## **CASE REPORT**

# ACUTE TOXOPLASMOSIS IN A BREASTFED INFANT WITH POSSIBLE TRANSMISSION BY WATER

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#### SUMMARY

*Toxoplasma gondii* transmission via breastfeeding has been discussed; however, no cases have been confirmed to date. This article describes a case of acute toxoplasmosis diagnosed in a mother and her six-month-old breastfed infant. The study accounts for the possibility of breast milk transmission and directs both clinicians and pediatricians to the hypothesis that both patients acquired toxoplasmosis via water ingestion.

KEYWORDS: Toxoplasma; Toxoplasmosis; Breastfeeding; Disease transmission; Infectious.

### INTRODUCTION

Breastfeeding mothers with acute infections are often concerned about the continuation of breastfeeding and the risk of microorganism transmission via breast milk. Such an infection may be caused by Toxoplasma gondii. Breast milk is a probable route of transmission for other animals, and the presence of Toxoplasma in the milk of several animals has been confirmed using polymerase chain reaction (PCR), cell culture, and antigen capture enzyme immunoassays (ELISA)<sup>6</sup>. The transmission of T. gondii via breastfeeding may occur due to the presence of cysts or tachyzoites in milk<sup>8,11</sup>, since the nutrients in milk may sustain viable cysts because of their resistance to gastric acidity<sup>10</sup>; the tachyzoites subsequently penetrate the oropharyngeal mucosa. However, oral transmission via breast milk in the setting of an acute infection is unlikely, as tachyzoites are extremely sensitive to proteolytic enzymes<sup>20,22</sup>. However, if gastric acidity is buffered by breast milk (decreasing pepsin digestion), tachyzoite penetration may occur via gastro-duodenal mucosa<sup>17</sup>. Maternal antibodies present in milk may exert protective effects for the infant, as previously demonstrated by the presence of anti-T. gondii antibodies in milk (with concentrations similar to serum levels)1. Although toxoplasmosis transmission to humans has occurred via ingestion of goat milk19,20, there has been only one reported case of probable transmission via breast milk following an outbreak of acute toxoplasmosis among guests at a party that included a breastfeeding mother<sup>3</sup>. In 2005, a two-month-old exclusively breastfed infant was diagnosed with acquired toxoplasmosis concomitantly with his mother; the infection was most likely transmitted by breastfeeding, as the mother was susceptible to T. gondii, and the newborn tested negative<sup>4</sup>.

The aim of this study was to describe the possible transmission *of T. gondii* via breast milk or via water ingestion in a breastfeeding infant,

and to draw the attention of clinicians and pediatricians regarding this situation.

#### CASE REPORT

An infant was referred to the Pediatric Infectious Disease Outpatient Unit of the University Hospital, State University of Londrina, Parana State, Brazil, with a diagnosis of acute toxoplasmosis. At the time, the limited epidemiological data regarding other transmission routes, such as the ingestion of water and food, suggested that the most feasible route of transmission was via breast milk.

The mother received prenatal care; however, serological tests for toxoplasmosis were assayed only during the first trimester (July 2012). Anti-T. gondii IgM and IgG antibodies were both not reactive, as determined via a chemiluminescence (CL) immunoassay. During pregnancy, the patient denied any risk of exposure to T. gondii, including the consumption of raw or undercooked meat, drinking unfiltered water, contact with cat feces, and gardening. Following childbirth, the woman reported consumption of raw meat; however, she drank only filtered water while in Brazil. In September 2013, she traveled to Mogadouro (Portugal) with her child (six-months-old), who was exclusively breastfed. Both mother and child stayed for 11 days, and the woman reported consuming colonial salami and goat cheese. During this period, she and her child drank water from a local mine and from a sink faucet, each of these locations being possible sources of T. gondii oocysts. The mother also reported that the only solid food that the child consumed was pear pulp and banana. Following their return to Brazil, the mother presented left cervical lymphadenopathy without fever. In November 2013, laboratory tests revealed the presence of anti-T. gondii IgG and IgM antibodies, and the diagnosis of acute toxoplasmosis was confirmed (Table 1). The

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Period	Mother						Infant			
	IFI IgG	IFI IgM	CL IgG	CL IgM*	ELISA IgA	IgG Avidity	IFI IgG	CL IgG	CL IgM**	IgG Avidity
November 18, 2013	1: 1,024	1: 4,096	-	-	-	-	-	-	-	-
December 20, 2013	-	-	200.0	21.4	4.0	-	-	-	-	-
January 8, 2014	-	-	-	-	-	-	-	> 200.0	17.3	-
January 17, 2014	1: 32, 000	-	1,394.0	41.2	-	Low (22.3%)	1: 128,000	1,736.0	24.8	Low (21.6%)
March 28, 2014	-	-	-	-	1.4	-	-	> 200.0	2.1	-

