Approach to the infants of mother with infected toxoplasmosis during pregnancy

Nedim SAMANCI, Fahri OVALI, Türkan DAĞOĞLU, Atıl YÜKSEL, Ergin BENGİSU

Dept. of Obstetrics & Gynecology, Neonatal Intensive Care Unit, Medical School of İstanbul University, İstanbul, TURKEY

*Toxoplasmosis is one of the most common infections in the world. In this study, fourteen cases with diagnoses of acquired maternal toxoplasma infection during pregnancy and their babies were reported. The diagnosis of maternal infection were confirmed by high antibody titers and seroconversion at the second or third trimester during pregnancy. Toxoplasma Ig **M** from cord blood samples was detected in only one case. Signs of congenital toxoplasmosis including chorioretinitis, intracranial calcifacation and hydrocephalus was presenet in the only one baby. The risk of fetal infection was **7.1** %. We recommend that spiramycin treatment should be started as soon as possible once the diagnosis of maternal toxoplasma infection during pregnancy. The therapy should be begun from the first day for all babies. After a mean follow up period of twelwe month, three infants had evidence of subclinical toxoplasma infection **(21 %).***
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Key Words: Toxoplasmosis, Chorioretinitis, Pregnancy

Toxoplasmosis is one of the most common infections in the world (1). Congenital toxoplasmosis is the result of intrauterine transmission of *toxoplasma gondii* from the mother to her fetus (2). Prenatal diagnosis of congenital toxoplasma infection is possible and prenatal treatment of confirmed fetal infection is effective (3).

Toxoplasmosis is usually an asymptomatic and innocent disease, but in fetuses and immunocopromised hosts it often takes a severe course (4).

The diagnosis of the disease in the neonate is complicated by the fact that many cases appear as silent infections and that the development of clinical symptoms may take several years (2,5).

Toxoplasma gondii exists in two infectious forms in humans. Oocyts may be ingested in soil, contaminated with cat feces, that is on unwashed food or hands. Tissue cysts may be acquired by handling or eating raw or inadequately cooked meat (1).

Following acquisition of this organism there is initial parasitemia and widespread dissemination throughout the body. When toxoplasma gondii infection occurs during pregnancy, the organism is often transmitted across the placenta to the fetus (6). If transmission occurs early in fetal life, it may cause stilbirth or fetal damage and delivery of a child with congenital toxoplasmosis.

The severity of the disease depends on the age of the fetus at the time of transmission. The period of highest risk is between weeks 10 to 24; the low-risk period is from 26 to 40 weeks. The earlier the fetus is infected, the more severe is the disease in the fetus. Although the icidence of transmission to the fetus is highest during this latter period, it results in mild infection in the newborn (5).

The incidence of toxoplasmosis during pregnancy has been estimated to be 3 to 6 cases per 1000 live births in high-risk countries and 1 to 2 cases per 1000 live births in low risk-countries (4). After maternal toxoplasma infection, the overall risk of transmission to the fetus has been estimated as around 40 %(7).

The purpose of this study was to assess the outcome of the 14 infants of mother with acquired toxoplasmosis during pregnancy.

MATERIALS AND METHODS

This study was performed at the neonatal insensive care unit of Department of Obstetrics and Gynecology of the Medical Faculty of Istanbul University between January 1993 and Septenber 1994. Fourteen 14 infants of mothers with serologically confirmed *toxoplas-*

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Correspondence: Nedim SAMANCI
Ömerpaşa cad, Güvenç sok. No: 13
D: 7 İstanbul, TURKEY

ma gondii infection during pregnancy were referred to our clinic for treatment and follow-up. Prenatal diagnosis was performed by screening prodecures. Toxoplazma infection was asymptomatic in cases.

