Management of toxoplasmic embryo-fetopathy at the teaching university hospital of Grand Yoff in Dakar: A case report and literature review.

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Abstract

Background: Congenital toxoplasmosis is an embryofoetopathy due to transplacental contamination of a parasite, Toxoplasma gondii. The disease may be undetected during pregnancy and this entity is rarely described in Senegal despite high seroprevalence among pregnant women. Lesions caused to the fetus can be fatal or cause neurological or ophthalmologic sequelae detected at birth and much later in life.

Case presentation: We report through this study a case of congenital toxoplasmosis detected during the ultrasound of the 2nd trimester of gestation. The fetus presented a bilateral ventriculomegaly and foci of cerebral calcifications. PCR on amniotic fluid confirmed the diagnosis of congenital toxoplasmosis. The prognosis was poor despite the start of therapy with the occurrence of fetal death in utero in a context of hydrocephalus at 28 weeks of gestation.

Conclusion: Congenital toxoplasmosis can be responsible for severe brain lesions. The lack of guidelines and adapted prevention policy in our regions make this embryo-fetopathy being a neglected disease that is probably underestimated in our practice.

Keywords: Congenital toxoplasmosis, Toxoplasmic embryo, Fetopathy, Toxoplasma gondii, Ventriculomegaly.

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Introduction

Congenital toxoplasmosis is an embryo-fetopathy characterized by ocular, visceral or intracranial lesions secondary to maternal primo-infection by Toxoplasma gondii.

Prenatal diagnosis of congenital toxoplasmosis is rarely reported in our regions. Lack of expertise is also addressed, and studies and scientific research involved in prenatal diagnosis and care in Africa are mainly from South Africa and Rwanda according to the bibliometric analysis of Poreau [1] Including 463 articles between 1956 and 2015. The prevalence of congenital toxoplasmosis remains unknown in Senegal.

Toxoplasma gondii is a unicellular flagellar protozoan, whose final hosts are the feline. Man can be considered as an intermediate host when it hosts the parasite in the form of tachyzoites and can present a chronic infestation in the form of bradyzoites, in brain or muscle tissue [2]. The geographical distribution of the infestation is global and in West Africa, this seroprevalence reaches 60% in certain regions [3]. During a primary infection with seroconversion in pregnant women, these lesions are particularly severe especially if an anti-parasite treatment is not undertaken in time.

For this reason, some countries with a high prevalence of toxoplasmosis have implemented a national screening program with serological surveillance for toxoplasmosis at monthly intervals throughout pregnancy, starting in the first trimester [4,5].

This policy, because of the cost of monthly serologies is difficult to implement in our regions. Thus, without screening, the first manifestation of fetal toxoplasmosis is most often malformations detected on ultrasound. Congenital toxoplasmosis can cause birth defects, fetal death, or long term disabling sequelae as blindness secondary to chorioretinitis. According to Rorman [6], the majority of newborns with congenital toxoplasmosis do not have any sign of the disease at birth.

The aim of our study is to describe the malformations identified in one case detected from ultrasound during pregnancy and the outcome.

Case Presentation

Mother's fetus

Mrs. AM is a 22-year-old primigravida referred to the reference ultrasound center at the Maternity of the teaching hospital of Grand Yoff in Dakar for a cerebral abnormality at the ultrasound of 22 weeks (Figure 1). The medical history was without any particularity.

Ultrasonography revealed hydrocephalus with significant bilateral and asymmetric ventricular dilatation (Figures 1A and 2A). There was a rupture of the medial septum (Figure 1A), and visible calcification in the forebrain (Figure 1B). No other abnormalities were reported. Fetal biometrics showed an

increase in head circumference above the 95th percentile while other biometric data were related to a gestational age of 22 weeks.

