Case Report

Congenital toxoplasmosis the overlooked disease: a case report

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INTRODUCTION

Toxoplasmosis is one of the most common human parasitic infections worldwide with a possible devastating outcome for immunocompromised patients, fetuses and newborn babies. It is caused by Toxoplasma gondii, which is an obligate, intracellular protozoan parasite. CT can occur secondary to acute primary maternal infection during pregnancy or within 3 months before conception and less frequently due to reactivation of previous maternal infection. The severity of the disease depends on the gestational age at the time of transmission, being more severe in early gestation. Infants with CT are asymptomatic at birth in over 70% of cases. Nevertheless, they may still develop significant neurodevelopmental sequelae and chorioretinitis months or even years after birth if are left untreated. Studies have demonstrated that screening and treatment for toxoplasmosis during pregnancy can help to decrease the vertical transmission and the clinical sequelae thereafter.  

CASE REPORT

A male preterm infant 35 weeks gestational age was born via normal vaginal delivery. His Apgar score was 7 and 8 at 1 and 5 minutes after birth, respectively. He received routine neonatal care in the labor room. His birth weight was 2,450 kg, his length was 45.5 cm and his head circumference (HC) was 32.5 cm, all were at the 50th centiles. The infant was born to a 34-year-old multi-gravida mother who had no previous miscarriages or abortions and her current pregnancy was uneventful with no history of fever, rash, medical illness or drug intake. The parents were healthy non-consanguineous and of East African descent. There was no family history of medical illnesses. The baby was delivered at a private hospital and was referred to our hospital on the 3rd day of life after the deterioration of his condition. Upon admission, he was looking very ill with skin mottling, cold extremities, deeply jaundiced and on a mechanical ventilator. He showed severe respiratory distress and his arterial blood gases revealed hypoxia and mixed acidosis.

ABSTRACT

The causative agent of congenital toxoplasmosis (CT) is Toxoplasma gondii, an obligate intracellular parasitic protozoan presenting as a zoonotic infection distributed worldwide. Congenital toxoplasmosis may lead to abortion, intrauterine growth restriction, hepatosplenomegaly, jaundice and several neurological and ocular manifestations. The classic pathognomonic manifestations are the triad of intracranial calcifications, hydrocephalus and chorioretinitis. However, the majority of infected infants are asymptomatic at birth. Herein, we reported a case of severe CT in a late preterm newborn. Interestingly, the majority of the manifestations reported for CT were observed in this case. The high anti-toxoplasma antibodies (IgM and IgG) in the infant and his mother confirmed the diagnosis.

Keywords: Toxoplasma gondii, Congenital toxoplasmosis, Hydrocephalus, Intracranial calcification, Chorioretinitis
Immediately, the ventilator settings were adjusted and a bolus of normal saline was given. Inotropes were commenced (dopamine and dobutamine). A partial septic screening was taken and the antibiotics were changed to amikacin and meropenem. Radiographs of the chest and abdomen revealed bilateral lung infiltrations and distended abdomen with enlarged liver and spleen. There was high indirect hyperbilirubinemia without evidence of hemolysis and the baby was started on intensive phototherapy. However, the total bilirubin continued to rise and an exchange transfusion was accomplished on the next day. Blood culture and sensitivity result (C/S) was positive for gram-negative bacilli (Klebsiella pneumoniae) that was sensitive to the above mentioned antibiotics. Physical examination noteworthy revealed large hepatosplenomegaly with no ascites. Comprehensive laboratory workup was initiated, including complete blood count (CBC) with differential count, peripheral blood smear, electrolytes and renal function tests. The results were within normal ranges. The repeated liver function tests revealed high liver enzymes with high total and direct bilirubin. Serum ammonia and lactate were normal. Urine for reducing substance was negative. Metabolic screening in urine and blood was unremarkable. The glucose-6-phosphate dehydrogenase (G6PD) enzyme assay was normal. The baby improved progressively and after 4 days, he could be extubated to oxygen via nasal prongs then room air.

On the 6th day of life, the father brought to us an antenatal U/S report that showed fetal ventriculomegaly. Brain U/S and CT scan were done and showed bilateral marked symmetrical dilatation of the supra and infratentorial ventricular system with diffuse cortical calcifications (Figure 1).

