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Congenital Toxoplasmosis or the Tip of an Iceberg. Report of Two Cases

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Abstract

Among the many parasitic diseases observed in the tropics, Toxoplasmosis is a fairly common occurrence. An infected pregnant woman can transmit it, transplacentally, to her foetus. Two cases of congenital toxoplasmosis are discussed in this study. One patient is at 7 days of life, while the other is at 9 days of life. The newborns displayed the typical symptoms of jaundice, hepatosplenomegaly, chorioretinitis, and cranioencephalic abnormalities. However, the uniqueness of these observations is the presence of umbilical haemorrhage, a symptom not described in the literature researched. The evolution of this finding, during treatment is distinguished by the symptoms persisting until six months of age, in addition to growth retardation of saturation-weight, with no retardation of psychomotor development in one patient, and with hydrocephalus accompanied by psychomotor retardation in the other one. Hence, it is recommended that pregnant women are systematically screened for toxoplasmosis, and seronegative women are monitored; in fact, the early and suitable management of congenital toxoplasmosis will significantly control this parasitosis.

Keywords

Toxoplasmosis, Congenital Toxoplasmosis, *Toxoplasma gondii*, Embryo-Fetopathy, TORCH Infections

1. Introduction

Toxoplasmosis, a disease caused by a protozoan, genus *Toxoplasma gondii*, is a type of anthropozoonosis. In the congenital manifestation of the disease, soon after the parasite is passed transplacentally during the primary infection in a pregnant woman, embryo-fetopathy is induced in the newborn and typified by

lesions, which are ocular, visceral and neurological.

It was Wolf *et al.* [1] who described the *princeps* case in 1939, after which congenital toxoplasmosis cases have been periodically reported in Africa [2] [3]. The reported first case, at the Centre Hospitalier Universitaire Pédiatrique Charles de Gaulle (Ouagadougou, Burkina Faso) was described in 2017 [4]. In this study, two cases of congenital toxoplasmosis are presented, detected in the same institution. The epidemiology, diagnostic, therapeutic and evolutionary features of this parasitosis are discussed to help enhance the management of this disease in our country.

2. Cases Presentation

Case ≠ 1

On 05/28/2020, BS, a male newborn at day 7 of life, was admitted into our hospital, with symptoms of jaundice and umbilical bleeding.

The mother was 35 years of age, G5P5. The pregnancy history revealed unexplained maternal fever in the 2nd trimester. Prevention measures were administered against malaria, anemia and tetanus. However, while the serologies for HIV, syphilis and viral hepatitis B were negative, the ones for rubella and cytomegalovirus were not performed. In this 2nd trimester, serology for toxoplasmosis was done, which was positive with IgG titers at 372.8 IU/ml and IgM at 35 IU/ml. Obstetrical ultrasound showed fetal abdominal ascites at 25 weeks of amenorrhea. The mother was placed on spiramycin tablets, 3 million IU (3 tablets/day) from the 25th week of amenorrhea until delivery.

The baby was born through normal delivery, with birth weight of 2100 g, cranial perimeter (CP) of 29 cm and CP/age ratio < −3 SD, and height of 48 cm.

On admission the physical examination noted a temperature of 36.5˚C, SpO_2 of 90%, respiratory rate of 67 c/min and heart rate of 134 b/min. Overall, the general condition of the newborn was poor, with flaming mucocutaneous jaundice and umbilical bleeding, accompanied by hepatosplenomegaly, generalized hypotonia and blunted archaic reflexes.

The toxoplasma serology result was positive and the IgG titer was 11,430 IU/ml, with negative IgM. The other exams showed: hemoglobin 8.2 g/dl, total bilirubin 330.14 µmol/l, and direct bilirubin 317.68 µmol/l; in addition, the prothrombin count was 59%, procalcitonin was 4.48 µg/l, Gamma Glutamyl Transferases were 77 IU (3 times the normal), ASAT transaminases were 256 IU (6 times the normal) and ALAT was 85 IU (2 times the normal).