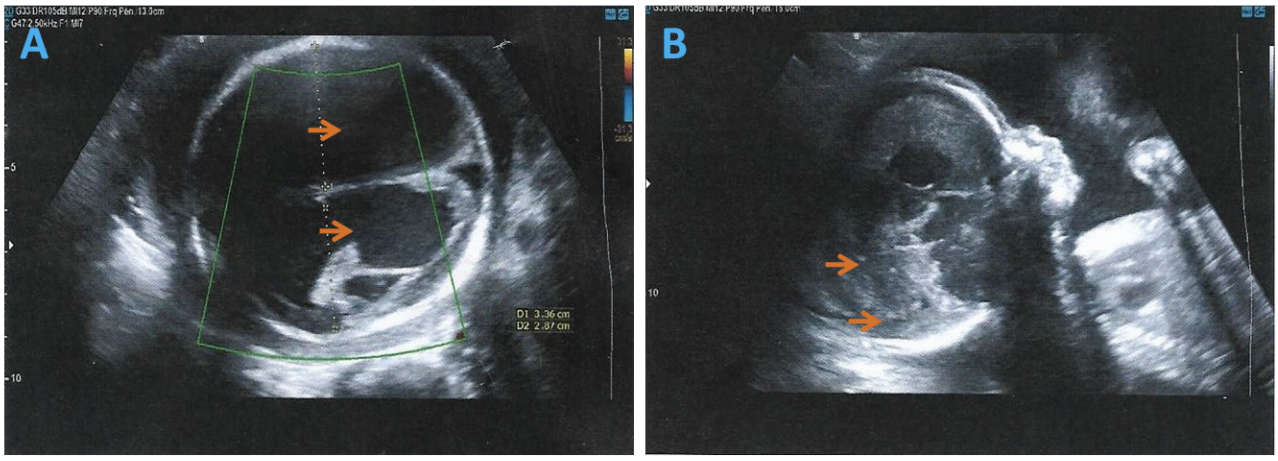

Figure 1. *(A) US coronal view of the fetal brain at 22 weeks of gestation. Bilateral and asymmetric ventricular dilatation; (B) US parasagittal view of the fetal brain. Foci of calcifications disseminated in the cerebral parenchyma in the forebrain (arrows).*

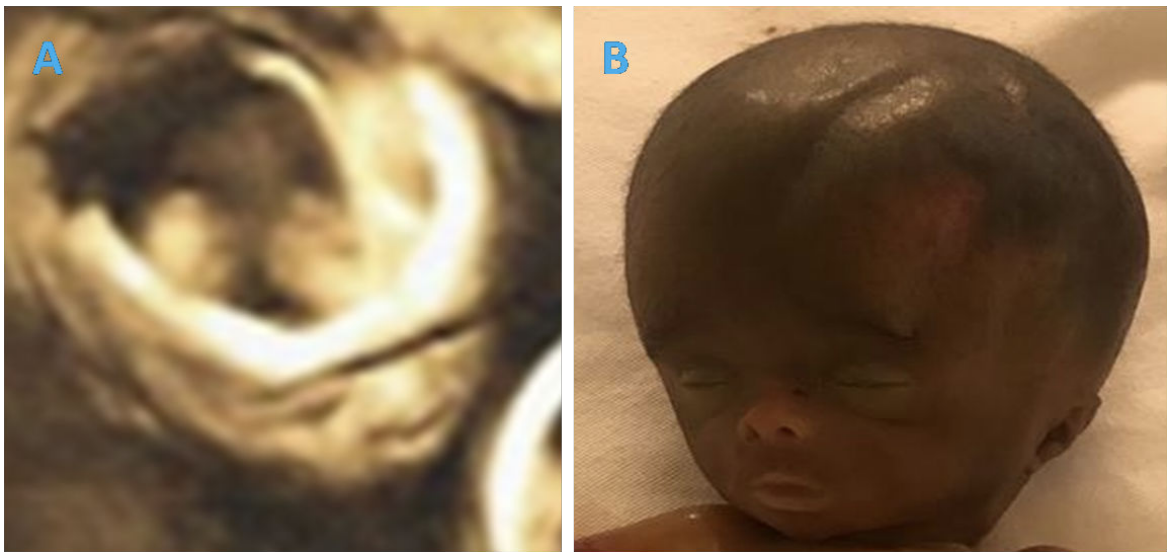

Figure 2. *(A) US 3D reconstruction after the 2D acquisition of coronal view of the fetal brain. Asymmetrical ventriculomegaly; (B) The Macrocrania and bulging fontanelles at birth.*

