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CASE REPORTS

CHALLENGES IN THE DIAGNOSIS OF MOTHER-TO-CHILD TOXOPLASMA GONDII INFECTION – CASE REPORT

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Abstract. We present the case of a newborn from a mother infected with Toxoplasma gondii during pregnancy. Born alive, the baby presented multiple organ failures, which in the end, despite of the treatment, led to his death. This case report is very instructive, and proves once again not only the necessity of assessing the possible teratogenic infections in pregnant women, but also the key role of prenatal investigations and of the risk factors.
Keywords: mother-to-child toxoplasmosis, pathologic pregnancy

Introduction

The study of the infectious pathology during pregnancy has become a very important issue due to the diagnostic difficulties and to the multiple treatment options.

The particularities of the infections must be well known in order to be able to make an early diagnosis, because most infections alter the physiological course of pregnancy, and they affect the quality of the conception product.

Some infectious diseases (viral, bacterial or parasitic) are acquired because of the physiological immunodepression during pregnancy, and they can have extremely severe clinical repercussions, varying from more or less vital malformations to the death of the fetus in utero.[1]

Some of the key-elements involved in mother-to-child transmitted infectious diseases are those classified as TORCH (Toxoplasma gondii, Other infections, Rubella, Cytomegalovirus, Herpes simplex virus).[2]

The infectious agents easily bypass the placenta, and depending on the moment of infection and on the involved infectious agent they can induce more or less specific fetal effects.

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Mother-to-child fetal toxoplasmosis plays a very important role in infectious etiology neonatal diseases.

Toxoplasmosis is a very frequent parasitic infection. In immunocompetent patients, the primo infection with T. gondii usually displays benign and self-limiting outlines, manifested through a mononucleosis-like syndrome (fever, micro polyadenopathy, hepatosplenomegaly, lymphomonocytosis). In immunocompromised patients, the primo infection with T. gondii may display extremely severe outlines. The HIV-related severe cellular immunodepression may induce the reactivation of a latent T. gondii infection, with severe disease outlines, such as cerebral toxoplasmosis, which rapidly leads to exitus if adequate treatment is not immediately administered.

Epidemiologic studies have shown that 22% of the pregnant women in London, 32% in New York (Stray Pederson, Lorentzen-Stry) and 87% in Paris (Desmonts) are immune to T. gondii, having specific antibodies, which protect the fetus from a congenital infection with T. gondii. Data indicates that 30% of the fertile women are negative for T. gondii, being prone to acquiring the primo infection during pregnancy and to passing it on to the fetus.[2,3]

Human transmission of T. gondii occurs in two ways: fecal-oral route (by ingesting oocysts from a cat) or transplacental, as is the case of congenital toxoplasmosis. [3,4]

In congenital toxoplasmosis, the outcome may vary according to the moment when the parasite passes through the placenta. In immunocompetent pregnant women, there is a risk of transmitting the disease to the fetus only during the primo infection with T. gondii, confirmed by the presence of anti T. gondii IgM.[5]

Congenital toxoplasmosis is characterized especially by neuromotor deficiencies and ocular toxoplasmosis (chorioretinitis and blindness gradually appear over the course of the child's development). Congenital toxoplasmosis is described by the following triad: intracerebral calcifications, chorioretinitis and hydrocephaly, although not all children with congenital toxoplasmosis are symptomatic at birth, and very few of these present the complete classic triad.[2,6]

Clinical signs in congenital toxoplasmosis include: congenital encephalomyelitis with hydrocephaly through stenosis of the Sylvius aqueduct, ocular damage and visceral forms in case of late fetal contamination.[2]

Encephalomyelitis usually appears in early infections and is clinical manifested by convulsions with other signs of neurologic impairment, being followed by cerebral calcifications and ocular damage.[7]

Ocular damage is generally characterized by chorioretinitis, being either unilateral or bilateral, pigmentary, maculary, scarring or evolving, and it can sometimes be the only clinical sign. The ocular effects may also include micro-ophthalmic syndrome and strabismus.[6]

The visceral outlines appear in late contaminations and they manifest through feto-placental anasarca, liver damage with jaundice in 50% of the cases, splenomegaly, lymphadenopathy, various cutaneous eruptions, thrombocytopenic purpura, pneumopathy, metaphyseal bone damage, anemia and fever.