On the abdominal ultrasound, the liver appeared homogeneous and hyperechoic with fluid effusion in medium abundance. On the transfontanellar ultrasound, multiple intraparenchymal calcifications were noted, related to left paraventricular hyperechoic formation and left subependymal hemorrhage (**Figure 1**). On the cerebral scanner, multiple calcifications appeared to be disseminated in the supratentorial cerebral parenchyma (**Figure 2**). On examination of the eye fundus, the intraocular pressure in both eyes was high, with visible large

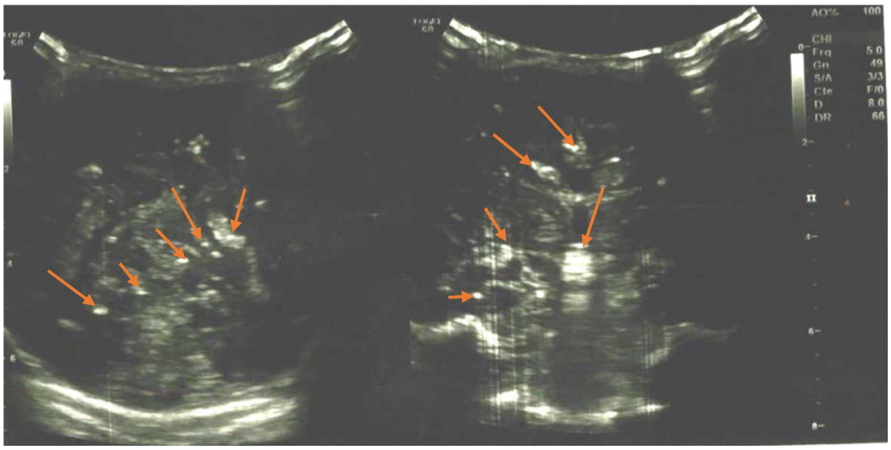

Figure 1. Transfontanellar ultrasound of SB revealing intraparenchymal calcifications.

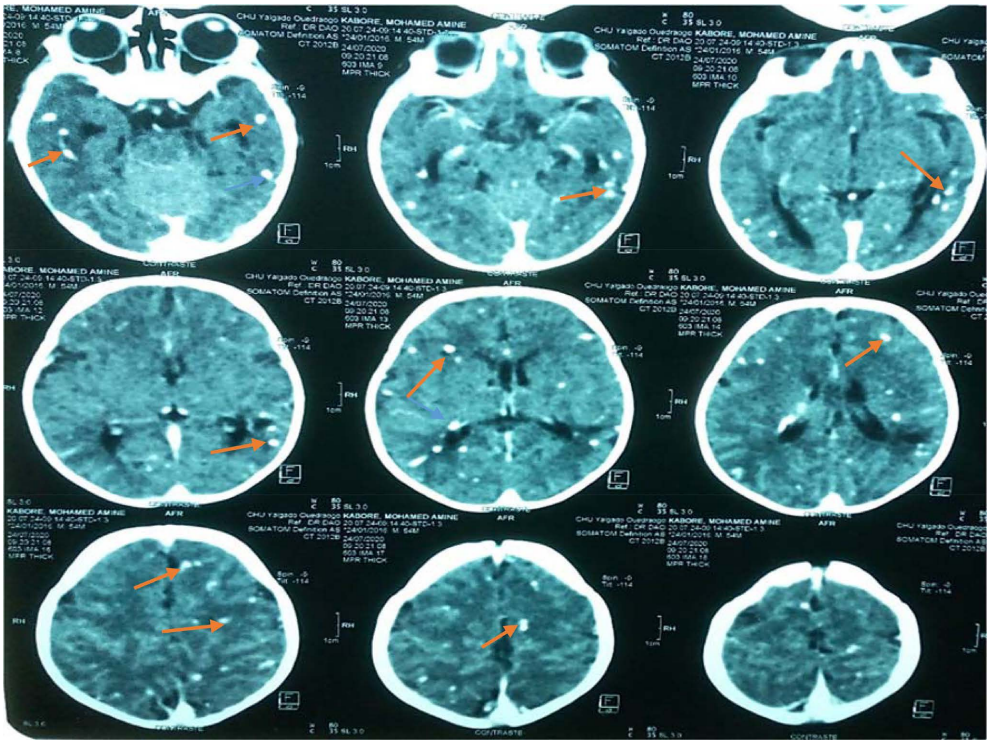

Figure 2. BS cerebral computed tomography displaying multiple disseminated calcifications.

papillary excavation and bilateral chorioretinitis scars.

