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Original article

Congenital toxoplasmosis in a reference center of Paraná, Southern Brazil

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ABSTRACT

This study describes the characteristics of 31 children with congenital toxoplasmosis children admitted to the University Hospital of Londrina, Southern Brazil, from 2000 to 2010. In total, 23 (85.2%) of the mothers received prenatal care but only four (13.0%) were treated for toxoplasmosis. Birth weight was <2500 g in 37.9% of the infants. During the first month of life, physical examination was normal in 34.5%, and for those with clinical signs and symptoms, the main manifestations were hepatomegaly and/or splenomegaly (62.1%), jaundice (13.8%), and microcephaly (6.9%). During ophthalmic examination, 74.2% of the children exhibited injuries, 58.1% chorioretinitis, 32.3% strabismus, 19.4% microphthalmia, and 16.2% vitreitis. Anti-*Toxoplasma gondii* IgM antibodies were detected in 48.3% of the children. Imaging brain evaluation was normal in 44.8%; brain calcifications, hydrocephaly, or both conditions were observed in 27.6%, 10.3%, and 17.2%, respectively, of the patients. Patients with cerebrospinal fluid protein $\geq$ 200 mg/dL presented more brain calcifications ($p = 0.0325$). Other sequelae were visual impairment (55.2% of the cases), developmental delay (31.0%), motor deficit (13.8%), convulsion (27.5%), and attention deficit (10.3%). All patients were treated with sulfadiazine, pyrimethamine, and folinic acid, and 55.2% of them exhibited adverse effects. The results demonstrate the significance of the early diagnosis and treatment of toxoplasmosis during pregnancy to reduce congenital toxoplasmosis and its consequences.

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Introduction

Toxoplasmosis is a worldwide infection caused by the protozoan *Toxoplasma gondii* (*T. gondii*), an obligatory intracellular parasite.[1] In Central and South America, 50–80% of individuals are seropositive for IgG antibodies against *T. gondii*, indicating their previous exposure to this parasite.[2] The prevalence of this infection acquired during pregnancy ranges from 10.3% to 75.2% in different countries.[3–7] In Brazil, the seroprevalence of anti-*T. gondii* IgG antibodies ranges from 49.2% to 91.6%,[8–10] and the incidence of congenital toxoplasmosis varies from 0.3 to 5.0 per 1000 births.[11–13]

The risk of fetal transmission depends on factors, such as the maternal immune response, the gestational age at infection, and the parasite virulence. The risk of congenital transmission varies from up to 2% at the periconceptional period, 10–25% in the first trimester of pregnancy, 30–45% in the second trimester, 60–65% in the third trimester, and up to 80% before childbirth.[1] However, the severity of congenital disease is high when transmission occurs in the beginning of the pregnancy and decreases with gestational age.[1,2,4,7,8]

The diagnosis of toxoplasmosis acquired during pregnancy is based on laboratory tests because more than 90% of infected pregnant women are asymptomatic. When clinical manifestations are present, in general, they are nonspecific and include fever, headaches, myalgia, lymphadenopathy, and rash.[14]

The majority of children with congenital toxoplasmosis do not exhibit signs or symptoms at birth, presenting instead as subclinical infections; nevertheless, infected children are at risk of developing late sequelae, mainly ocular and neurological. For the symptomatic children, the severity of clinical manifestations is related to the trimester of pregnancy when transmission occurred, as follows: fetal death in the first trimester; retinochoroiditis, microcephaly, and mental retardation in the second trimester; and lymphadenopathy, hepatosplenomegaly, eye injuries, and brain calcifications in the third trimester.[15] All of the children whose mothers presented acute toxoplasmosis during pregnancy, symptomatic or not, may have congenital toxoplasmosis. Children born with signals or symptoms of congenital disease are also at risk and should undergo serological investigation to detect specific anti-*T. gondii* antibodies.[15]

The purpose of this study was to describe the demographic, clinical, and laboratory characteristics of children with congenital toxoplasmosis that received treatment for congenital toxoplasmosis at one medical center in southern Brazil.

Materials and methods

Population and study design

The study included a retrospective cohort of 236 medical records of suspected congenital toxoplasmosis from the Outpatient Reference Centre for Pediatric Infectious Diseases, which is the reference service for congenital toxoplasmosis at the Outpatient Clinical Hospital, University of Londrina, Paraná State, Brazil. The study identified 31 cases of congenital toxoplasmosis that occurred from January 2000 to December 2010. This study was approved by the Ethical Committee Involving Humans from the University of Londrina, Londrina, Paraná, Brazil.

Diagnostic criteria

Cases were defined as congenital toxoplasmosis when the infant exhibited one of the following features: anti-*T. gondii* IgM and/or IgA antibodies after 10 days of life, persistently elevated or increasing titers of IgG anti-*T. gondii* (after three-week intervals between the samples), seropositive for IgG after 12 months of life, retinochoroiditis and/or hydrocephaly/cerebral calcifications, and anti-*T. gondii* IgG seropositivity and response to specific treatment.[16]

During the period of the study, anti-*T. gondii* IgG antibodies were detected by indirect immunofluorescence (IFI) with *T. gondii* fixed on a glass slide.[17] For the detection of anti-*T. gondii* IgM antibodies, the methods varied in the period evaluated, but included indirect enzyme immunoassay (ELISA), chemiluminescence, and IgM capture ELISA.

Statistical analysis

Data were recorded in a database, and the statistical analysis was performed using the Epi Info 3.4.3 and GraphPadPrism 5.00 software. Continuous variables were expressed in minimum and maximum values, mean, standard deviation, and median. Categorical variables were reported in absolute frequency (*n*) and percentage (%). Comparisons between groups of categorical variables were performed by Chi-square analysis or Fisher's exact test, when appropriate. An odds ratio (OR) and 95% confidence interval (CI) were also calculated. The results were considered significant when the *p*-value was less than 0.05 (5%).

Results

Description of the population

Of the 31 children evaluated, 20 (64.5%) were male and 11 (35.5%) were female. Their birth weights ranged from 1150 to 3800 g (median 2585 g), and 11 children (37.9%) had birth weights < 2500 g. Gestational age at delivery ranged from 26.2 to 41 weeks (median 36 weeks). Maternal age ranged from 14 to 42 years (median 26 years), and 23/31 (85.2%) pregnant women received prenatal care.

Clinical analysis of pregnant women

Among the 31 pregnant women evaluated, 16 (51.6%) did not have a record of any clinical symptom, eight (25.8%) were asymptomatic, and seven (22.5%) showed symptoms, such as fever (6.5%), adenomegaly (6.5%), flu-like symptoms (6.5%), and myalgia (3.2%). The toxoplasmosis infection was not diagnosed in 20/31 (64.5%) during pregnancy. Four women (12.9%) had not received prenatal care, and 16 (51.6%) had a serology requested. Eleven (35.5%) pregnant women were suspected cases of recent *T. gondii* infection, indicated by positive tests for IgM anti-*T. gondii*. However, this suspicion was not