Serological tests for antenatal infections were sent and the results were negative except for toxoplasma. The toxoplasma serological tests in the infant’s blood were IgG level of 166.4 IU/ml and IgM level of 4.23 index, measured by chemiluminescent microparticle immunoassay (CMIA). The reactive cutoff for IgG ≥3.0 IU/ml and IgM ≥0.60 index. The serological tests of the mother’s blood showed a toxoplasma IgG level of 94.3 IU/ml and IgM level of 1.3 index (measured also by CMIA). Ophthalmological examination revealed chorioretinal changes in both eyes and uveitis with pigments at the anterior lens surface of the right eye. An ENT specialist was consulted, and no abnormalities were reported. The pediatric neurologist shared the entire process of management and follow-up. Considering these clinical, serological and imaging findings, the diagnosis of congenital toxoplasmosis was made. The infant (Figure 2) was commenced on a regimen of sulfadiazine (100 mg/kg/day), pyrimethamine (1 mg/kg/day), folinic acid (10 mg/day, 3 times/week) for 12 months. Prednisone (1 mg/kg/day) was given till the eyes active lesions had subsided (for about 48 days). During the full treatment period, no adverse effects related to the medications were observed. The baby was discharged home at the age of 52 days in stable health condition. Nevertheless, the head circumference was 37 cm (90th centile) and he weighed 3.40 kg (10th centile). The parents were provided with detailed instructions regarding the medications and the multidisciplinary follow-up appointments. During the follow-up period, the hepatosplenomegaly diminished in size but remained palpable for about three months. The most striking clinical feature was a rapid increase in hydrocephalus. Head circumference at the age of 4 months was 45.6 cm which was above the centiles (Figure 3). Immediately, a brain CT scan was done and it showed a marked increase in the hydrocephalus size (Figure 4).

Figure 2: The baby at the age of 18 days; he was still jaundiced with a distended abdomen (hepatosplenomegaly).

Figure 3: The child at the age of 4 months showed marked hydrocephalus with the sunset sign.
mometry test showed a normal hearing.

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Cataracts, microphthalmia, nystagmus and strabismus can 7
neovascularization, retinal detachment and visual loss.

Chorioretinitis is usually bilateral and can lead to 8
hydrocephalus, although they are seldom seen at birth.9
Chorioretinitis is usually bilateral and can lead to 8
neovascularization, retinal detachment and visual loss.
Cataracts, microphthalmia, nystagmus and strabismus can
also be seen. Neurological manifestations include micro
or macrocephaly, hydrocephalus, seizures, cerebral
calcifications, meningoencephalitis, motor and cerebellar
dysfunctions and sensorineural hearing loss.9 Other
clinical manifestations may include rashes (petechial,
maculopapular or blueberry muffin), lymphadenopathy,
hepatosplenomegaly, jaundice, pneumonitis, myocarditis
and endocrinopathies.10

Antenatal maternal diagnosis can be carried out by
performing toxoplasma serology tests (IgM, IgG and
IgA). Fetal infection can be confirmed by positive
amniotic fluid toxoplasma PCR and ultrasound
scanning.11 Evaluation of a newborn suspected of having
CT should include CBC with differential count and
peripheral blood smear, which may show abnormalities
such as anemia, thrombocytopenia and/or eosinophilia.
Characterestic CSF findings include mononuclear
pleocytosis and high protein content.12 The presence of
toxoplasma-specific IgM and IgA in a newborn confirms
the diagnosis of CT. Toxoplasma IgG test should be
performed and typically reflects maternal antibodies.
However, the persistence of toxoplasma IgG antibodies
by one year of age is considered the gold standard
evidence of congenital infection. PCR positive results in
any body fluid such as blood, spinal fluid and urine also
confirm the diagnosis.5

Neonatal imaging studies including brain ultrasound, CT
scan and MRI are recommended to look for intracranial
calcifications, hydrocephalus and cortical brain atrophy,
whereas abdominal ultrasound can help in detecting
intrahepatic calcifications and/or hepatosplenomegaly.2

Studies have shown that prenatal treatment results in
decreasing the number of both severe and mild infections
and reducing the incidence of sequelae at birth as well as
the late sequelae. Spiramycin is given to mothers with
acute primary toxoplasmosis in the first trimester of
pregnancy and should be continued till delivery.
Pyrimethamine, sulfadiazine and folinic acid
combinations (PSF) are given after confirmation of fetal
infection by amniotic fluid PCR or imaging. PSF regimen
should be avoided in the first 14 weeks of gestation due
to its teratogenicity.1

