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Short communication

Neonatal fever: A puzzling case

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ABSTRACT

Toxoplasmosis is a potentially serious fetal infection associated with maternal seroconversion of toxoplasmosis during pregnancy. Follow-up and treatment vary between different countries. We present a case of congenital toxoplasmosis with unusual physiopathology and symptomatology. The mother was immunized before the beginning of pregnancy but immunosuppressive treatments for Crohn disease maintained during the pregnancy could explain toxoplasmosis reactivation in the mother and congenital toxoplasmosis. The baby presented reversible B lymphopenia and hypogammaglobulinemia.

1. Introduction

Toxoplasma gondii is a single-cell protozoan parasite. Usually, in otherwise healthy people the infection is asymptomatic; however, the situation can become complicated when the primary infection appears during pregnancy.

The worldwide incidence of congenital toxoplasmosis (CTP) varies between 0.6 and 3.4 cases per 1000 births depending on the country and the socioeconomic group [1]. Fetal manifestations can vary considerably: from no symptoms to fetal death. Sometimes, CTP causes fever, but this symptom is rarely isolated [2]. Systematic screening programs and prophylactic treatment differ from one country to another. In North America screening is only recommended for immunocompromised mothers (human immunodeficiency virus (HIV) carriers and others) or when an anomaly is detected by ultrasonography [3]. The literature reports several cases of HIV-infected women having toxoplasmosis reactivation late in pregnancy with severe consequences for their babies [4]. Toxoplasmosis reactivation can also occur during pregnancy in women with other types of immunodeficiency [5]. Here, we report the case of a newborn girl presenting CTP through a rare mode of contamination.

2. Observation

The first child of a Caucasian couple was born at 39 weeks of gestational age, weighing 3950 g (height: 49.5 cm, cranial perimeter: 35.5 cm) in a French maternity unit. The mother had not been traveling and had no notable past medical history apart from being on ongoing treatment for Crohn disease, with 125 mg/day azathioprine (throughout the pregnancy) and 5 mg/kg infliximab every 8 weeks (except during the third trimester).

Serological results obtained during pregnancy were negative for HIV, cytomegalovirus (CMV), syphilis, and hepatitis B virus (HBV), and revealed immunization for rubella and toxoplasmosis (two positive IgG results 1 month apart, high avidity). A vaginal swab was positive for *E coli*.

The delivery occurred in a level 2 maternity unit by emergency caesarian due to suspected chorioamnionitis (maternal fever (38.1°C), high C reactive protein (CRP) (29 mg/L), and abnormal fetal heart rate with tachycardia and decelerations). There was no rupture of the membranes. The amniotic fluid was meconial. The baby girl's initial Apgar score was 2–10–10. She needed positive pressure ventilation for 2 min due to bradycardia and apnea. The baby had fever (38.2°C) without any other symptom. There was no indication of splenomegaly or hepatomegaly.

In the first few hours the baby presented respiratory distress and was transferred to a neonatal unit in the same hospital. The

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leukocyte count was 17 G/L (lymphocytes, 1.02 G/L) and CRP at 12 h of life were high (29 mg/L). Blood and lumbar puncture cultures were performed. Antibiotics cefotaxime (200 mg/kg/day for 48 h then 100 mg/kg/day) and gentamicin (3 mg/kg at 48 h intervals) were started in the 1st h of life. After 48 h, the fever was still present and was associated with episodes of tachycardia, tachypnea, and peripheral hypoperfusion. During these episodes, the baby needed a high-flow nasal cannula (HFNC) due to desaturations and signs of respiratory distress. Between spikes of fever the clinical examination was normal. The chest x-ray was normal. Intravenous acyclovir (60 mg/kg/day) and amoxicillin (100 mg/kg/day) were added. The cerebrospinal fluid, stools, and respiratory secretions were screened for viruses.

During the first 10 days the baby was breastfed and grew slowly, but was oxygen-dependent via HFNC and fever was always present. At 6 days of life, while the lymphopenia persisted (leukocytes, 13 G/L; lymphocytes, 0.88 G/L) CRP dropped to 9 mg/L. It was decided to perform basic screening for immunodeficiency.

At day 9 all bacteriological (blood, cerebrospinal fluid, urine, gastric juice cultures) and virological test results (Rotavirus, Enterovirus, Herpes virus, Varicella zoster virus and Influenza virus) were negative. Antibiotics were stopped. At day 10 immunophenotyping revealed few B cells (1% equivalent 0 G/L) and hypogammaglobulinemia (IgG 5.46 g/L (normal, 7–13), IgA < 0.05 g/L (normal, 0.07–0.22), IgM < 0.05 g/L (normal, 0.04–0.26)).

The baby was transferred to our neonatal intensive care unit (level III) for the specialist's advice. Clinical symptoms were poor with febrile episodes (Fig. 1) including tachycardia, tachypnea, low O2 saturation, and prolonged capillary refill without specific symptoms. There was still no sign of splenomegaly, hepatomegaly, or jaundice; CRP varied between 6 and 10 mg/L, and blood pressure was normal.