Besides these signs, congenital toxoplasmosis may induce abortion, premature birth or death of the fetus in utero or at birth.

Laboratory diagnosis is based on ELISA tests, assessing the presence of IgM and IgG specific anti-Toxoplasma gondii antibodies.[9]

The diagnosis of the disease in pregnant women is mainly serologic, being based on the early development of IgM antibodies (in the first few days after infection), which reach the maximum titer after 2-3 weeks then disappear after 4 months from the infection.

When confirming toxoplasmosis in a pregnant woman it is extremely important that she understands the risks the fetus is exposed to, and that she is entitled to therapeutic abortion.

If the pregnant woman decides to continue the pregnancy, an emergency treatment is administered, mainly with spiramycin 3g/day (50mg/kg/day) per os, twice daily, until birth.[2]

We have to mention that this is the standard treatment protocol in our country, other countries and international guidelines describing other types of treatment, such as an association of pyrimethamine with sulfadiazine and folinic acid (both in the USA and in Europe).[2]

Case report

V.F., a 27-year-old female patient, from urban area, domestic, G III, P I, pregnant in 31 weeks, live fetus, cranial presentation, is admitted for premature rupture of membranes and painful uterine contractions.

Personal physiological history is noncontributory.

The patient's personal pathological history includes the following: Toxoplasma infection during current pregnancy, treated according to the guidelines indicated by the infectious diseases specialist physician (rovamycin 3g/day up to admittance, respectively up to 31 weeks of pregnancy)

The positive diagnosis of pregnancy toxoplasmosis was established according to the results of repeated serologic tests at 28-29 weeks (positive IgM). T gondii serology had been negative in the beginning of the pregnancy (negative IgM and IgG) and the ultrasound exams performed during pregnancy follow-up did not reveal malformations suggestive of toxoplasmosis, except for small areas of periventricular cerebral calcifications.

The physical examination was within normal parameters. The genital clinical examination revealed the following: short cervix allowing the index, mobile skull, ruptured membranes, fetal heart beat of 178 bpm.

Considering prematurity, the lack of cervical changes and the fetal cardiac activity, we decided to perform a transverse segmental Cesarean-section. We extracted a live, male fetus: 1400g/38 cm, cranial perimeter of 28 cm, thoracic perimeter of 26 cm, Apgar score of 5, 6 at 5 minutes. The newborn was admitted to the neonatal intensive care unit, presenting acute respiratory distress syndrome.

The newborn's clinical examination revealed: pale skin, diminished tone, dyspnea. We decided upon ventilatory prosthesis.

The ultrasound examination was suggestive of hydrocephaly and cerebral calcifications, and it generated the suspicion of congenital infection. Given the pathologic medical history of the mother, we performed IgM determination for the TORCH profile, together with the usual laboratory tests. The test results were as follows: Hb 10.5g%, Ht 30.8%,

leukocytes 13800/mm^3, thrombocytes 425000/mm^3, AST 140 U/L, ALT 55 U/L, TBil 9.08 mg%, DBil 4 mg%, positive Toxoplasma IgM. These lab results assent with a positive diagnosis of toxoplasmosis.

We started antibiotic and supportive toxoplasmosis treatment (spiramycin 100mg/kg/day, i.v. glucose 10% - 4ml/hour. Ranitidine 1ml every 12 hours, under monitoring of oxygen saturation).

The newborn received endotracheal synthetic surfactant (orotracheal intubation) 5ml/kgbw dissolved in normal saline.

The patient required administration of parenteral fluids: 60-70ml/kgbw/day during the first day, gradually increased to 100ml/kgbw/day.

The hydroelectrolitic imbalance was corrected through administering NaHCO3 (8.4% or 84‰) 1-3ml or mEq/kgbw/day mandatorily administered in 5% glucose (1ml NaHCO3 contains 1mEq Na).

The evolution was unfavorable during the next few days, the newborn presenting repeated cyanosis episodes, generalization of jaundice, abdominal bloating followed by hematemesis.

We requested a CT exam. Cerebral-ventricular imaging showed a deep recent intraparenchymal hematic collection of 2.7/1.6 cm, located in the frontal-temporal-parietal left region, diffused into the ventricular system, in the anterior horn of the left lateral ventricle and the posterior horns of the lateral ventricles. Internal hydrocephaly, intra- supra- and infra- tentorial with periventricular activity. Simplified cerebral gyrations in both hemispheres.