Serologic data

A "TORCH" serological assessment (for the detection of antibodies against toxoplasmosis, mumps, rubella, CMV and herpes simplex virus) was carried out after this discovery and revealed a toxoplasmic serology related to Immunoglobulins (Ig) type M negative and positive G-type. The CMV, HSV1 and HSV2, Rubella, and Syphilitic serologies were negative.

The analysis of the medical file revealed that the patient initially followed in a peripheral health center had a toxoplasmic serology at 7 weeks of amenorrhea. IgM level was slightly increased compared to the norm of the laboratory without serological control thereafter.

Amniotic fluid analysis

An amniocentesis was proposed to the patient for an etiological approach and a sample of amniotic fluid was taken. A systematic karyotype in way to exclude associated genetic etiologies was performed. It was normal with a chromosome formula 46, XX. However, Real-time PCR was performed and highlighted the parasite DNA signing the diagnosis of congenital toxoplasmosis.

A curative treatment began so, by the administration of sulfadiazine (3 g per day) and pyrimethamine (50 mg per day) with and supplementation with folic acid (50 mg) twice a week at 24 weeks of gestation. The patient stopped the preventive treatment that started a week before, based on spiramycin (3 million IU, 3 times a day).

Post mortem examination

Fetal death in utero occurred at 28 weeks of gestation. Post mortem examination in the histopathologic unit confirmed that the female fetus had macrocephaly with bulging fontanelles. Examination of the face did not reveal any dysmorphism (Figure 2B). In the absence of parental consent, the autopsy could not be performed.

Discussion

Prevalence

The various studies carried out in Senegal indicate a seroprevalence for toxoplasmosis which varies between 18 and 40% in the pregnant woman according to whether the study was carried out in urban or rural area [3]. The tendency is the same in other countries in West African, like in Burkina Faso [7].

The prevalence of congenital toxoplasmosis is difficult to determine because few studies are devoted to this entity in the sub-Saharan area. The lack of prophylactic guidelines and gestational screening process are responsible for underestimate or unknown diagnosis. These data are making congenital toxoplasmosis being a neglected disease in our context [8]. Indeed we don't have data, or any study concerning the prevalence of congenital toxoplasmosis in Senegal Sarvi [9], extrapoiled the prevalence of congenital Toxoplasma among Iranian population using some meta-analysis including 2230 Iranian neonates and he found 4.10% (95% CI=2.68-5.77%). This number is important and justify a screening at birth; This methodology is an interesting model that could help to estimate the prevalence of the disease in our population. The main limitation remains the lack of study. According to Helieh [10], the prevalence is high in the US and in Europe (from 30 to 80%). When there is maternal exposure the diagnosis is considered as often undetected according to Moncada [11].

One of the most important meta-analyzes was published in 2013 in the World Health Organization (WHO) bulletin [12] and reported an incidence of 190,100 cases each year.

Brain lesions

Toxoplasma is described as having a tropism for central nervous system.

Macroscopically: The studied fetus had mainly, brain lesions with bilateral ventricular dilatation and cerebral calcifications. The brain lesions often described are: microcephaly or hydrocephalus which is associated with periventricular or cortical calcifications [6].

Histologically: The suggestive sign is the cyst. In cases of cyst rupture, inflammatory and necrotic foci are numerous around these broken cysts. Lesions may include periventricular necrosis or surrounding the Sylvius aqueduct, associating vasculitis, thrombosis, and calcification. These lesions are then visible in the form of spots or small hyperechogenic features during ultrasonography [13,14]. These lesions are secondarily responsible for hydrocephalus by obstruction of the Sylvius aqueduct.