However, another blood test confirmed immune-deficient B lymphopenia (CD 19; 0.3%, 0 G/L). Hypogammaglobinemia was also confirmed (IgG 4.8 g/L, IgA < 0.08 g/L, IgM < 0.21 g/L) and treated with two injections of polyvalent immunoglobulins (0.4 G/kg) at 48 h intervals.

The initial hypothesis was reversible toxicity arising from medication, but to confirm this a T-cell receptor excision circle (TREC) assay was performed.

Secondly, wide-ranging complementary infectivity tests were performed. The results of serological tests for hepatitis A and C, CMV, Epstein Barr virus (EBV), PCR for CMV in urine, norovirus, fungal blood and stool cultures, and antigenemia for Candida albicans were all negative. A TORCH serology screen (toxoplasmosis, rubella, CMV, syphilis, Herpes virus) and Parvovirus B19 were performed on a blood sample.

All serological results came back negative except for toxoplasmosis serology. The detection of G, M, and A anti-Toxoplasma immunoglobulins with ELISA and ISAGA methods in serum samples of the mother and the infant are shown in Tables 1 and 2. The comparative IgG and IgM Western blot was noninformative (LDbio Diagnostics, Lyon, France). Analysis of maternal serum revealed high IgG levels indicating reactivation of chronic toxoplasmosis (Table 1). The infant's extensive work-up for toxoplasmosis was negative; cranial ultrasonography and fundal ophthalmological examinations were all normal. According to French guidelines, treatment with sulfadoxine (100 mg) and

Table 1
The results of detection of M, G and A anti-Toxoplasma immunoglobulins by ELISA and ISAGA methods in the mother's serum samples during pregnancy (weeks' gestation, WG) and after birth (day 20)..

	10 WG	17 WG	Day 20
IgM[a]			
Considered positive if > 0.6 index	0.09	0.14	0.77
IgG[a]			
Considered positive if > 3 IU/mL	7.30	6.30	452.90
IgM[b]			
Considered positive if > 0.65 index	0.10	0.09	0.41
IgG[b]			
Considered positive if > 8 IU/mL	22.0	21.0	> 300.0
IgM[c]			
Considered positive if > 9 index	NA[e]	NA	12.0
IgG avidity[c]			
High if > 0.3 IU/mL	0.558	NA	NA
IgA[d]			
Considered positive if > 8 index	NA	NA	9.0

[a] ELISA – Architect Toxo® (Abbott Diagnostics, Wiesbaden, Germany).
[b] ELISA – VidasToxo® (bioMerieux, Marcy l'Étoile, France).
[c] Toxo-ISAGA® (bioMerieux).
[d] Vidas Toxo IgG avidity (bioMerieux).
[e] Not available.

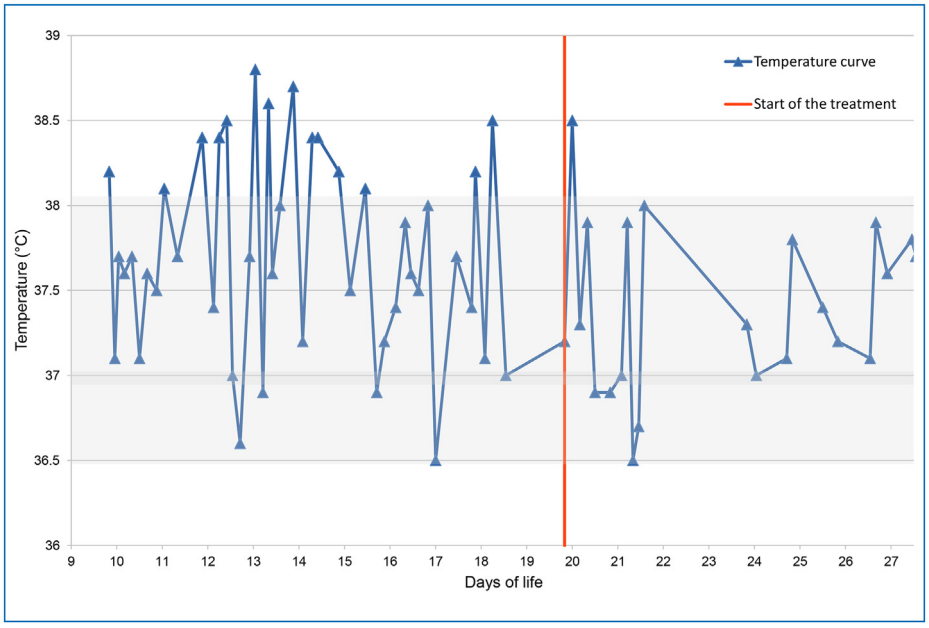

Fig. 1. Infant's rectal temperature curve before and after treatment.