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Congenital Toxoplasmosis with Aplastic Anemia: A Rare Association

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ABSTRACT

Congenital toxoplasmosis is caused by transmission of an intracellular obligate coccidian protozoan (*Toxoplasma gondii*) via vertical transmission during pregnancy. The clinical manifestations are wide ranging from asymptomatic to intracranial calcifications, seizures, developmental delay, chorioretinal lesions and even fetal death. Aplastic anemia is one of the rare presentations of congenital toxoplasmosis. Hence, we are reporting a case of a 23-year-old male who presented to us with aplastic anemia due to congenital toxoplasmosis. Thus, congenital toxoplasmosis should always be considered as a cause when evaluating a case of aplastic anemia.

Keywords: Aplastic anemia, congenital toxoplasmosis, *Toxoplasma gondii*

Toxoplasmosis is a parasitic disease caused by *Toxoplasma gondii*, an intracellular obligate coccidian protozoan. It usually spreads by eating poorly cooked food that contains cysts, exposure to infected cat feces or from infected mother to baby during pregnancy. It rarely spreads through blood transfusion.[1] Toxoplasmosis is a disease having worldwide distribution. In United States, 13.2% of individuals greater than 6 years of age had serological evidence of exposure, as per data from a 2009-10 survey.[2] The exact incidence of toxoplasmosis in India is not yet documented but few studies have shown prevalence rate of 22.4% among women of childbearing age (8.8-37.3%).[3]

Toxoplasmosis may present clinically with different presentations like acute toxoplasmosis and congenital toxoplasmosis. Acute toxoplasmosis is usually asymptomatic and self-limited and remains unrecognized in 80-90% adults; whereas the clinical manifestations of congenital toxoplasmosis are wide ranging from asymptomatic to intracranial calcifications, seizures, developmental delay, chorioretinal lesions, hematological complications and even fetal death.[1] Maternal infection is by far the most common in third trimester; however, more serious infectious sequelae occur with first and second trimester infection. If prenatal infection is severe, it may cause multi-organ dysfunction and intrauterine fetal deaths.

Aplastic anemia is a potentially fatal bone marrow failure disorder, and if left untreated, it is associated with high mortality. It appears to be 2- to 3-times more common in Asia compared to Europe.[4] Congenital toxoplasmosis is usually associated with hemolytic anemia, but in our case, it was associated with aplastic anemia and therefore, we are reporting this case.

CASE REPORT

A 23-year-old male presented to us with complaints of easy fatigability and shortness of breath on exertion for past 3-4 months. He also had 1 episode of gum bleeding 4 months back. He had history of repeated blood transfusions (5 units whole blood in last 10 months). He had no history of any addiction and consumed a mixed diet. He also had no history of reddish or yellowish discoloration of urine, drug or toxin ingestion and radiation exposure. On general physical examination, patient was conscious, poorly nourished (body mass index [BMI] 17.5 kg/m^2), anemic and had mild pedal edema. He had nonparalytic squint (concomitant)

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in right eye. There was no lymphadenopathy and icterus. On per abdomen examination, there was mild hepatomegaly but no splenomegaly.

On cardiac auscultation, there was loud first heart sound and hemic murmur was heard. On neurological examination, mental function of the patient was normal but there was decreased distant vision (was able to do finger counting only from 1 meter distance) and decreased color vision (primary colors) in both eyes. Nystagmus was present bilaterally in horizontal gaze. The motor, sensory and cerebellar system examination did not reveal any abnormality and there were no signs of meningeal irritation. For further evaluation, ophthalmologist reference was taken and they found bilateral macular scarring along with few Roth spots on fundus examination, suggestive of congenital toxoplasmosis as shown in Figure 1.

On the basis of history and clinical examination including fundus finding, we made our provisional diagnosis of anemia with congenital toxoplasmosis.

For confirmation of above diagnosis, patient was thoroughly investigated and the following results were found: Complete blood count (hemoglobin [Hb] - 2.1 g/dL, total leukocyte count [TLC] - 1.96 × 10^3/uL, platelet count - 14 × 10^3/uL). Differential leukocyte count (DLC) was neutrophils - 22.9%, lymphocytes - 65%, monocytes - 9.2%, eosinophils - 0.4% and basophils - 4.5%. Mean corpuscular volume (MCV) - 95.7 fL, mean corpuscular hemoglobin (MCH) - 30.2 pg, MCH concentration - 31.5 g/dL, hematocrit - 6.1%. Peripheral blood film (PBF) showed normocytic normochromic red cells; leukopenia with neutropenia and no immature cells seen; thrombocytopenia with platelet morphology normal. Reticulocyte count was 0.30%, thus making reticulocyte production index = 0.02%; which reflects hypoproliferative anemia. On further investigation, iron profile, vitamin B12, thyroid profile, Coombs test, renal and liver function tests, lactate dehydrogenase, urine examination and autoimmune profile were all normal. Patient was also tested for human immunodeficiency virus (HIV), hepatitis B, C and E virus and was found negative. USG abdomen showed mild hepatomegaly. So, the next step in the algorithm was to perform bone marrow aspiration, which showed hypoplastic bone marrow with normal morphology, thus making the diagnosis as aplastic anemia. Various causes of aplastic anemia were ruled out like drugs and radiation exposure, infections like HIV and hepatitis E, autoimmune conditions and paroxysmal nocturnal hemoglobinuria (PNH). The most likely cause for aplastic anemia was toxoplasmosis; which was further confirmed by serology testing for toxoplasma IgG, which came out to be positive. On further enquiring, it was found that patient's family had cats as pet for past 25-30 years, which could be the source of toxoplasmosis.