 Table 1

 Comparison of serological results of mother and infant

Indirect immunofluorescence (IFI): reference values (RV) IgG <1:16 and IgM = nonreactive; Anti- *T. gondii* IgG by chemiluminescence (CL) RV <1.6 UI/mL; \*Anti- *T. gondii* IgM by CL - RV index <0.5; \*\*Anti- *T. gondii* IgM by CL - RV index <0.83; Anti- *T. gondii* IgA by enzima immunoassay (ELISA) - RV index <1.0; Avidity of anti-*T gondii* IgG by CL- RV: low <49.9%; intermediate 50.0 – 59.9%; high > 60.0% IFI IgM and ELISA IgA not done in infant

mother was treated with sulfadiazine, pyrimethamine, and folinic acid. During this period, the child presented fever and rash on the trunk that lasted for three days, symptoms that occurred a few days before the mother's adenopathy developed. A physical examination revealed the presence of multiple 1.5 cm diameter nodes in the right occipital chain without hepatosplenomegaly, but no serological tests were performed. In December 2013, the serological tests were repeated using maternal serum samples, and the presence of anti-*T. gondii* IgG, IgM and IgA antibodies was noted. In January 2014, the mother finished treatment, and additional tests demonstrated no reactivity of antibodies against human immunodeficiency virus types 1 and 2 (anti-HIV-1/2), decreased anti-*T. gondii* IgA.

In Brazil, the child drank only filtered water and consumed fruit pulp; the mother has denied exposing the child to other risk factors for T. gondii. In January 2014, serological tests of the child's serum samples for toxoplasmosis detected anti-T. gondii IgG and anti-T. gondii IgM antibodies (Table 1); the child was subsequently referred to the Pediatric Infectious Disease Outpatient Unit of the University Hospital. New serological tests for toxoplasmosis revealed low avidity for IgG anti-T. gondii (CL). A positive PCR test identified T. gondii DNA in a blood sample taken from the child (Fig. 1). The child was then treated with sulfadiazine, pyrimethamine and folinic acid. Following seven days of treatment, the child presented anemia (hemoglobin: 10.0 g/dL, hematocrit: 30.9%) and neutropenia (780 cells/mm<sup>3</sup>). The dose of folinic acid was increased, and the neutropenia subsequently improved slightly (836 cells/mm<sup>3</sup>). An ophthalmologic examination and a brain computed tomography (CT) scan revealed no abnormalities. Treatment was maintained for 28 days, and folinic acid was maintained for an additional seven days thereafter. One month after discontinuing the drugs, a second ophthalmological examination was performed. No lesions were noted, and the ganglia sizes were reduced; a second hematologic evaluation demonstrated recovery from the anemia (hemoglobin: 11.2 g/dL), but the neutrophil count remained decreased (871 cells/mm3). Treatment with ferrous sulfate was initiated, and folinic acid was re-introduced. The neutrophil count finally recovered (1,520 cells/ mm<sup>3</sup>) following these treatments.

#### DISCUSSION

In the present case report, serological tests for toxoplasmosis were performed only during early pregnancy, and the results were characteristic of a profile of susceptibility to infection. However, the serological profile

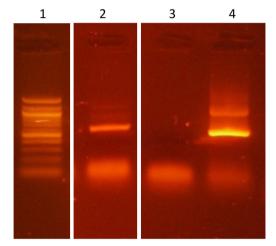


Fig. 1 - Electrophoretic profile of 529 bp DNA fragment of *Toxoplasma gondii* (Gen-Bank n°. AFI46527) amplified from peripheral blood sample of a child diagnosed with acute toxoplasmosis. Method of polymerase chain reaction (PCR), agarose gel 2%, stained with SYBR® Safe DNA Gel Stain (Invitrogen, Life Techonology, USA). Line 1: molecular marker 100 pb. Line 2: peripheral blood samples of children with acute toxoplasmosis. Line 3: negative control (no DNA). Line 4: positive control (529 pb of sample with DNA of Tachyzoites of the RH strain)

at the time of diagnosis, which was performed when the child was eight months old, was compatible with an acute infection, as demonstrated by the presence of anti-*T. gondii* IgG antibodies with low avidity, which excluded the possibility of a congenital infection. Additionally, the infant's symptoms began prior to the onset of maternal symptoms, and the incubation period was consistent with the acquisition of the disease while traveling abroad. There is a small possibility that the child's infection was the result of contact with its mother's hands after she handled the colonial salami and goat cheese. Moreover, during the clinical history, it was revealed that the water in Portugal was the only likely common source of toxoplasmosis transmission for mother and child.