Postnatal treatment is started when the diagnosis of CT is
confirmed even if the infant is asymptomatic and
continues for one year.12 Laboratory surveillance
including CBC, renal and liver function tests should be
done regularly to detect medications adverse reactions
such as bone marrow suppression and possibly hepatitis.
Evaluation for G6PD deficiency should be done before
commencing treatment especially for those who are
coming from areas with high incidence.13 Prednisone is
considered in cases of severe chorioretinitis or elevated
CSF protein concentration ≥1 g/dl. It is continued until
the resolution of active chorioretinitis that threatens
vision.14 For hydrocephalus, neurological evaluation,
serial HC measurements and prompt placement of a

Figure 4: CT scan brain at the age of about 4 months showed marked hydrocephalus and decreased cortical
calcifications.

An urgent neurosurgical referral was arranged and a
ventriculoperitoneal (VP) shunt was inserted at the age of
about 4.5 months. After surgery, the head circumference
started to decrease and it was 46 cm (80th centile) at the
age of 9 months. The child completed the one-year course
of treatment. The last visit at the age of 14 months
revealed a moderate psychomotor and cognitive
developmental delay with some visual impairment.
However, the audiometry test showed a normal hearing
sense. The head circumference progressively stabilized at
75th centiles for his age.

DISCUSSION

In pregnant women, toxoplasmosis is acquired through
the consumption of undercooked meat infected with
tissue cysts or through ingestion of oocysts excreted by
cats via eating contaminated food, vegetables or drinking
contaminated water. Seroprevalence varies worldwide
and within countries and this variation is mostly
attributed to cultural habits and food consumption
rituals.5 The estimated incidence of CT globally, ranges
from 0.1 to 6/1000 live births, with the highest being in
the Middle East and South America.6 During maternal
parasitemia toxoplasma may invade the placenta with the
subsequent passage into the fetal circulation and tissues.
The severity of CT is inversely proportional to the
gestational age, but the rate of transmission to the fetus
increases with the gestational age progress.

The most severe forms occur in early pregnancy
infections and can induce spontaneous abortion,
deleterious lesions, hydrops fetalis or stillbirth.7 At birth
CT has a wide range of clinical presentations, from being
subclinical and asymptomatic to serious devastating
sequelae including prematurity, intrauterine growth
restriction, neurological and ocular complications and
perinatal death. The classic triad of neonatal CT includes
chorioretinitis, intracranial calcifications and
hydrocephalus, although they are seldom seen at birth.8
Chorioretinitis is usually bilateral and can lead to
neovascularization, retinal detachment and visual loss.
Cataracts, microphthalmia, nystagmus and strabismus can

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ventriculoperitoneal shunt are crucial for improved outcomes.\(^8\)

The outcome of CT is variable from severe impairment to completely normal children and young adults. It has been shown that children who are born with moderate or severe clinical signs at birth when treated, exhibited markedly better outcomes compared to those who were not treated or treated only for a short course. In treated children, cerebral calcifications may be resolved partially or completely during the first year of life.\(^9\) Close monitoring and regular follow-up of infants during and after treatment is paramount with particular concentration on disease progression, chorioretinitis recurrences, adverse reactions of medications and therapeutic response. A multidisciplinary team is highly recommended including a neonatologist, pediatric neurologist, ophthalmologist, audiologist, radiologist, and infectious disease pediatrician. Parents involvement in the care of the patient is of great importance.\(^7\)

**CONCLUSION**

Congenital toxoplasmosis can be prevented or reduced by providing prompt and timely medical care and decreasing the chance of exposure to the infection during pregnancy. Although treating the pregnant mother or the newborn does not guarantee a cure of the disease or the absence of lesions, it is the most effective way to prevent relapses and more serious sequelae in the long term. Infants evaluation should include serological studies, ophthalmological, neurological and hearing examinations to improve the outcomes. Currently, optional medications for the treatment of toxoplasmosis are lacking and some medications have serious adverse reactions. We reported this case to emphasize the importance of this neglected disease and to highlight the urgent need for appropriate prevention and management strategies to reduce the effect of this burdensome infection as far as possible.

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**REFERENCES**