

Clinical Article

Congenital Toxoplasmosis

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Abstract

The aim of study was to make an overview of clinical signs caused by congenital toxoplasmosis and methods of diagnosis in Budapest, Hungary. The most frequent sign of congenital infection among our patients were cerebral ultrasonographic changes (calcification, hydrocephalus, microcephaly), neurologic disturbances (muscle tone disturbances, seizures) and chorioretinitis. We observed hepatic failure rarely. The differential diagnosis of ultrasonographic changes included as other causes of hydrocephalus (hemorrhage, CMV or other infections) as other causes of calcification (CMV or other infections) too. The differential diagnosis of eye lesions included colobomatous defect, other inflammatory lesions (HSV, CMV), birth injury (intraocular hemorrhage) circulatory disturbances or neoplasm. *Int Pediatr.* 2000;15(1):33-36.

Key words: congenital toxoplasmosis, calcification, hydrocephalus, microcephaly, seizures, chorioretinitis

Introduction

The most common method of diagnosis of congenital toxoplasmosis is serologic testing of neonate together with his/her mother. For serologic testing we used IgM, IgG, IgA antibody determination by Vidas Toxo Competition kits. We diagnosed congenital toxoplasmosis in 16 infants. Early treatment may prevent the further progress of the infectious process and the development of handicaps in children. Congenital toxoplasmosis may be a preventable congenital infection. This prevention is possible by both the identification of fresh infections with serologic screening of pregnant women and the treatment of seropositive cases.

Toxoplasmosis is a zoonosis, distributed all over the world. In immunocompetent persons the infection mainly causes inapparent infection. Clinically it can rarely mimic the infectious mononucleosis syndrome. Human contamina-

tion occurs by contact with the stool of infected cats or by consumption of unwashed vegetables, fruits or uncooked meat of infected animals. Except for maternal-fetal infection, there is no human transmission.¹⁻³ Contamination may also occur by transplanted organs.⁴

Worldwide, about 0.5% to 1% of pregnant women become contaminated by *Toxoplasma gondii*.⁵

Method

We used Vidas Toxo Competition (Bio Mérieux) kits during our study. The following new methods of diagnosis are known in Hungary, but they have not been routinely used yet:

1. ELISA detection of IgM and IgA antibodies against the parasite membrane P-30⁶.
2. PCR has already been introduced in Hungary, but it was not available at the time of this study.⁷

Presentation of Cases

At the 2nd Pediatric Department of Semmelweis Medical University, and at the Szent László Municipal Hospital of Infectious Diseases in Budapest, we treated 16 infants with congenital toxoplasmosis between January 1995 and June 1998. In eleven infants the diagnosis was made by clinical signs of congenital infection in the neonatal period (Table 1). The most frequent signs were cerebral ultrasonographic changes (in 12 infants). Seven infants show neurologic signs: muscle tone disturbances, convulsions, EEG changes. Eight infants had chorioretinitis. Six infants presented all three previously named signs, and toxoplasma antibody level were diagnostic in these cases. Nine mothers of our 16 patients had *Toxoplasma* antibodies characteristic to primary infection during pregnancy. Their newborns for that reasons were investigated after birth. Hepatic failure was detected in one infant, and in another infant visual disturbances was found as a sole clinical manifestation.

The history, clinical signs and the result of serologic tests are summarized in Table 1. Congenital CMV infection was investigated but not detected in all cases.

Results

Severe neurologic signs, gross intracranial calcification and/or hydrocephalus were found in 3 patients. In these pa-

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Table 1. - Clinical data of patients with congenital toxoplasmosis

Patients (N°16)	N°	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
History																	
Ultrasonographic changes before birth		+						+									
Serologic test during pregnancy (IgM, IgA, high IgG titers)		+	+		+	+	+					+			+	+	+
Clinical signs																	
Cerebral ultrasonographic changes		+	+	+		+	+	+	+	+	+		+		+		+
Neurologic signs		+						+	+	+	+		+	+			
Chorioretinitis		+		+				+	+	+	+		+	+			
Hepatic failure in infancy															+		
Serologic changes after birth																	
Ig M pos mother		+	+	+	+	+		+								+	+
IgM pos neonate		+		+	+			+			+	+				+	+
IgA pos neonate		+		+									+				
IgG pos neonate		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Start of therapy																	
Age (weeks)		2	3	3	4	2	3	3	6	6	10	3	3	15	2	2	3

tients, therapy prevents the progression of the disease only by improving the chance of a good quality of life. Moderate neurologic signs observed in 4 cases (eg. moderate ventriculomegaly, muscle tone disturbances) and/or cerebral sonographic changes (subependymal cyst formation, less prominent calcification) improved or fully resolved during therapy.

As a consequence of the therapy progression of chorioretinal lesions were never observed. Six patients had an improvement of their vision, orienting well in their environment.

The therapy of 4 children is still in progress.

One patient's parents discontinued their infant's therapy after six months in hope of a spontaneous improvement (this patient was asymptomatic at birth, but he was IgM positive).

Discussion

If the primary toxoplasma infection of the mother occurs during pregnancy, she can contaminate her fetus transplacentally. The earlier the fetus is infected during the pregnancy, the more prominent clinical signs of infection the neonate has at birth. In the case of a maternal infection during the first trimester of pregnancy, the transmission rate is 10-20%. Whereas during the third trimester 50-60% of the fetuses will be infected at birth. Infection in the early pregnancy may lead to abortion or stillbirth.⁸

If there is suspicion of a recent infection of a mother and her fetus during pregnancy, diagnosis can be made by isolation of the parasite from cord blood, placenta, amniotic fluid or tissues.^{9,10,11,12} After birth, early diagnosis can be made with serologic tests. However, their interpretation warrants experience.