This was the case of our patient, born with macrocrania and bulging fontanelles.

Hydrocephalus is an unfavorable sign in case of congenital toxoplasmosis and it can lead to fetal death in utero as in the case of Kasonga study [15] where the fetus was in anasarca thus achieving a hydraps fetalis. At birth, there is a high risk of mental retardation, and other neurosensory and neurological disorders, including convulsions [16]. This is due to obstruction of the Sylvius aqueduct or periventricular abscesses. In the most severe cases, diffuse cortical involvement can be observed [17]. The ventricular dilations observed during toxoplasmosis are specifically bilateral and rapidly progressive. They are often associated with intracerebral densities and other cortical lesions, or even the midline lesions. In our study, the fetus had bilateral ventricular dilatation as well as calcifications in the forebrain. The autopsy was not performed in accordance with the respect of parental choice.

Inoculation with the mouse to establish the diagnosis is less and less practiced or abandoned to be replaced by a PCR on the amniotic fluid [18]. However, the animal model remains a tool of choice to understand the pathogenicity of the parasite. Inoculation with the animal revealed a pre-spotting location in the brain tissue [19,20].

The Ferguson [20] study also revealed the persistence of pathogenic activity of the parasite in the brain with the destruction of the parenchyma even after seroconversion and appearance of a maternal immune response with positive IgG.

According to Lima [21], Rodents are interesting models for studying parasite immunity. In a recent study in 2019, she shows how Toxoplasma gondii reprograms key metabolic pathways in the host cell to establish its replicative niche. The study of this molecular mechanism involving "Human Immune Evasion", are important to be able to fight more specifically the parasite.

Extra-cerebral signs of the fetopathy may be placentomegaly, ascites or, more rarely, pleural or pericardial effusions. Fetopathy may also associate with hepatomegaly with intrahepatic densities that can be visualized by imaging [15].

In the last trimester of pregnancy, after 28 weeks, the essential risk is the pigmentary chorioretinitis. This chorioretinitis persists for several years, requiring long-term surveillance, sometimes even into adulthood [22]. In these cases, the fundus exam can detect foci of macular pigmented cicatricial chorioretinitis [23].

Prevention and new recommendations

There is now heterogeneity of European policies and practices regarding prenatal screening for toxoplasmosis, which highlights questions and uncertainties about this screening [24].

In Senegal, this screening is not accessible for the main part of the population because of the expensive cost of monthly serologies. Access to performant laboratories offering the test, especially in rural areas is difficult meanwhile the exposure to the parasite is higher. The severity of the lesions caused by the parasite and the difficulty of the diagnosis justifies the establishment of strategies of screening and treatment adapted to our regions to fight against this neglected disease

The diagnosis of congenital toxoplasmosis during the prenatal period is based on amniocentesis. Emphasis should be placed on primary prevention because this strategy has proven effective in other geographical localities with declining seroprevalence [24]. This orientation is reinforced by the fact that the prophylactic and curative treatments reduce the severity of the lesions but their real effectiveness remains a controversial subject by many authors [25].

Conclusion

The diagnosis of congenital toxoplasmosis is poorly reported in the sub-Saharan zone despite significant exposure of pregnant women to toxoplasmosis: The discovery of bilateral ventricular dilatation associated with intracerebral calcifications is an important sign of orientation towards the diagnosis of congenital toxoplasmosis. This one should be confirmed by the search of the parasite by PCR in the amniotic fluid following the practice of an amniocentesis. This makes possible the starting of curative treatment in the event of the discovery of fetal contamination. In addition, strategies concerning primary and secondary prevention during prenatal consultations and effectiveness of chemoprophylaxis and curative treatment should be studied and adapted in our context to improve the prognosis of this neglected disease that is alarming for the fetus.

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