In our country, routine serological screening to detect maternal toxoplasma infection is not compulsory. In our faculty there is an ongoing toxoplasma screening procedure. The aim of the screening programme is to identify seronegative pregnant women. All pregnant mothers were tested at the first antenal visit, and seronegative women there after in every trimester. In this way, the onset of infection could be timed, we detected toxoplasma specific Ig G and IgM antibodies using enzyme-linked immunosorbent assay (ELISA). The titers of 135 IU/ml or more were considered as recent primary infection. Diagnosis was based on the detection of seroconversion from negative to positive tests, presence of Ig M antibodies, a marked increase in antibody titers over several weeks. When a recently acquired toxoplasma infection was diagnosed in ppregnancy, prenatal diagnosis was performed by fetal blood samplingy and ultrasonography at 20-24 weeks of gestation. Fetal blood tested for specific ELISA IgA, IgG and nonspecific signs of infection such as leucocyte count, eosinophil count, platelet count, lactate dehydrogenase (LDH) and gamma glutamyl transferase (GGT). Ultrasound examination was done to detect any enlargement of cerebral ventricles and periventricular calcification. The condition of the fetus was evaluated by ultrasonography performed fortnightly.

All women received spiramycin, 3 gm daily throughout the pregnancy from the time maternal infection was proved. Spiramycin was administered without interruption. Once the fetal infection was suspected, pregnant woman had 3 week courses of pyrimethamine, 50 mg, and sulfadiazine. 3 mg/day, alternating with 3 weeks of daily spiramycin. Folinic acid was included in this regimen.

Delivery occured between weeks 32 and 40 of gestation (mean 37±2 weeks), and the infants weighed 1550 to 3910 g (mean 2950+630 g). Intrauterine growth retardation was observed in one baby. Signs of congenital toxoplazmasis including chorioretinitis, intracranial calcification, and hydrocephalus was present in the only one baby. Cord blood samples were obtained, and toxoplasma IgM and IgG were determined. The condition of the neonat was checked by ophthalmoscop, skull radiographs, cranial ultrasonography, and in some babies lumbar puncture.

We begun therapy for all babies on the first day. The therapy of the infants depended on signs and laboratory results (Table 1). Subclinical congenital toxoplasma infection was diagnosed in patients showing no symptoms at all. They had highly positive specific Ig G results at first day of birth. Serologic follow-up procedure was performed at the end of first month and twelwe month (Table 2). The infants were followed for twelwe months.

RESULTS

Maternal toxoplasma infection was diagnosed in patients showing no symtoms at all. The diagnosis of maternal infection was confirmed by high antibody titers (IgG>135 IU/ml) and seroconversion at the second or third trimester during pregnancy.

In our study the overall risk of fetal infection was 7.1 %. Thirteen women were treated with spiramycin

Table 1. Guidelines for treatment of congenital toxoplasma infection in the infant.

1- Manifest congenital toxoplasmosis: -Pyrimethamine 1 mg/kg per day orally for 2 or 6 moths, then this dose three times a week.
Sulfadiazine 100 mg/kg per day in two divited doses

Folinic acid. 5 mg every 3 days during treatment with pyrimethamine, if bone marrow toxicitiy occurs at this dose, increase to 10 mg every 3 days.

Spiramycin, 100 mg/kg per day orally in 2 doses.
Treatment is continued for first year of life in alternating
Courses: Pyrimethamine and sulfadiazine for 21 days and spiramycin for 30 to 45 days.

2- Overt congenital toxoplasmosis with evidence of inflammatory process (chorioretinitis, high level of cerebro spinal fluid protein, gereralized infection) As in no1 above+-corticosteroids (prednisone: 1 mg/kg per day in two divided doses)

3- Subclinical congenital Toxoplasmosis pyrimethamine+sulfadiazine for 6 weeks, there after alternate with spiramycin as above. Treatment is continued for one year.

4- Healthy newborn with negative serology; mother shown to have acquired toxoplasmosis during pregnancy. One course of pyrimethamine+-sulfadiazine for 1 month obtain consultation to determine necessity for continued theraphy. This desicion must be made on serologic test titers clinical in infants.

5- Heathy newborn; mother has high titer but timing of infection is undefined. Spiramycin for 1 month and then as in no 4 above.

Table 2. Out come of 14 infants of mothers with toxoplasmosis acquired during pregnancy.