When it is possible, an investigation should begin with a serologic test of the pregnant woman.⁹ Serologic testing of the neonate is always carried out together with the mother. The presence of anti-toxoplasmic IgM or IgA in the neonate is the most specific sign of congenital infection because these antibodies are produced by the neonate itself (i.e. they do not pass across the placenta).¹³ At the same time, the absence of IgM does not rule out acute congenital toxoplasmosis, because IgM antibodies can only be detected in about 20% of congenital infections. This is due to the phenomenon, that high levels of maternal IgG antibodies to *Toxoplasma* compete for antigenic sites on the surface of the organisms.¹⁴

Sometimes after maternal infection high IgM and IgG antibody levels persist in the mother for years, suggesting chronic infection. The fetuses of such mothers will be not infected.^{14,15}

Duration of treatment of congenital toxoplasmosis was 1 year. During the first 6 months, Sulfadiazin (80-100mg/kg/day) and Pyrimethamin (1-2mg/kg/day) with calcium leucovorin (5mg/3day against bone marrow depression as a side effect) was used. Absolute neutrophil count was regularly checked. If an infant had active chorioretinitis, steroid treatment was added to this regimen. After 6 months of therapy the combination of the above mentioned drugs alternated monthly with spiramycin (100mg/kg/day).¹⁶

By the European Research Network on Congenital Toxoplasmosis⁹ the likelihood of *Toxoplasma gondii* infection was separated into five mutually exclusive categories: definite, probable, possible, unlikely and not infected. According to that classification, ten of our patients had definite and six of them had probable congenital *Toxoplasma* infection.

In Hungary, the number of live births were at approximately 90 000 annually. Using 50% fetal transmission rate, 2-

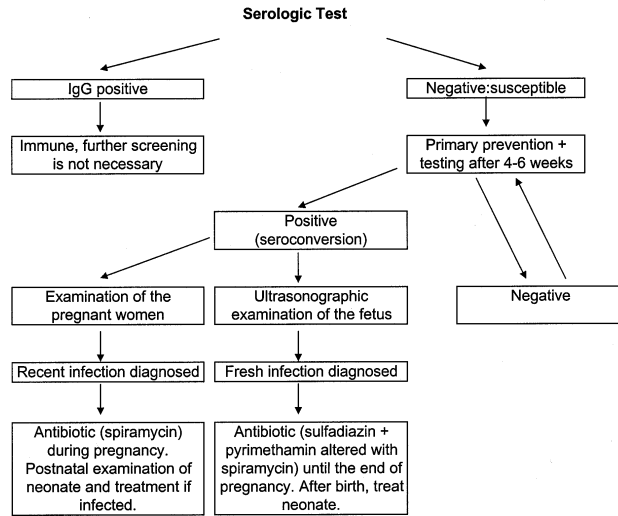


Fig 1. - Serologic screening of pregnant women for recent toxoplasma infection

300 offspring could have been infected without screening and treatment programme.¹⁵ Without a screening programme of pregnant women, the diagnosis of congenital infection is more difficult, because the primary infection of the pregnant remains undiagnosed. We suppose an underestimate of congenital toxoplasmosis, because infected neonate may be without symptoms and still be at risk of developing sequelae such as chorioretinitis.¹⁷ Thus the diagnosis is frequently suspected when one observes cerebral ultrasonographic or ocular changes. Hopefully introducing new techniques (i.e. PCR) will make the diagnosis easier.

Clinical signs and sequelae of infection is listed on Table 2 and 3.

The most frequent signs of infection among our patients were cerebral ultrasonographic changes (e.g. ventriculomegaly, calcification, subependymal cysts). Neurologic disturbances were seen in 7 infants. The more severe the intracranial calcification, the more severe the consequence of infection. Small areas of calcification may resolve, not causing any clinical signs thereafter.¹¹ Hepatic failure in one infant improved. More than half of our patients showed chorioretinitis. If it is the only manifestation, it usually remains undiagnosed for years, and may be a cause of blindness in adolescence.¹⁷

The consequence of French, Austrian and Hungarian studies are, that congenital toxoplasmosis may be prevented.^{2,3,15}

The following recommendations for pregnant women for the prevention of congenital toxoplasmosis¹ were suggested:

1. Cook meat to >66°C, smoke it, or cure it in brine.
2. Wash fruits and vegetables before consumption.
3. Avoid touching mucous membranes of mouth and eye while handling uncooked meat or unwashed

Table 2. - Clinical signs of congenital toxoplasmosis

Hepatosplenomegaly
 Jaundice, hepatic failure
 Hydrocephaly, microcephaly
 Intracranial calcification
 Seizures
 Cerebrospinal fluid involvement (elevated protein count, lymphocytic sediment)
 Chorioretinitis
 Rash
 Lymphadenopathy
 Anemia
 Pneumonitis

Table 3.—The sequelae of congenital toxoplasmosis

Mental retardation
 Seizures
 Muscle tone disturbances
 Hydrocephaly and/or microcephaly
 Vision disturbances (blindness)
 Hearing loss

fruits or vegetables.

4. Wash hands and kitchen surfaces thoroughly after contact with raw meat or unwashed fruits and vegetables.
5. Prevent access of flies, cockroaches, and other coprophagic insects to fruits and vegetables.
6. Avoid contact with materials that are potentially contaminated with cat feces, such as cat litter boxes, or wear gloves, when handling such materials and when gardening.
7. Disinfect cat litter box for 5 minutes with nearly boiling water.

By performing serologic screening of pregnant women it becomes possible to discover recent infections, to treat the mother, and thus decrease the rate of fetal infection. After birth it is possible to diagnose subclinical infections of neonates of infected mothers. With the strategy shown on Figure 1, congenital toxoplasmosis can become a preventable congenital infection in Hungary as well.

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