Patient underwent 3 units whole blood transfusion and was treated with tablet sulfadoxine-pyrimethamine combination (800/160) b.i.d. and tablet folic acid 5 mg o.d., which will be continued for 1 year as per the

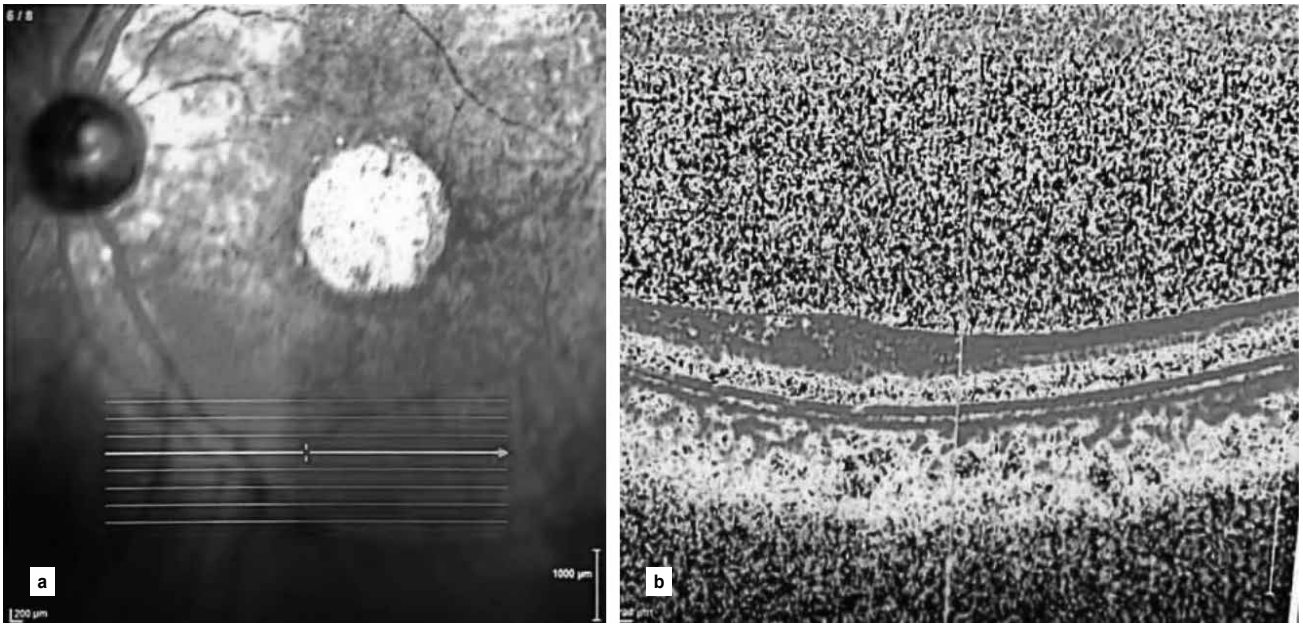

Figure 1. Macular scarring near the optic disc on fundus examination **(a)**; thinning of fovea on optical coherence tomography of the patient **(b)**.

guidelines. He was discharged from the hospital and advised regular follow-up.

DISCUSSION

Toxoplasmosis is caused by a coccidian parasite, *T. gondii*. The disease is primarily spread through exposure to oocysts present in contaminated water, food or soil or by ingesting cysts from undercooked meat. There is also transplacental route of transmission. There are 3 stages of the parasite: tachyzoite, bradyzoite and sporozoite. Tachyzoites are seen in the acute infectious form of the disease, while bradyzoites are periodic acid-Schiff (PAS) positive dormant cyst stage awaiting reactivation as the host gets immunocompromised. Sporozoites exist within oocyst and are the form in which the parasite is spread through the environment.[1] Although most congenitally-infected children are asymptomatic at birth, they may develop some symptoms later in life. Loss of vision is the most frequently observed sequelae in congenitally-infected children. Hydrocephalus, chorioretinitis, psychomotor retardation, intracerebral calcifications, loss of hearing and death (very rarely) may occur.[5] Ocular toxoplasmosis can be a prodrome to central nervous system (CNS) toxoplasmosis.

There have been cases reported by Rawat et al[6] and Nelson et al[7] in which toxoplasmosis has presented with hemolytic anemia and hepatosplenomegaly.

