular response during pregnancy, which might interfere with the parasite control and the clinical course of maternal infection and subsequently increase the risk of vertical transmission.[1-3]

The impact of reinfection on the occurrence of human congenital toxoplasmosis is also largely unknown. Cases resulting from reinfection have also been reported,[4] with the detection of IgM, and especially IgA antibodies due to the immune response of the gastrointestinal tract to the ingestion of oocysts.[5-7] Fetal involvement is variable.[4,8]

In the Brazilian State of Minas Gerais, neonatal screening of 146,307 newborns from November 2006 to May 2007 identified 190 cases of congenital toxoplasmosis (prevalence of 1/770 liveborns).[9] Among these, there was an infant whose mother was chronically infected and had a

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Financial support: Secretaria do Estado de Saúde de Minas Gerais, Brazil.

No conflicts of interest declared concerning the publication of this article.

Suggested citation: Andrade GM, Vasconcelos-Santos DV, Carellos EV, Romanelli RM, Vitor RW, Carneiro AC, et al. Congenital toxoplasmosis from a chronically infected woman with reactivation of retinochoroiditis during pregnancy. J Pediatr (Rio J). 2010;86(1):85-88.

Manuscript submitted Jun 8 2009, accepted for publication Aug 7 2009.

doi:10.2223/JPED.1948

clinical and serological picture consistent with reactivation of toxoplasmic retinochoroiditis during pregnancy. The purpose of this paper is to report this case and review the literature on the subject.

Case description

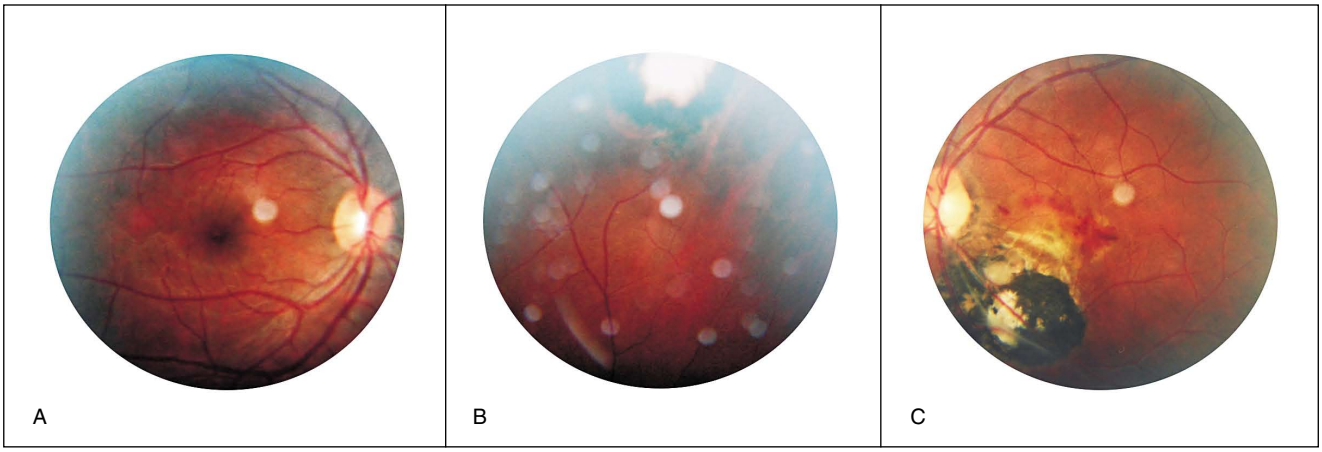
In 2006, a primiparous woman gave birth to a male infant at 39 weeks of gestation. At birth, his weight was 3,410 g, length 50 cm, and head circumference 37 cm. A pediatric examination found no abnormalities. The mother reported an episode of toxoplasmic retinochoroiditis in the left eye 10 years before pregnancy. She referred serological tests which were consistent with the diagnosis, and was treated with standard antiparasitic drugs, as well as oral and topical corticosteroids. She had no apparent immunodeficiency neither used immunosuppressive drugs. In the 24th week of gestation, she had reactivation of retinochoroiditis in her left eye, with further decreased vision and a satellite lesion at the margin of a perimacular pigmented scar. She was then treated only with topical corticosteroids. The serological screening for toxoplasmosis in the 25th and 28th weeks showed low and stable IgG levels and no IgM antibodies (Table 1). In the 25th week, HIV tests had negative results. Ten days after birth, as part of a research project on neonatal screening, a dried blood sample from her infant tested positively for anti-*Toxoplasma gondii* IgM antibodies. Confirmatory serological tests for toxoplasmosis on the infant yielded positive results for IgG and IgM (Table 1). Clinical examination revealed splenomegaly and transfontanel ultrasound and hearing assessment were unremarkable. One month after birth, ophthalmologic examination of the baby revealed multiple active retinochoroidal lesions in the peripheral retina of both eyes. Two weeks later, the mother experienced slightly decreased vision and floaters in the right eye and examination disclosed active toxoplasmic retinochoroiditis in the superior periphery of the right eye. The left eye had a large pigmented perimacular scar. The mother was initially treated only with topical steroid and mydriatic. However, vision further decreased in the right eye, requiring classical treatment (sulfadiazine, pyrimethamine and folinic acid) with oral prednisone (1 mg/kg). The lesion eventually healed, with recovery of visual acuity, but 1 year later she developed further decreased vision in the left eye, with choroidal neovascularization at the margins of the old perimacular scar in the left eye (Figure 1).

