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CASE REPORT

Congenital Toxoplasmosis: An Incidental Finding

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Abstract

Congenital toxoplasmosis occurs through trans-placental transmission and features may not be apparent until later in life. If untreated, it can lead to significant disabilities such as mental retardation, blindness, deafness, epilepsy and death.

We report a case of congenital toxoplasmosis to raise awareness of the often-forgotten challenges associated with the management of congenital infections.

A late preterm neonate conceived via in-vitro fertilization was delivered with microcephaly. The mother had a positive history of contact with cats and cat's litter. No toxoplasma screening was done during antenatal care. Physical examination findings revealed microcephaly (OFC = 29cm) only. Laboratory results were normal except for T. gondii immunoglobulin G and M seropositivity in the baby and the mother. The baby was placed on Pyrimethamine.

Perinatal care should focus on health education and increased vigilance for these congenital infections so as to aid in prevention, early detection and management.

Key-words: Congenital toxoplasmosis, Congenital infection, Cats.

Key Messages:

Congenital toxoplasmosis is an avertible infection which can have long-term devastating consequences and can also lead to death. Perinatal care should focus on health education, with mandatory efforts targeted towards making diagnostic tests and treatment options available to limit preventable morbidity and mortality.

Introduction

Congenital toxoplasmosis (CT) is a preventable, trans-placentally acquired infection caused by Toxoplasma gondii with devastating consequences in the new-born or later in life.[1] In the new-born, it commonly develops following acute infection during pregnancy and less commonly from maternal infection shortly before conception or as a result of reactivation of a previous quiescent infection in an immunocompromised mother. Transmission of infection is also known to occur at the time of delivery. Breastmilk transmission however has not been reported.[2] The primary source of maternal infection is mainly through the feaco-oral route by eating uncooked or undercooked meat containing the parasite, contaminated fruits, vegetables, water or contact with infected cats or soil. Infection has been known to occur following organ transplantation and blood transfusion. [2]

Globally, toxoplasmosis is a very common infection, affecting 25-30% of the population.[3] The prevalence increases with age [4], with approximately 85% of women of childbearing age predisposed to the infection. [1,5] In Europe, the seroprevalence of CT is low at 10%, while in some areas in Brazil and Madagascar, a seroprevalence rate as high as 80% has been documented. [6] In the United States, the estimated incidence of CT infection ranges between 1/3000 to 1/ 10000 live births[2] and is as high as 1.5 to 2.5 /1000 births in some parts of Africa.[7] In a bi-centre study in Nigeria, a high prevalence (75.4% and 80.5%) of toxoplasmosis in pregnant and postpartum women was reported [8] and may be linked with poor hygienic and alimentary practices as well as high seroprevalence of toxoplasmosis among some domestic animals, with confirmed high preponderance and spread of veterinary toxoplasmosis to humans.[9]

The overall risk of congenital infection from acute *T. gondii* infection in untreated pregnant women varies according to the trimester the disease is acquired and ranges between 20% and 65%, [2,10] it being highest during late gestation as a result of the decrease in placental barrier function and immune control of infection.[4] In contrast, the risk of severe symptomatic disease is inversely proportional to the gestational age at which the mother seroconverts, and is utmost between 10 and 24 weeks of gestation. [1,5,11] Approximately 10% of congenital infections without prenatal therapy results in abortion or neonatal death. [1]

After delivery, clinical disease has a wide spectrum of presentation with approximately 75% having no clinical symptoms.[2] The hallmark of the disease is a triad of chorioretinitis, intracranial calcifications and hydrocephalus. It can also lead to preterm delivery with or without growth restriction, skin rashes, jaundice, anemia, hepatosplenomegaly, lymphadenopathy, seizures and abnormal head size (microcephaly or macrocephaly). As the infant grows, delay in motor and developmental milestones, seizure disorder and mental retardation may occur. At present, the outcome of a new-born that is asymptomatic cannot be predicted. Its manifestations may not be apparent until the second or third decade of life [1,12] with approximately 80% developing hearing and visual impairment as late as 30 years after birth.

Therapy using pyrimethamine-sulfadiazine combination therapy for a period of at least one year is recommended irrespective of clinical presentation. Prednisone is advocated for active CNS disease and ventricular shunting in case of hydrocephalus advocated[1].

In Sub-Saharan Africa, the burden of CT is often underestimated and it remains untreated due to lack of routine serologic screening especially during antenatal visits [12,13] largely due to unavailability of testing kits for disease verification and monitoring as well as shortage of essential drugs for adequate therapy. Still, majority of maternal and neonatal infections have no overt clinical symptoms[14] which further militate against effective diagnosis and management.

This report aims to highlight a case of incidental diagnosis of CT, in order to raise awareness of the often-forgotten CT linked with pregnancy, management challenges and the need for routine universal screening of pregnant women and babies.

Case History:

A one-hour old female neonate was delivered via emergency caesarean section to a 29-year-old primipara with gestational diabetes (GD), pregnancy induced hypertension (PIH) and history of decreased fetal movement at 36weeks. The baby's APGAR scores were normal.

Pregnancy was conceived via in vitro fertilization following 6 years of infertility. The mother

developed GD and PIH at 30weeks gestation and was managed with Insulin, Aldomet and Nifedipine. She had a previous history of spontaneous miscarriage at six weeks gestation, one year prior to the index pregnancy. There was a positive history of domestication of cats and contact with cat litter for two years. No history of ingestion of undercooked meat, fever during pregnancy or smoking/alcohol ingestion. Venereal disease research laboratory screen and obstetric scan done during antenatal visit were normal.

