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HYDROPS FETALIS SECONDARY TO TOXOPLASMA GONDII AND TREPONEMA PALLIDUM COINFECTION: CASE REPORT AND BRIEF LITERATURE REVIEW

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Abstract

Background

Hydrops fetalis is a pathological condition in which fluid accumulates in the fetus in an extracellular environment, leading to subcutaneous edema and possible accumulation in the fetal body and abdominal cavity. The most common causes in this region are infectious, making systematic monitoring during pregnancy essential. However, it is difficult to apply this guideline in urban areas, and even more so in rural areas with few resources for investigation, as in this patient's case, monitoring was ineffective.

The aim was to carry out infection studies in maternal blood samples taken after giving birth to a newborn in hydrops.

Case presentation

A 36-year-old rural woman in her 6th pregnancy presented with uterine contractions in what was thought to be a full-term pregnancy. The progress of this pregnancy had not been monitored throughout the antenatal period for unknown reasons despite a clinical presentation characterized by breathlessness and generalized edema. The obstetric gynecology clinical examination revealed a mattress-like appearance suggestive of placenta previa, and a cesarean section was indicated with the extraction of a newborn with hydrops fetalis who died despite resuscitation efforts. An infectious disease investigation after delivery revealed the presence of both *Treponema pallidum* and *Toxoplasma gondii* in the maternal blood sample.

Conclusion

This state of hydrops fetalis was secondary to this co-infection, which is very difficult to manage in such conditions, facilitated by the lack of systematic biological monitoring for pathogens that could harm both the fetus and the mother.

Recommendation

Facilitate prenatal visits to women, especially in rural areas where access to services is limited, through home visits from health workers and community relays.

During the monthly antenatal visit, pregnant women should be subjected to compulsory infectious screening to provide suitable conditions for the fetus.

Keywords: *Hydrops Fetalis, Syphilis, Toxoplasmosis, Co-Infection, Delivery.*
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Introduction

Hydrops fetalis (HF) is a condition in which abnormal extracellular fluid accumulates in at least two compartments within the fetus: serous cavities and tissues. Clinically, this accumulation appears as subcutaneous edema. However, it can spread throughout the fetal body, including the heart (pericardial effusion), lungs (pleural effusion), and even the abdominal cavity (ascites) (1,2).

Several factors can cause fetus hydrops, most of which remain unknown, apart from immunological and genetic (phenotypic) causes. Infectious causes are the most common in this environment and account for 4-15% of fetoplacental hydrops (FPH) (1,3).

In conditions where investigative resources are limited, rapid diagnostic tests are most commonly used to detect infectious agents in clinical settings, where infectious agents are often sought in the etiology of HF, including *Toxoplasma gondii*, *Treponema pallidum*, *cytomegalovirus*, and *parvovirus B19*, which have been implicated in fetal and placental hydrops (1,4).

Despite the importance of surveillance through screening of pregnant women for pathogens such as *Toxoplasma gondii* and *Treponema pallidum* during their antenatal check-ups, a policy of systematization of these check-ups has not yet been put into practice in our country. *Toxoplasma gondii* and *Treponema pallidum* are both responsible for intrauterine fetal and adnexal abnormalities, mainly if they co-occur in a pregnant woman (co-infection). The pathogens involved in HF still need to be better understood, and there are few studies conducted in the region.

The aim of this study was therefore to perform infection studies in mother sample blood after the birth of a neonate in a state of hydrops, which is likely to be the cause.

A case of neonatal HF in which toxoplasmosis-syphilis co-infection was diagnosed following a biological investigation during postoperative cesarean delivery is presented.

Case presentation

Maternal and parental informed consent is obtained and signed to ensure patient confidentiality and safety. The newborn was the result of a cesarean delivery in a state of fetoplacental hydrops (FPH) for a pregnancy estimated to be at term. The delivery was performed at the Muhungu-Etat health center, in the Ibanda urban health zone in the city of Bukavu, South Kivu, Democratic Republic of the Congo.