The treatment administered to BS included sulfadoxine + pyrimethamine per os 50 mg, once every 10 days, folic acid per os 1.25 mg once every 7 days, and vitamin K1 injection 5 mg every two days. Ophthalmic dorzolamide hydrochloride was also given and the newborn continues to undergo motor physiotherapy sessions, at present.

At 6 months of age, the evolution was marked by persistent jaundice, cholestasis syndrome, hypertonia, and brisk osteotendinous reflexes, particularly in the lower limbs, as well as malnutrition (weight of 5.4 kg and weight/age ratio < −3 SD, height of 60 cm and height/age ratio < −3 SD); apart from these,

microcephaly was evident (CP of 35.5 cm and CP/age ratio < −3 SD). However, normal head and axial posture, eye tracking, and reaction to noise were evident.

Case ≠ 2

On 05/22/2020, NB, a female newborn, on day 7 of life, was admitted to our hospital for umbilical cord bleeding and jaundice.

The mother, 31-years-of age, G4P3, had experienced poor monitoring, throughout the pregnancy. While negative results were recorded for the HIV, syphilis and viral hepatitis B serologies, no serology tests were done for rubella, cytomegalovirus and toxoplasmosis. On obstetric ultrasound, the fetus showed hydrocephalus at 37 weeks of amenorrhea. Delivery was at term, and normal. Birth weight was recorded at 2730 g, CP at 38.5 cm (CP/age ratio > 3 SD), weight 32 cm and height 50 cm.

On admission, the physical examination revealed a poor general condition, with mucocutaneous jaundice and pallor. Active bleeding from the umbilicus was present. Temperature recorded was 38.6˚C. Weight was of 2725 g, CP of 38.5 cm with CP/age ratio > 3 SD.

The result was positive for the toxoplasma serology, giving an IgG titer value of 680 IU/ml, but negative for the IgM test. Transaminases AST were 297.9 IU (8 times the normal), while ALT was 130.8 IU (4 times the normal). The transfontanellar ultrasound enabled the diagnosis of hydranencephaly and calcifications of the left vitreous (Figure 3). As shown in Figure 4, the brain scan revealed triventricular hydrocephalus.

NB received a treatment which included sulfadoxine + pyrimethamine per os 50 mg once every 10 days, and folic acid per os 1.25 mg once every 7 days. A hydrocephalus shunt was inaccessible; no physiotherapy or ophthalmological treatment was performed.

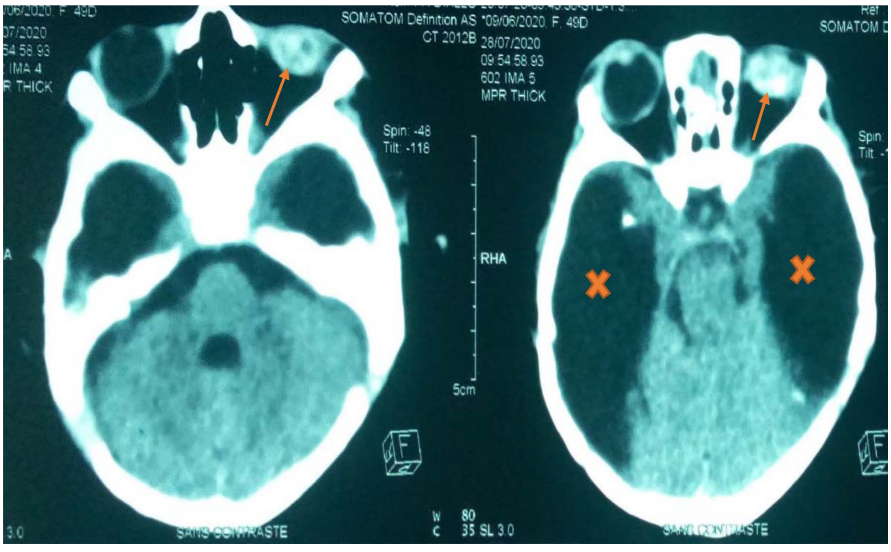

Figure 3. Transfontanellar ultrasound of NB indicating calcifications of the left vitreous and hydranencephaly.