Despite the positive serologic results (IgM and IgG), the sera collected from mother and offspring (1 and 2 months after birth) were also analyzed by immunoblotting as described by Gavinet et al.[6] The IgG antibodies of the

Table 1 - Results of serological tests to confirm toxoplasmosis in mother and offspring

		Antibodies		
Dates	**Method**	**IgG**	**IgM**	**IgA**
Mother LMP -16/03/06				
08/01/06	Chemiluminescence	52.7 UI/mL (positive ≥ 8.0)	Negative	NP
08/25/06	Chemiluminescence	44.2 UI/mL (positive ≥ 8.0)	Negative	NP
12/05/06	ELFA-VIDAS	> 300 UI/mL (positive ≥ 8.0)	Negative	NP
Offspring DOB - 11/11/06				
11/21/06	ELISA*	NP	0.333 (positive)	NP
12/05/06	ELFA-VIDAS	54 UI/mL (positive ≥ 8.0)	4.48 (positive ≥ 0.75)	
12/05/06	ELISA†			17.3 (positive ≥ 5.0)
01/24/07	ELFA-VIDAS	>300 UI/mL (positive ≥ 8.0)	5.39 (positive ≥ 0.75)	
01/24/07	ELISA†			9.0 (positive ≥ 5.0)
02/12/08	ELFA-VIDAS	> 300 UI/mL (positive ≥ 8.0)	Negative	NP

DOB = date of birth; ELFA-VIDAS = enzyme-linked fluorescent assay-vitek immunodiagnostic assay system; ELISA = enzyme-linked immune sorbent assay; LMP = last menstrual period; NP = not performed.
* Q-PREVEN TOXO IgM kit (Symbiosis Diagnóstica Ltda, Leme, Brasil)® – dried blood sample.
† ETI-TOXOK-A reverse PLUS kit (Diasorin Biomédica, Sallugia, Italy).



A = Normal posterior pole of the right eye.
B = Superior periphery of the right eye, showing the retinochoroidal scar with central atrophy and pigmented margins.
C = Posterior pole of the left eye, showing a large and predominantly pigmented retinochoroidal scar involving the macula. Retinal hemorrhages are seen in the superior margin of the lesion, indicating presence of a choroidal neovascular membrane.

Figure 1 - Color fundus photographs of the mother 14 months after delivering the offspring with congenital toxoplasmosis; the patient had been treated for recurrent toxoplasmic retinochoroiditis in her left eye 12 months before

newborn recognized three *T. gondii* proteins (87 kDa, 54-58 kDa e 31-33 kDa) which were not recognized by the mother, confirming infection of the offspring.

Two blood samples from the infant (collected 5 and 8 weeks after birth) were also tested by polymerase chain reaction (PCR) targeting *T. gondii* B1 gene as described by Vidigal et al.,[10] with negative results. Blood from the same samples was also inoculated in Swiss-Webster mice. The animals were evaluated daily, having their peritoneal fluid analyzed under the microscope for tachyzoites, and being sacrificed after 30 days. A serologic test for *T. gondii* was performed and the brain was examined for tissue cysts. These tests also gave negative results.