On 6 April 2022, a 36-year-old parturient from a rural area (Ngweshe, Walungu territory in South Kivu) was consulted for lumbopelvic pain in the form of uterine contractions in a pregnancy of 40 weeks of amenorrhoea and two days from the date of the last menstrual period. She was in her 6thpregnancy, including five live births. Still, the progress of this pregnancy had not been monitored throughout the prenatal period by the health facilities, including an antenatal ultrasound. This was despite a clinical presentation characterized by feelings of suffocation and generalized edema. The parturient was of blood group O and rhesus positive, with no medical or surgical history. It should also be noted that the spouse's group was unknown during the examination.

The physical examination revealed a general state marked by an arched posture. Vital signs were within normal limits, in particular blood pressure of 122/60mmhg, heart rate of 102 beats per minute, and respiratory rate of 28 cycles per minute, as well as oxygen saturation varying between 92-98%. Elsewhere, we noted edema of the lower limbs from the middle third of the legs to the feet, painless but taking up the bucket.

The gynecological and obstetrical examination revealed a uterine height of 37cm, a fetal heartbeat of 140-154 per minute, a fetus in cephalic presentation laboriously objectified, and a position that did not identify a wooden and slightly tender abdomen. Contractile regimes of sound intensity and regular rhythm; vaginal touch, cervix 80% effaced and dilated to 8cm on arrival.

Figure 1: Hydrops fetalis newborn

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An untimely rupture was performed and revealed a mattress-like appearance, suggesting the diagnosis of a non-hemorrhagic overlying placenta previa. A cesarean section was immediately indicated, and the extraction of a newborn (figure 1) of female morphotype, weighing 3200g with an APGAR score of 6-4-4, despite resuscitation efforts according to the ABCD rule. Biological investigation on the newborns showed the blood group O and rhesus positive, hemoglobin 16g/dl and hematocrit at 43%, leukocytes at 23000 cells/mm3 in a state of hydrops, and the placenta oedematous. However, delivery by cesarean section (approach) and the placental insertion site (anterior) did not allow a better assessment of the placental state. However, it should be noted that the newborn did not adapt to life outside the womb in the hours following birth, despite the various therapeutic approaches adopted as part of his management.

The diagnosis of hydrops fetalis (HF) was made, and maternal biological investigations to find the etiology likely to be involved in this state were launched.

Most of the paraclinical examinations did not attract our attention. The particularity came from the biological analyses carried out using the immunochromatography technique, a rapid diagnostic test for toxoplasmosis and syphilis. The methods and diagnostic approach were performed following the manufacturers' recommendations. For *Toxoplasma gondii*, the rapid diagnostic test (Sure Biotech, New York, USA) examined immunoglobulin (Ig) G (IgG) separately, with a sensitivity of 90% (CI 95%: 73.4%-97.9%) and specificity of 99.1% (CI 95%: 96.8%-99.9%) versus immunoglobulin M (IgM) with a sensitivity > 99.9% (CI 95%: 88.7%-100%) and specificity of 99.5% (CI 95%: 97.5%-100%) but combined on the same cassette; the test came back positive for IgM.

The syphilis test also came back positive with a sensitivity of 95% and a specificity of 94.9% after analysis according to the manufacturer's protocol (bioline: SD syphilis 3.0; standard diagnostic, China) for the antigens: TpN15, TpN17, TpN47 for the qualitative detection of IgG, IgM and IgA anti-treponemal antibodies.

Discussion

Toxoplasmosis and syphilis are pathologies that are most often asymptomatic but are known to be capable of causing congenital malformations in the fetus during pregnancy. To minimize the transmission of these pathogens from mother to fetus, it is essential to conduct regular screening during pregnancy, even if the rate of positive test results is low compared to the rate of seroconversion. This screening is critical for preventing congenital infections (1,5,6).

FPH consists of an accumulation of fluid in an extracellular space and may be secondary to an immunological or non-immunological etiology. From an immunological point of view, with the incorporation of anti-D immunoglobulins (Ig) in the management of rhesus alloimmunization, non-immunological causes remain the most frequent(2).

Despite the various etiologies, the main hemodynamic mechanisms involved in the development of FPH associated with the immaturity of the fetus's organs concern, on the one hand, the heart, due to its inability to pump blood (anemia caused by haemoconcentration), will increase the pressure on the walls and thus cause fluid to pass into the tissues (pericardial effusion: congestive heart failure) where edema appears as the kidneys eliminate less and less salt and water. This hydro-sodium retention causes the fetus to gain weight sufficiently quickly. On the other hand, when the water potential of the vacuole is higher (less negative) than that of the external environment, water tends to leave the cell (low osmotic pressure) (7,8).