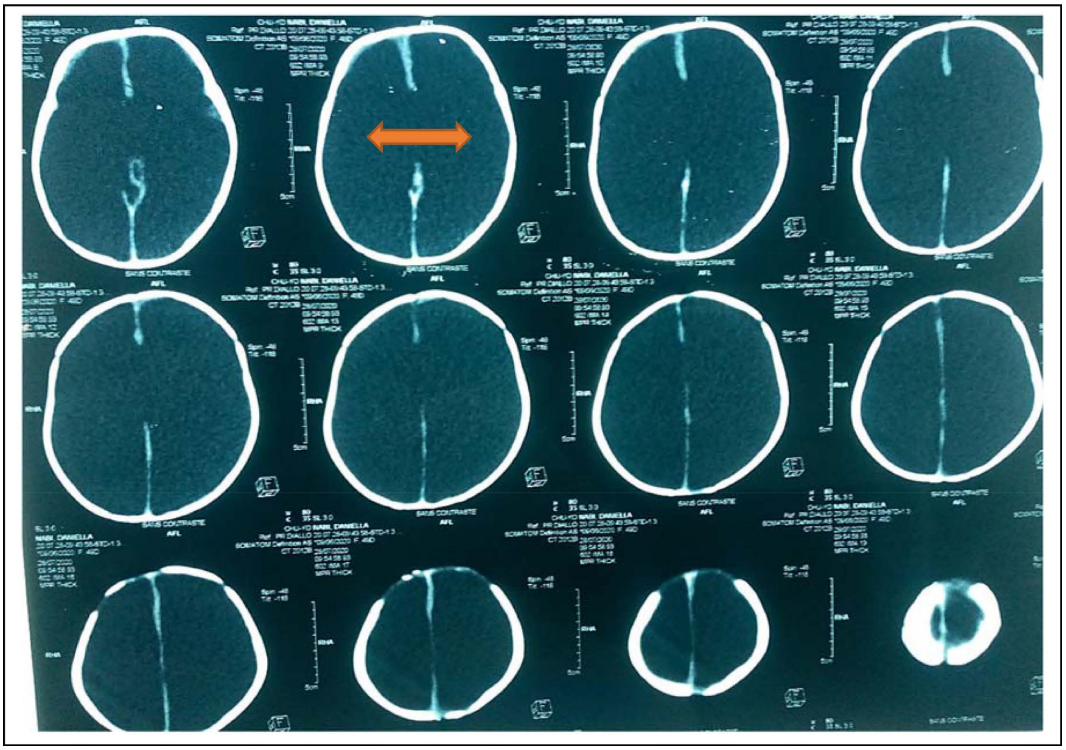

Figure 4. Brain computed tomography of NB presenting triventicular hydrocephalus.

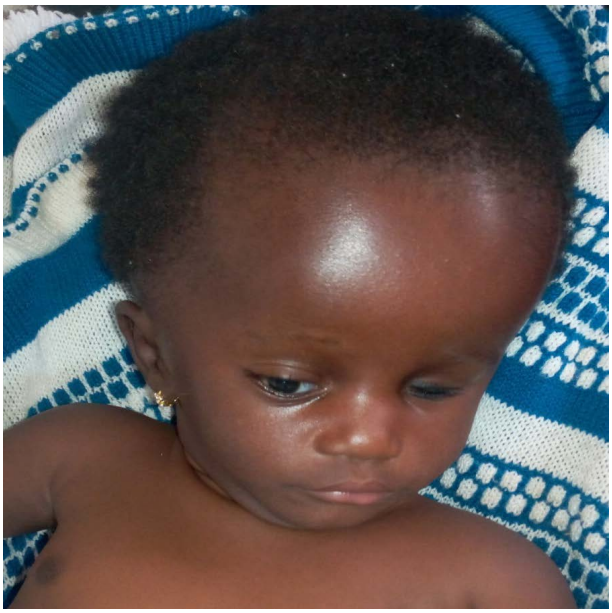

Figure 5. Photograph of NB showing macrocephaly, left microphthalmia.