The child was treated with sulfadiazine, pyrimethamine, and folinic acid for 12 months,[5] and is now under follow-up without ophthalmologic, auditory or neurologic sequelae.

Discussion

We present a case of a woman with chronic infection who had a clinical and serological picture consistent with reactivation of toxoplasmic retinochoroiditis in her left eye during pregnancy and transmitted the disease to her offspring. The mother reported a first episode of ocular toxoplasmosis that was treated 10 years before conception, and results of serological tests during pregnancy evidenced only low IgG levels, with no IgM antibodies. Congenital infection was confirmed by serological tests (Table 1), as well as by comparative immunoblotting.

In immunocompetent pregnant women, only primary *T. gondii* infection is regarded to pose a significant risk of vertical transmission,[5,11] although this primary infection may be acquired shortly before conception.[3,12] Congenital toxoplasmosis resulting from chronically infected immunocompetent pregnant women is considered a rare event,[2,10-12] being attributed to either reinfection or reactivation.[3,5,13]

Reinfection is accompanied by an intense immune response, often manifested by the elevation of IgG levels and the appearance of IgM antibodies. In an immunocompetent pregnant woman with a serological profile of latent infection (no IgM and IgA antibodies, and low IgG levels), indicators of acute toxoplasmosis (IgM and/or IgA results and high IgG levels) suggest reinfection, which might result in transmission to the fetus.[6] Gavinet et al.[6] reported a case of congenital infection from an immunocompetent mother in which early serological investigation during gestation suggested a chronic *T. gondii* infection. Sequential serological tests showed emergence of IgM and IgA and an increase in titers of IgG antibodies, suggesting a possible reinfection.

Two other publications reported cases of toxoplasmosis transmitted by chronically infected mothers with congenital infection diagnosed early in the neonatal period.[7,8] Retrospective analysis of blood samples indicated that in both cases there was an increase in serum titers of IgG antibodies and the appearance of IgA antibodies. The maternal immune system was not compromised in either case and there was also no evidence of reactivation during pregnancy, so reinfection was the most likely explanation. Silveira et al.[2] described a case of congenital toxoplasmosis diagnosed through a routine screening, in which the mother had been infected 20 years before pregnancy. They suggested the possibility of reinfection by the same or different strains of the parasite. Reinfection may be associated with exposure to a large number of parasites, to a more virulent strain or to a parasite of a different genotype. Lebas et al.[4] reported

a severe case of congenital toxoplasmosis in a woman infected before pregnancy and suggested that she may have been infected by a different parasite strain. Experimentally, chronically infected animals may deliver offsprings with congenital infection when they are reinfected with different strains of the parasite.[14] Recently, natural mixed infections, resulting from coincident or sequential exposure to parasites of different genotypes have been observed in humans,[15] although it is still unclear whether the protection triggered by the primary infection is genotype-specific.

In the present report, the mother was immunocompetent and had no serological evidence of recently acquired infection or of reinfection. Clinical history and ophthalmological examination were consistent with reactivation of retinochoroiditis during pregnancy, but reinfection cannot be definitely excluded. Reactivation of retinochoroiditis is more common during pregnancy,[1] but is usually regarded to be a localized process, with no systemic implications and a presumed low risk of fetal infection.[1] Immunocompromised pregnant women, especially those infected with the human immunodeficiency virus (HIV), are at higher risk of reactivation during pregnancy (about 1%), mainly in advanced stages of the disease,[12] with the risk of fetal involvement estimated to range between 2 and 5%.[3,5] Episodes of reactivation correlate with stable or increased serum IgG titers, but IgM antibodies are invariably not detected, as observed in our case. Interestingly, our patient also had an episode of active retinochoroiditis in the left eye 6 weeks after delivery. One year later, she developed choroidal neovascularization in the margins of the perimacular scar in her right eye.

In areas of high prevalence of toxoplasmosis, systematic neonatal screening may identify children with congenital toxoplasmosis caused by reinfection or reactivation during pregnancy, possibly indicating that such events might have been underestimated. This may influence the decision to treat reactivating ocular disease in pregnant women. We warn to the need for preventive education at the start of prenatal care, including monitoring of ocular symptoms, whether or not the patients are susceptible.

Acknowledgements

To Dr. Edilaine Fernandes for her contribution regarding part of the ophthalmologic data.

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