The newborn's state deteriorated progressively; in day 12, the newborn presented apnea episodes with cyanosis, followed by non-resuscitable cardiac arrest.

The causes of deaths were: intracerebral hemorrhaging, hydrocephaly, prematurity, liver failure and cardiac arrest.

The results of the anatomopathologic examination concurred with the main cause of death, confirming massive cerebral hemorrhage and renal, hepatic and pulmonary impairment.

The necropsy protocol revealed the following: massive cutaneous and sclera jaundice, cachexia. Regarding the skull: anterior fontanelle 3/2.5 cm, with partial ossification of the cranial bones, meningeal edema and punctiform hemorrhaging, cerebral edema, simplified cerebral gyrations, enlarged brain of soft consistency, hydrocephaly, dilated lateral ventricles containing a fibrinohematic material and clots. The surrounding cerebral tissue was yellow and it contained necrotic substances, being soft, with nervous matter liquefaction. The old lesions had resolved into a rarefied, alveolar-like nervous matter. There was deep hemorrhaging in the thalamus and the basal nuclei and the surrounding nervous matter was rusty in color through hemosiderin impregnation. The vascular structures were visible due to blood stasis.

The thoracic cavity presented lungs with marble-like aspect, with atelectatic, hemorrhagic areas; the heart and the great blood vessels presented normal aspect.

The abdominal cavity inspection revealed icteric liver with increased volume, a red-purple spleen, dilation of the renal pelvis of the right kidney with moderate renal calyx dilation, and normal looking left kidney. The exam also revealed hypertrophy of the suprarenal glands and gastric bleeding.

The anatomopathologic diagnosis confirmed the clinical diagnosis: meningeal bleeding, hydrocephaly, diffuse cerebral bleeding in the lateral ventricles and the thalamus, post-hemorrhagic cerebral edema with liquefying of the nervous matter. Secondary diagnostics: right hydronephrosis, gastric bleeding, cachexia.

We present all these elements in order to emphasize the pathologic modifications that T.gondii induces in different organs, especially in the brain, but also affecting other organs.

In this case we performed a differential diagnosis with intracerebral bleeding and premature birth related multi-organ failure.

The differential diagnosis may also consider other infectious diseases which produce hydrocephaly and cerebral calcifications, such as rubella and cytomegalovirus infections, but in this case the diagnosis was confirmed by the laboratory results and by the fact that the mother had also been infected with T. gondii.

Also, the differential diagnosis is performed for other causes of neonatal respiratory distress, such as airways obstructions by malformations, pneumonia and aspiration syndrome, respiratory failure caused by a cardiac disease such as Fallot tetralogy, bronchopulmonary dysplasia caused by an insufficient development of pulmonary bronchioles, other central nervous system diseases, pulmonary bleeding. All these diagnoses can be excluded by thorough clinical examination and by laboratory tests, which in this case confirmed the congenital toxoplasmosis diagnosis.

The particularity of this case consists in the fulminant evolution of the toxoplasmosis in the fetus despite the adequate treatment administered to the mother in the prenatal period in order to prevent both the fetal and the newborn infection. Another important characteristic is the manner in which the infection was acquired during pregnancy, the initial serology being negative. We also have to mention that the patient had not been monitored from the beginning of the pregnancy up to the 29th week.

Conclusions

The association of toxoplasmosis with pregnancy greatly increases the risk of premature birth, which most of the times is secondary to toxoplasmosis

Congenital toxoplasmosis may sometimes display extremely severe outlines

The neurologic signs of congenital toxoplasmosis are the most severe manifestations. [10]

The screening of pregnant women for infectious diseases is extremely important. Positive pregnant women must be counseled and the serology must be monitored in dynamics. Negative pregnant women upon initial examination will be re-tested every trimester for an early diagnosis of a primo infection or of a re-infection. In cases of conflicting results, with high titers of IgG antibodies, the importance of avidity test must be emphasized. [11,12]

The role of preconception advice is crucial in preventing neonatal affections.

Considering the complexity of the clinical outline, the extremely reserved prognosis and the difficult etiologic diagnosis, the interdisciplinary consult between the obstetrician, the neonatologist and the infectionist is of the outmost importance.

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