At 3 months of age, a positive IgG titer at 1120 IU/ml was recorded, while the IgM returned negative. This notable evolution was regarded as consistent with active infection. At 6 months of age, the follow-up revealed regression of the cutaneous/mucosal jaundice, accompanied by psychomotor delay and lack of head and axial posture, as well as lack of ocular pursuit and reaction to noise.

Anthropometric measurements indicated macrocephaly (CP of 54 cm with

CP/age ratio > 3 SD). Archaic reflexes although present were blunted; cranial suture disjunction was observed, macrocephaly with sunset eye sign was evident, as well as inability to open the left eye (**Figure 5**).

3. Discussion

Incidence of congenital toxoplasmosis

These two cases of congenital toxoplasmosis discussed in the present study were among the 800 newborns our Neonatology unit admitted, in 2020. This represents a hospitalization frequency of 3.75 per 1000 newborns. Although a third case was diagnosed, it has been excluded here, as the file is incomplete. Congenital toxoplasmosis, a basically cosmopolitan disease, reveals variations in incidence, based on geography. In fact, its incidence in Latin America is estimated at 3.8 per 1000 births [5], while the annual number of cases globally is deemed to be around 190,100, with 26,500 to 37,000 of the cases occurring in Africa [6]. However, in Africa, these figures appear to be an underestimation, due to the lack of toxoplasmosis screening or monitoring programs; further, the obtainable data are scattered, from hospital sources, and fail to accurately present the true picture of occurrence in the general populace. Burkina Faso is in no way different, very little knowledge is available, regarding the epidemiology of congenital toxoplasmosis, screening is not mandatory for pregnant women, and this does not rank as a notifiable disease. However, after surveillance was implemented, significant seroprevalence of toxoplasmosis of 31% among pregnant women was reported in the city of Bobo-Dioulasso [7] [8].

Diagnostics

In the present work context, the prenatal diagnosis of toxoplasmosis is highly inadequate. In the event of one of the two patients showing a normal ultrasound, it is possible to identify ascites in the other. This examination enables the possibility of diagnosing a foetus, in 20% of the cases, by the appearance of typical intracranial calcifications related to ventricular dilatation as well as other less characteristic anomalies, namely, hepatomegaly, ascites, pericardial effusion, intestinal hyperechogenicity and the increase in placenta size [9] [10]. In the likelihood of the availability of ultrasound in our country, for the vast majority of pregnant women it remains an inaccessible facility, especially to the poor and/or those in rural areas. More advanced diagnostic tests like the identification of Toxoplasma or its DNA in the amniotic fluid, and magnetic resonance imaging remain, until date, unavailable in our country. Obstetricians or midwives fail to routinely prescribe prenatal blood tests, which include screening for TORCH infections (Toxoplasmosis, Other Agents, Rubella, Cytomegalovirus, Herpes simplex). However, after the Burkinabè government implemented the policy, in 2016, offering free healthcare for pregnant women and children under the age of five, access to such examinations will probably enhance the toxoplasmosis screening. Sadly, no legislation favouring compulsory prenatal screening is in place, as some developed countries like France enjoy.