Aplastic anemia is pancytopenia with hypocellular bone marrow. There is biphasic age of distribution, with a major peak in teenage and the twenties and a second surge in older adults. Men and women are equally affected.[8] The incidence of aplastic anemia is reported to be higher in Asia than in the Western countries. The exact incidence in India is not known because of a lack of epidemiological studies. About 20-40% of pancytopenic patients in referral centers have aplastic anemia.[9] The clinical presentation of aplastic anemia is usually lassitude, weakness, shortness of breath and bleeding. Lymphadenopathy and splenomegaly are highly atypical of aplastic anemia. There are various causes of aplastic anemia like constitutional, radiation and drug exposure, viruses (Hepatitis E, HIV, Epstein-Barr virus), immune diseases, paroxysmal nocturnal hemoglobinuria and pregnancy. Congenital toxoplasmosis is not a documented cause of aplastic anemia but in our case, it is the probable cause of aplastic anemia.

Congenital toxoplasmosis is a fatal disease that can be prevented and treated. Spiramycin is the drug of choice for preventing transplacental transmission of the parasite.[10] Most experts use spiramycin to treat pregnant females who have acute toxoplasmosis early in the pregnancy and pyrimethamine/sulfadiazine/folinic acid to treat women who seroconvert after 18 weeks of pregnancy or in cases of documented fetal infection. Congenitally-infected neonates are treated with daily oral pyrimethamine (1 mg/kg) and sulfadiazine (100 mg/kg) along with folinic acid for 1 year.

Since there is no effective vaccine against toxoplasmosis, the only option is to prevent the disease by not eating undercooked meat and avoiding oocyst contaminated material (cat's litter box). Litter boxes should be changed every day as freshly excreted oocysts will not be infectious. Also, these should be changed by HIV negative and nonpregnant persons preferably. Thorough washing of hands should be practiced after changing litter boxes and further it is advisable that all pregnant women should be screened for toxoplasmosis during antenatal period, so to treat and prevent transplacental transmission to fetus.

CONCLUSION

Congenital toxoplasmosis can have various clinical presentations, including aplastic anemia. Hence, whenever a patient presents with recurrent anemia despite repeated blood transfusions, especially aplastic anemia, we should search for congenital toxoplasmosis as a cause and treat it.

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ARTICLE RETRACTION

Title: To Study the Efficacy and Safety of a Polyherbal Formulation in Nonalcoholic Fatty Liver Disease Patients

Authors: Pravin Rathi, Prabha Sawant, Dipesh Waghmare

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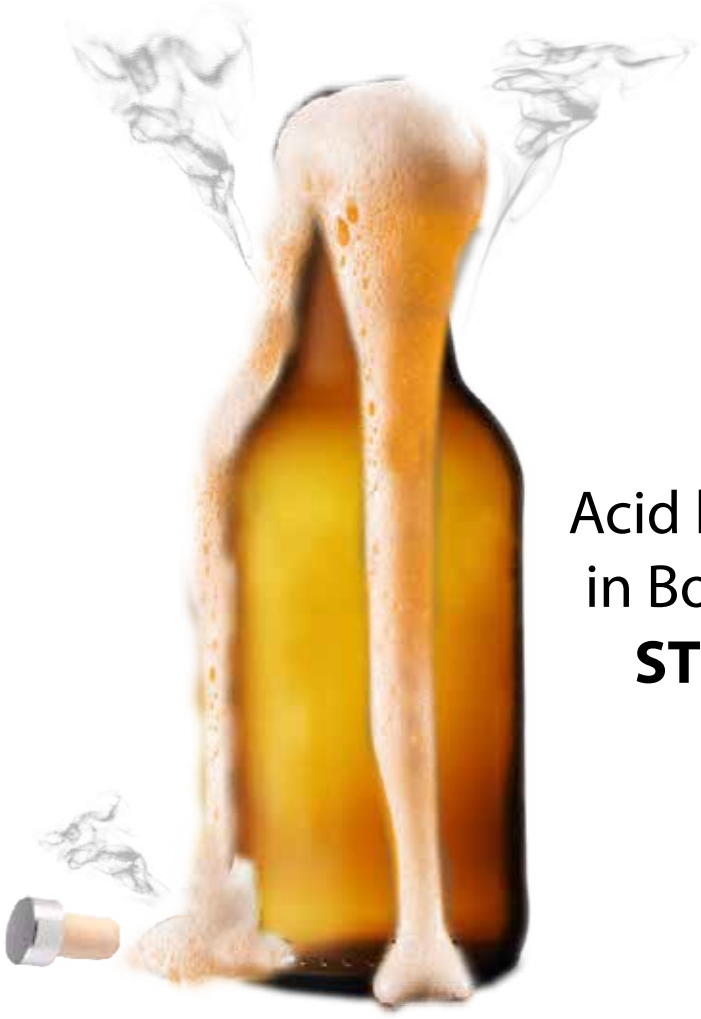
The article has been retracted from the journal and all the authors are intimated about this. The article was published after receiving a signed cover letter from the corresponding author on behalf of all the co-authors and after due diligence and completion of all required formalities.

However, due to an impending dispute between the stakeholders, a decision has been taken to retract the article from the journal.



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