Water is an important vehicle for the transmission of toxoplasmosis. In a study of seroprevalence in Brazil, where municipal water distribution was addressed, 84.0% of the population with a low socioeconomic status, and 23.0% of the population with a high socioeconomic status presented toxoplasmosis seroreactivity. The most important risk factor for seropositivity among the people with a low socioeconomic status

CAPOBIANGO, J.D.; MITSUKA-BREGANÓ, R.; MONICA, T.C.; FERREIRA, F.P. & REICHE, E.M.V. – Acute toxoplasmosis in a breastfed infant with possible transmission by water. Rev. Inst. Med. Trop. Sao Paulo. 57(6): 523-6, 2015.

was drinking unfiltered water, which demonstrates the importance of transmission via waterborne oocysts in that region<sup>2</sup>. This may be due to the contamination of water reservoirs, particularly wells with shallow water in which oocysts from soil may contaminate the water during floods<sup>2</sup>. Oocysts remain viable for long periods of time in both soil and water9. In another study conducted in Poland, the presence of T. gondii was demonstrated in water wells, and 64.6% of the country's rural population tested positive for T. gondii. Higher percentages of seropositivity were observed among people who drank well water compared with those who drank filtered water<sup>21</sup>. In late 2001, there was a large toxoplasmosis outbreak resulting from the contamination of the city's tank water supply in Santa Isabel do Ivai, Parana State, southern Brazil7. These studies demonstrate that waterborne infections are a constant concern in public health, and there have been several recent cases of toxoplasmosis transmitted via water. Mogadouro is a village in northern Portugal, and studies conducted in the northeastern region of Portugal were characterized by seropositivity for anti-T. gondii in 72.4% of domestic cats, 38.0% of dogs, 7.5% of cattle, 33.6% of sheep, 18.5% of goats, and 9.8% of pigs<sup>12,14,15</sup>. These results demonstrate the prevalence of environmental contamination with T. gondii, which was responsible for these animal infections. Another seroprevalence study from this region demonstrated that the majority of women in childbearing age are susceptible to primary infection with T. gondii; therefore, the risk of congenital toxoplasmosis remains high in this region<sup>13</sup>.

In this case report, the specific treatment for acute toxoplasmosis was continued until ophthalmological injury, damage to the central nervous system, and possible congenital infection were excluded. Acquired infections usually do not require specific treatment unless the symptoms are both severe and persistent, vital organs are involved, or the infection has occurred in an immunosuppressed patient<sup>16,18</sup>. Treatment was maintained for four weeks due to the persistence of parasite DNA positivity, which was revealed by PCR during the third month following infection, and because the child was less than 12 months of age. However, the risk of side effects should always be considered, even though they are reversible upon discontinuation of treatment<sup>5,18</sup> (as was observed in this study).

Finally, we emphasize that transmission of toxoplasmosis via breastfeeding in humans remains unproven, which underscores the necessity of excluding other routes of transmission. The lack of data proving disease transmission via breastfeeding and the favorable clinical outcomes noted are enough to recommend the maintenance of breastfeeding, even when the mother presents acute toxoplasmosis. When breastfeeding children, we should exclude other possible routes of toxoplasmosis transmission, such as congenital disease and intake of water and other contaminated foods. The consumption of water, contaminated with oocysts, may be an important transmission route and may be responsible for acute infections among pregnant women, breastfeeding mothers, and infants, justifying the intensification of public health measures in several countries with prophylactic guidelines for drinking only boiled or filtered water in order to reduce the transmission of toxoplasmosis via this route.

## RESUMO

#### Toxoplasmose aguda em um lactente durante a amamentação, com possível transmissão pela água

A transmissão do *Toxoplasma gondii* através do aleitamento materno tem sido discutida; no entanto, até o momento nenhum caso

foi confirmado. Este artigo relata um caso de toxoplasmose aguda diagnosticada na mãe e no seu bebê com seis meses de vida, que estava em amamentação exclusiva. Embora apresente a possibilidade de transmissão pelo leite materno, o estudo chama a atenção de clínicos e pediatras para a mais provável hipótese de que ambos adquiriram toxoplasmose pela ingestão de água.

#### AUTHOR CONTRIBUTIONS

JDC conceived and designed the study; performed data analysis and interpretation; and prepared the manuscript. EMVR performed data interpretation and manuscript revision. RMB, TCM and FE performed the laboratory tests. All the authors read and approved the final manuscript.

### ACKNOWLEDGMENTS

We thank Dr. João Luis Garcia (Department of Veterinary Preventive Medicine of UE) for his assistance with the laboratory procedures.

### CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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Received: 30 September 2014 Accepted: 01 April 2015