

Microcephaly due to congenital toxoplasmosis in times of Zika virus epidemic in Brazil

Microcefalia por toxoplasmose congênita em tempos de epidemia por Zika vírus no Brasil

(A versão em Português desta carta está disponível na mesma página eletrônica.)

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To the Editor,

Brazil has one of the highest prevalence rates of congenital toxoplasmosis worldwide [1]. As a result, the Ministry of Health of Brazil published an ordinance that made the notification of gestational and congenital toxoplasmosis compulsory [2], paving the way for the necessary implementation of a program specifically oriented to the prevention and treatment of gestational and congenital toxoplasmosis in the country. We report briefly a case of congenital toxoplasmosis that occurred in the setting of the National Public Health Service and refers to the pertinence and urgency for the implementation of public policies to institute preventive measures for women susceptible to *T. gondii* infection in Brazil and to ensure the diagnosis and treatment of the infection acquired during pregnancy. This letter was written in accordance with the ethical standards of the Helsinki Declaration as revised in 2013. Patients' identities were preserved, confidentiality and data protection were maintained, and all ethical principles of research involving human beings were respected.

The case refers to a female newborn born by cesarean section due to premature amniorrhexis, with a gestational age of 36 weeks, weight of 2380 g, length of 45 cm, and a head circumference of 31 cm (value above the -2 Z score for gestational age, according to the current recommendation of the Ministry of Health [3]). The newborn's Apgar score was 8 and 9 (at the first and fifth minutes, respectively). The neonatal physical examination was normal, the infant evolved uneventfully, and on the third day of life she was discharged with her mother. The red reflex test and auditory screening, both normal, were performed before discharge. This was the mother's first child at the age of 20; the pregnancy was uneventful, and she was in good health throughout the gestational period. The prenatal care consisted of seven consultations at the Basic Health Unit at the pregnant woman's neighborhood. Six ultrasound scans were performed throughout the pregnancy, and no abnormalities were observed in the fetus. Maternal serology for toxoplasmosis in the first trimester of pregnancy was negative for immunoglobulin (Ig) M and IgG. No examination was performed in the second trimester. In the third trimester the serology for toxoplasmosis was not repeated,

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but serological tests for HIV, Hepatitis B and C, cytomegalovirus and syphilis were performed, and all were non-reactive.

Suspicion of microcephaly occurred in the child's third month of life and then serological tests for congenital infections and a skull radiography of the child were performed along with IgM and IgG for toxoplasmosis with avidity test for the mother. At that time, the head circumference of the infant was 35 cm, a microcephaly level (below the -2 Z score).

The serological tests were performed only in the fifth month of child's life, and were negative for syphilis, rubella, cytomegalovirus and herpesviruses. However, IgG and IgM were positive for toxoplasmosis, both in the mother and in the child. The mother's IgG avidity test result was moderate, which indicate that toxoplasmosis was probably acquired in the second trimester of pregnancy.

At six months of life, on return to the consultation, the infant presented with strabismus in the left eye (alternating endotropy) and the fundoscopic examination revealed retinochoroidal scars in both eyes. The skull radiography was suggestive of a reduction of the skull / face ratio, and the nuclear magnetic resonance of the skull revealed a reduction in the supratentorial parenchyma and reduction of the parietal-occipital white matter with lateral ventricular ectasia. Extensive alteration of the cortical-subcortical signal in both cerebral hemispheres, small subcortical cysts at the temporal poles, and multiple foci of calcification distributed in the supratentorial compartment were observed.

The diagnosis of congenital toxoplasmosis was concluded when the child was seven months old, and microcephaly due to toxoplasmosis was confirmed by radiological as well as clinical criteria, identified as a significant delay in neuromotor development. In the apposition of the head circumference measures on the chart of the child's record of Ministry of Health [4], the infant remained below the -2 Z score from the fifth to the ninth month of life, even when considering the corrected gestational age. Treatment with pyrimethamine, sulfadiazine and folinic acid was started, and the child was referred for follow-up at the pediatric infectious disease clinic, as well as for pediatric neurology, physiotherapy, speech therapy and occupational therapy. The child also continued to receive care at the municipal outpatient clinic for congenital infections.

This case of congenital toxoplasmosis occurred during the Zika virus epidemic in Brazil. The Ministry of Health began to adopt from March 2016 an international standard definition for microcephaly referenced by the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) [5]. We advocate in favor of public health measures that ensure the diagnosis and treatment of other congenital infections that also cause microcephaly in newborns and/or infants. In the case of toxoplasmosis, such measures should be based on serological tests during pregnancy and after child birth.

This case reported shows that when the subject is microcephaly due to congenital infections in Brazil one must be attentive to other possibilities besides Zika virus infection, in particular one should be aware of congenital toxoplasmosis, which is highly prevalent in Brazil [1]. Toxoplasmosis treatment, if provided in due time, may prevent irreversible neurological damage resulting from the inflammatory reaction established in the child because of the *T. gondii* parasite reproduction in noble tissues such as brain and retina.

As in the case herein reported, microcephaly due to congenital toxoplasmosis may manifest itself only months after birth. In fact, most congenital toxoplasmosis infections are asymptomatic at birth, clinically manifesting severe consequences of irreversible visual and / or neurological changes in the following months or years after birth. Therefore, the serological screening of susceptible mothers throughout pregnancy is fundamentally important for the early diagnosis of congenital infections and the immediate treatment initiation, ideally still *in utero* or at least immediately after birth. The present case corroborates data from the natural history of toxoplasmosis microcephaly reported in a published Danish study in 1960 [6] prior to the establishment of regular screening programs for toxoplasmosis. In that study, of the 11,253 infants examined, 156 presented with positive serology for congenital toxoplasmosis. Of these children, 69% had no apparent disease either at birth or in the first two months of life. However, the vast majority of them developed severe neurological sequelae after the third month of life. In that Danish study, 13 infant cases with microcephaly were identified to be the result of a *T. gondii* infection, and none were diagnosed at birth but only after the third month of life, similar to the present reported case.

Therefore, we believe that it is very pertinent that the Ministry of Health developed this ordinance making the reporting of cases of gestational and congenital toxoplasmosis in the country mandatory, and we

fully support this ordinance. Ideally, the actions that will be implemented from the guidance of the Health Ministry Ordinance 204, of February 17, 2016, will result in a national program specific for congenital toxoplasmosis, aiming to benefit children throughout the country by preventive health education measures, besides screening and treating gestational and congenital toxoplasmosis in Brazil.

NOTES

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Conflicts of interest disclosure

The authors declare no competing interests.

Authors' contributions

All the authors declare to have made substantial contributions to the conception, or design, or acquisition, or analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content; and to approve the version to be published.

Availability of data and responsibility for the results

All the authors declare to have had full access to the available data and they assume full responsibility for the integrity of this report.

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