On examination, the baby had a temperature of 36.5^0C, with no skin rashes/petechiae nor any other dysmorphic features beside an occipito-frontal circumference (OFC) of 29cm which was below the 10^{th} centile on the intrauterine growth chart. The weight and length were 3000g and 45cm respectively. Other examination findings were normal.

Other investigations done included an oxygen saturation of 96% in room air, capillary haematocrit of 78% and blood glucose of 5.8mmol/l. The baby was managed as a high risk perinate: infant of diabetic mother with polycythaemia and microcephaly (? cause), at risk of jaundice and hypoglycaemia.

Baby was commenced on breastfeeding with top-up feeds and prophylactic phototherapy.

She developed jaundice on the second day of life. Her total bilirubin level was 8.1mg/dl, and due to the known association of jaundice with haemolysis, a repeat haematocrit was done to determine its extent and was found to be normal. Other parameters of the liver function test were within normal limits (alkaline phosphatase: 98 IU/l, alanine transaminase:18.5 IU/l and aspartate transaminase: 20 IU/l). Blood group of the baby was O positive while that of the mother was B positive. The baby's infection screen was normal with a total white blood cell count of 9.4 x 10^3/ul, granulocyte count of 3.3 x 10^3/ul and lymphocyte count of 4.0 x 10^3/ul. Likewise, trans-fontanelle ultrasound scan using 3.5mHz transducer showed normal cerebral and cerebellar hemispheres including the ventricular systems and extra-axial fluid spaces. Retroviral screening was non-reactive by ELISA. Results of cytomegalovirus immunoglobulin (Ig) G and M assay were negative. Toxoplasma gondii IgG and IgM assay could not be done at the time due to lack of diagnostic kit. Baby remained stable and was discharged on the 4^{th} day of life. Toxoplasma gondii IgG and IgM assays were done at 2 weeks old and was positive for both the baby and mother. Fundoscopy and brain CT scan was normal. Auditory brainstem response revealed severe hearing impairment in the right ear, while the left ear showed mild hearing loss. She was commenced on Pyrimethamine 2mg/kg/day 12 hourly for 2days, then 1mg/kg/day for 2 months, then 1mg/kg/day on alternate days and it was continued for 1year. Serial OFC measurements were 34.5cm, 36.5cm, 37.5cm, 38.5cm, 39.5cm at 10weeks, 14weeks, 16weeks, 6 months, 7months respectively. Neurologic examination and developmental milestones were normal. Repeat toxoplasma IgM assay was negative at 8 months of life, while IgG was still positive.

Discussion:

This report demonstrates that CT requires a high index of suspicion, as presentation is asymptomatic in majority of cases.[1] This patient had no obvious clinical symptoms on presentation that were suggestive of any form of infective process except microcephaly.[15] In particular, the history of domestication of cats and maternal contact with their litter, previous early trimester miscarriage; and the late preterm delivery in the index pregnancy which was attributed to GDM and PIH may all be linked with maternal toxoplasma infection and thus, be a possible cause of microcephaly in the baby. All this history may suggest a prior infection during her first pregnancy which resulted in a miscarriage, and a reactivation of the quiescent

infection late in the index pregnancy (likely attributed to gestation-induced immunosuppression) despite the lack of maternal symptoms or disease confirmation.

The normal obstetric scan during the index pregnancy may also suggest that maternal infection was acquired late in pregnancy, as it has been reported that most foetuses infected in the second and almost all infants infected in the third trimester have mild or subclinical disease in the new-born period.[1,6] Similarly, the positive IgG and IgM assays, the 'gold standard' diagnostic test for CT in the absence of PCR,[1,6] in both the baby and the mother suggests an active, recent infection. Although the exact timing of primary infection in the mother could not be confirmed due to lack of IgG avidity test, the asymptomatic case presentation and positive maternal and neonatal IgM assay suggests a late trimester infection.[10]

Approximately 85% of women of childbearing age are predisposed to infection with the parasite.[1,5] In Europe and USA, the seroprevalence of CT is low at 10% and 11% respectively, while in some areas in Brazil and Madagascar, a seroprevalence rate as high as 80% has been documented.[6] In a bi-centre study in Nigeria, a high prevalence (75.4% and 80.5%) of toxoplasmosis in pregnant and postpartum women was reported,[8] suggesting poor hygienic and alimentary practices in these regions. Furthermore, the high seroprevalence of toxoplasmosis among some domestic animals, with confirmed high preponderance of zoonotic infection may account for the high prevalence of CT in these areas.[9] In this report, the history of contact with cats and cat litter indicates the source of infection. This substantiates the need for mandatory active infection screen in prospective mothers, given the reports of increased seroprevalence in both domestic animals and humans.[9]

Screening program revealed that majority (96%) of CT cases were unlikely to be detected without screening due to its asymptomatic nature.[16] Transmission of CT in this case could have been prevented if routine first trimester screening had been offered to the mother during pregnancy to establish baseline results and proactive screening during each trimester due to the risk of potential exposure which the mother had from her pets. This, in addition to new-born screening could have avoided the delay in detecting the baby's infection. Appropriate counselling and information dissemination about modes of disease transmission including preventive strategies during pre-conceptional care, which in our setting is not commonly done due to unplanned nature of pregnancies, as well as early antenatal care could have averted exposure to the parasite.

Limitations encountered include lack of antenatal surveillance and incomplete maternal prenatal infection screening. This hindered early institution of treatment for the mother during pregnancy and the baby at delivery. Also, lack of quantitative IgG /IgA assays, absence of PCR and appropriate culture medium; and unavailability of certain drugs like sulfadiazine and folinic acid were a major challenge.

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