Frequently, under the conditions here, the diagnosis of toxoplasmosis is suspected only at birth, when a newborn presents clinical signs of embryofetopathy. This enables ruling out those other conditions but retaining toxoplasmosis, through a significant titre of IgG or IgM antibodies that match the clinical picture the newborns present. In a large percentage of the cases with congenital toxoplasmosis, the newborn patients are asymptomatic at birth [11] [12]. It's only later in childhood and even in adulthood that the condition is revealed by poly visceral manifestations [13], particularly the ophthalmological manifestations [14] [15]. In fact, among all the newborn cases with toxoplasmosis, only 23.8% revealed signs at birth [2]. When congenital toxoplasmosis is exhibited, the clinical signs are categorised under the typical Sabin's tetrad, which includes chorioretinitis, hydrocephalus, intracranial calcifications, and convulsions. At differing frequencies, the other signs include intrauterine growth retardation, low birth weight, microcephaly, microphthalmia, jaundice, hepatomegaly, splenomegaly, and thrombocytopenia [11]. These signs are evident in both these observations, and other authors have also reported them [2]. The umbilical haemorrhage described here, however, appears atypical and exceptional. One possible explanation can be hepatocellular insufficiency and thrombocytopenia, noted in these two newborn patients.

In front of this maternal-foetal condition, not covered by any government legislation whatsoever in the developing countries and which presents protean characteristics, it is only by discussing a mix of epidemiological, anamnestic and newborn examinations that offer the clinician clues that can raise the suspicion for the diagnosis of congenital toxoplasmosis, and prompt him/her to ask for confirmatory examinations and implement treatment procedures, with no delay.

Treatment

Although controversy continues to rage over the futility of the drugs employed and their almost countless side effects [16], a treatment protocol for congenital toxoplasmosis is extensively shared and many treatment procedures are in use [17] [18] [19]. In Burkina Faso, in the absence of an undivided and accepted protocol, each healthcare team chooses to implement a therapeutic plan, according to its own rationales. Following a protocol different from the earlier case, where the patient was given pyrimethamine-spiramycin [4], in this study, a combination of sulphadoxine-pyrimethamine and folic acid was administered. Currently, both newborn patients continue to receive this treatment. In our context, the disadvantage is the lack of paediatric dosage forms, necessitating the use of tablets, which becomes a constraint in usage and approximations in the doses given. One of the patients is yet to benefit from neurosurgeon services for the hydrocephalus diversion required. The treatment of these two congenital toxoplasmosis cases clearly calls for the services of a paediatrician, ophthalmologist, and physiotherapist, demonstrating the management of this disease is multidisciplinary in nature.

Evolution and prognosis

Under treatment, a mixed short-term evolution of signs was observed in these two patients. While some signs persisted, others improved. Therefore, the evolution of congenital toxoplasmosis is related to the impediments occurring when beginning the treatment; obviously, early treatment enables the symptoms to decrease [20]. The prognosis, for these two patients, continues to be 'reserved'. In fact, among the factors of poor prognosis, infection precocity is very significant. It is well recognised that the earlier the onset of foetal infection, the greater the severity of the lesions [21], and in light of the abundance of signs these two patients presented, it is highly probable that these foetal infections appeared as early as the first trimester of pregnancy. Poor prognosis is also true for hydrocephalus, even in developed countries, in spite of good and available treatment protocols [22]. In our context, referring to countries with limited resources, introducing a ventriculoperitoneal shunt during the neonatal period continues to pose challenges. This further obscures the prognosis of the disease in one of the patients where the signs of intracranial hypertension are already evident. A codified follow-up plans are also absent in countries like ours, although they need to be implemented urgently and made mandatory for patient monitoring [18]. While ocular lesions, either new or arising from sequellar chorioretinitis in most cases, cause no major changes in visual function [23] [24], they can result in eventual blindness in some patients [15] [25]. In these two patients, the tenacity of the jaundice raises an alarm regarding possible bilirubin encephalopathy. The sequelae of neurological (epilepsy, cerebral palsy), sensory (blindness, deafness), and cognitive (lower intellectual coefficient) symptoms, which are clearly explained [23] [24] [25] [26], warrant patient monitoring to manage an adequate load. Therefore, it is crucial that a national program be established and monitoring of patients be made mandatory in our countries.

4. Conclusion

In Burkina Faso, manifestation of congenital toxoplasmosis in its severe form continues to be relevant. With no vaccine available, primary prevention persists as the only effective strategy to combat toxoplasmosis. A large-scale study on the incidence of congenital toxoplasmosis will throw much light on the extent of this condition prevailing in Burkina Faso and promote the institution of a national program to confront and overcome this long-ignored parasitic disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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