The time of maternal infection was proved	Gestational age at (weeks)	Cord Blood IgG IgM (specific) IU/ml	First Month IgG IgM (specific) IU/ml	Twelth month IgG IgM (specific)	Duration of therapy	Clinical findings	Outcome
2. trimestr	40	135 (-)	135	(-) (H	One month	—	Healthy
3. trimestr	39	135 (-)	(-) (-)	(-) (H	One month	—	Healtthy
2.trimestr	40	>240 (—)	>240 (—)	78 (-)	One year	—	Healtthy
3. trimestr	40	>240 (—)	(-) (-)	(-) (-)	One month	—	Healtthy
3. trimestr	40	135 (-)	(-) (-)	(-) (-)	One month	—	Healtthy
2. trimestr	38	>240 (—)	240 (-)	(-) (-)	One year		Healtthy
2. trimestr	32	>240 (49)				+	Exitus
2.trimestr	36	>240 (—)	(-) (H	(H (H	One month	—	Healtthy
3.trimestr	39	>240 (—)	6 6 (-)	(-) (H	One month	—	Healtthy
3. trimestr	36	135	66 (—)	/__) ^_)	One year		Healtthy
2. trimestr	37	>240 (—)	>240 (—)	(—) (—)	One year	—	Healtthy
3. trimestr	39	135	66 (-)	(-) (-)	One month	—	Healtthy
2. trimestr	40	>240 (—)	66 (H	(-) (H	One month	—	Healtthy
3. trimestr	39	135	(-) (H	(-) (-)	One month	—	Healtthy

only, one pregnant woman treated with pyrimethamine plus sulfadiazine. Treatment was started as soon as possible. Toxoplasma were not isolated from amniotic fluid in any of these cases. There was abnormality in nonspecific laboratory measurements such as GGT and LDH in only one case. Fetal toxoplasma IgM was positive in only one fetus who had been abnormal non specific laboratory measurements. This mother was treated pyrimethamin plus sulfadizine. All of the laboratory results was shown in Table 2. Subclinical toxoplasma infection was diagnosed in three infants showing no symptoms at all. Only one small for gestational age baby was observed. In our cases, ultrasonographic evaluation was performed. In all case, ultrasonography of fetal head showed ventriculomegaly; but delivery occured preterm at 32 weeks of gestation. Cord blood Ig M was positive. After delivery, we observed choriorenitis, hydrocephalus, intracranial calcification and abnormal cerebrospinal fluid (protein concentration 380 mg/dl) in this baby. This infant's mother had been treated pyrimethamine plus sulfadizine during pregnancy. This infant had died at third day of birth in neonatal invensive care unit.

The other 13 infants were followed for periods of twelve mounth. The overall rate of subclinic infection was 21 %. Tolerance to postnatal treatment was good. Any complication attributed to postnatal treatment was not seen. Thirteen infants had normal development and nerologic status during twelwe months. They had no problem during the follow-up.

DISCUSSION

The availability of prenatal diagnosis, allowing determination of whether or not the fetus has been infected with *toxoplasm gondii* may prevent unnecessary termination of a pregnancy involving an uninfected fetus (1). Once the diagnosis of toxoplasma infection during pregnancy is proved or suspected, treatment with spiramycin or pyrimethamine plus sulfadiazine should be started as soon as possible. This can be explained by the fact that transmission to the fetus via the placenta is delayed by treatment, leading to less serious lesions. Another hypothesis is that spiramycin prevents the spread of infection in the fetus (3).

After maternal toxoplasma infection, the risk and severity of fetal infection depends on the time during prenancy. The risk of transmission to the fetus increases from 25 % in the first trimester to 65 % in the third trimester, where as the risk of severe manifestations in affected infants decreases from 75 % in the first trimester to 0 % in the third trimester (8). Because the risk of fetal infection dose not correlate with maternal symptoms, their presence or absence is not helpful in predicting outcome. Congenital toxoplasmosis with clinical manifestations of disease in the newborn occurs when the fetus is infected before the 26 th weeks of gestation (5).

We don't know the true incidence of maternal toxoplasma infection among pregnant women, since our hospital is a reference clinic. High antibody titers (IgG>135 IU/ml) or sero conversion were detected in 14 women. All of cases, especially, was diagnosed at second or third trimester during pregnancy. Ultrasonographic examination to detect abnormal morphologic signs in the fetus resulting from toxoplasma infection also provides important information. The sign most frequently noted is cerebral ventricular dilatation that generally is bilateral and symmetrical (9). It has been suggested that detailed ultrasonography allows diagnosis of 98% to 99% of cases of clinical toxoplasmosis (1)-

We suggest that spiramycin treatment during pregnancy reduces the risk of fetal toxoplasma infec-

tion. Testing of fetal blood for nonspecific signs of infection such as platelet counts, GGT and LDH has been suggested as a usefull adjunctive measure (10). In only one case, we observed abnormal results of GGT and LDH, and this fetus had severe congenital toxoplasma infection.