This observation is of particular interest because there is the notion of a co-infection, and this would be more common in women with their first pregnancy, bearing in mind that most of those who have already had several pregnancies develop secondary acquired immunity during a primary infection. We found *Toxoplasma gondii*and *Treponema pallidum* indirectly present in the blood samples taken from the pregnant woman; a rather specific notion of co-infection with immature fetal organs would further accentuate the occurrence of hydrops(8).

The way these two pathogens affect the immune systems of immunocompromised individuals, specifically pregnant women in this case, is particularly concerning. This holds regardless of whether the infection is singular or a co-infection. Each pathogen, on its own, has a detrimental impact on fetal development (1,9).

In the course of these two infections, transplacental transmission occurs; apart from the death of the embryo-fetus, we can cite intracerebral calcifications (toxoplasmosis) leading to hydrocephalus (figure 1) but also at the hepatic level through the formation of biliary lithiasis (icterus) or obstruction of the bloodways at the base of a portal hypertension syndrome leading to fetal ascites (syphilis) (8–10).

The transplacental passage of germs at the level of the vascular endothelium may also be obstructed due to lymphatic dysplasia once the pathogen has reached the lymphatic tract in the study by Yaméogo et al., aortic insufficiency at the cardiac level led to congestive heart failure (edema) (2,11).

This co-infection, combined with the vulnerability of the fetus (immature organs), may have contributed not only to the onset and establishment of the hydrops state but also to its maintenance and persistence throughout the fetus' intrauterine life.

The serodiagnostics used to assess bacterial and parasitic infections were those of immunochromatography, highlighting the specific humoral immune response. This indirect technique using antibodies is effective, but it may not definitively determine the presence of the pathogen and the timing of the infection, which is crucial for assessing the risk (12).

The interpretation for toxoplasmosis, characterized by the presence of anti-toxoplasmosis Ig M, would suggest a recent infection during the last trimester of pregnancy and that the parturient would not be immune, hence the possibility of fetal transmission. For syphilis, on the contrary, the presence of three antigens in the same test zone (a test marked by three biomarkers) makes it challenging to create a better interpretation of the dating of the infection.
Hence, there is a need for rigorous infection surveillance during prenatal visits to pregnant women in the region.

Conclusion

The pathogenesis of HF involves a variety of immunological and non-immunological causes.
This very difficult condition has been exacerbated by the lack of systematic biological surveillance for pathogens that could harm the fetus and the mother.
This case of HF in newborn due to concomitant maternal infection with *Toxoplasma gondii* and *Treponema pallidum* highlights the importance and benefits of antenatal care in health facilities, where an appropriate range of investigations, including infectious tests, can allow aetiological diagnosis and early and rational intrauterine management of both the newborn and the mother.

Recommendation

Facilitate antenatal visits for pregnant women in general, especially in rural areas where access to care is complex, through systematic searches in villages for women who have been lost to follow-up or who have not been identified but whose pregnancies are eligible for antenatal care to bring them back into the health system or schedule home visits by community contacts.
Systematic screening during antenatal visits should be strongly encouraged to improve the prognosis of pregnancies and reduce the incidence of infections, such as toxoplasmosis and syphilis, to protect the fetus.

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List of abbreviations

hydrops fetalis (HF), fetoplacental hydrops (FPH), immunoglobulin (Ig).

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Conflict of interest

We have no conflicts of interest related to this study.

Authors' contributions

MML, MMG, and KKA designed and supervised the study.
MML, ABC, and NMR received agreements from the patients to participate in the study, collected patient information for data, and acted a cesarean delivery.
MML and ABJ analyzed blood samples and interpretation of the data.
MML, CMS, GMS, and BAC drafted a case presentation.
MML drafted the manuscript.
NKG, MMG, and CMS did a critical analysis of the manuscript
MML, ABC, MMG, CMS, NMR, GMS, BAC, KNG, ABJ, and KKA revised the manuscript.
All authors have read and approved the final manuscript.

Ethical Aspects and confidentiality

Informed consent was obtained from the patient after the guarantee of confidentiality and security of the data was explained and clarified, by the principle of the local ethics and deontology committee.

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