We observed positive Ig M results in only one fetus. Because the high levels of maternal IgG antibodies to toxoplasma may compete for antigenic sites on the surface of the organisms with the relatively low IgM antibody levels usually found in the fetus or the neonate. Detectable specific IgM antibody is usually absent in the sera of most neonates with congenital toxoplasmosis because of high levels of maternal specific IgG antibodies.

We continued therapy in infants with subclinical congenital toxoplasmosis for six months. We didn't observe any complication such as chorioretinitis, or neurologic signs. The results are promising. The study still continues because complications such as chorioretinitis might appear much later in life **(3).**

Hamilelik süresince toksoplazma ile infekte olan annelerin yeni doğan çocuklarına yaklaşım

Toksoplasmozis dünyadaki en yaygın enfeksiyon hastalıklarından biri olup bu çalışmada gebelikte edinsel maternal toksoplasma enfeksionu tanısı konulan 14 anne'nin bebeklerindeki klinik ve laboratuar bulguları bildirildi. Maternal infeksiyonun teşhisi gebeliğin ikinci veya üçüncü trimestirinde yüksek antikor türeleri veya serokonversiyon ile konuldu. Sadece bir olguda kordon kanında toksoplasma IgM tayin edildi. Koriyoretinit, intrakranial kalsifikasyon ve hidrosefali gibi konjenital toksoplasmaya özgü bulgular sadece bir olguda gözlendi. Fetal infeksiyon riski %7.1 olarak bulunduğundan dolayı gebelikte toksoplasma infeksionu geçiren tüm gebelere teşhis edilir edilmez spiramycin tedavisi başlanmalıdır. Tüm bebeklere 1. günden itibaren tedavi başlanmalıdır. Bizim olgularımızda 12 aylık takip sonrası subklinik infeksiyon oranı % 21 olarak bulundu.

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REFERENCES

1. Matsui, D. Prevention, diagnosis, and treatment of fetal toxoplasmosis. Clinics in Perinatology 1994; 21: 675-89.
2. Stray-Pedersen, B. A prospective study of acquired toxoplasmosis among 8043 pregnant women in the oslo area. Am J Obstet Gynecol 1980; 136: 399-406.
3. Hohlfold P, Daffos F, Thulliez P et al. Fetal toxoplasmosis outcome of pregnancy and infant follow-up after in utero treatment. J Pediatr 1989: 115: 765-69.
4. Koskiniemi J, Lappalainem M., Hedman K. Toxoplasmosis needs evaluation. An overview and proposals. Am J Dis Child 1989: 143: 724-28.
5. Remington JS, Mc Lead R., Desmots G. Toxoplasmosis. In Remington JS, Klein JO. infectious Diseases of the Fetus and Newborn Infant, ed. 4 Philadelphia, WB Saunders, 1995: 140-267.
6. Desmonts G, Forestier F, Thulliez PH, et al. Prenatal diagnosis of congenital toxoplasmosis. Lancet 1985: 1: 500-4.
7. Peckham C.S, Logun J. Screening for toxoplasmosis during pregnancy. Arch Dis Child 1993: 68:3-7.
8. Carter AO, Frank JW. Congenital toxoplasmosis. Epidemiological features and control. Can Med Assoc J 1986: 135: 618.
9. Thuliez P, Daftos F, Forestier F. Diagnosis of toxoplasma infection in the pregnant woman and the unborn child. Current problems. Scand J infect Dis 1992: 84(Suppl) 18-26.
10. Daffos F, Forestier F, Capella-Pavlousky M, et al. Prenatal management of 746 pregnanies at risk for congenital toxoplasmosis. N Engl J Med 1988; 31: 271-275.
11. Flice GA, Yeager AJ, remington JS. Diagnostic signifiance of immunglobulin M antibodies to toxoplasma gondii detected after speration of immunglobulin M from immunglobulin G antibodies J Clin Microbiol 1980; 12: 336-42.