Reversible non-immune hydrops in twin pregnancy due to CMV infection which was treated by IV Gancyclovir "Case report"

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### <u>Abstract</u>

A 28 years old primigravida 19 weeks pregnant carrying Diamniotic dichorionic twin pregnancy was suffering from jaundice due to CMV infection and fetal ascites which was successfully managed by IV Ganciclovir. Fetal infection by CMV leading to NIHF could be reversed completely by early detection and proper management using antiviral treatment. Despite the rarity of the cases and the difficulty of confirming the diagnosis, CMV should be considered in the differential diagnosis of NIHF, putting in consideration that early start of treatment will lead to better prognosis.

### **Introduction**

Non-immune fetal hydrops is diagnosed when there is fluid accumulation in more than two extravascular spaces, in addition to soft tissue edema such as the skin or scalp, or fluid in body cavities such as ascites pleural effusion, pericardial effusion, or hydrocele (1, 2).

Many causes may result in such condition as (3): Intrauterine infections represent 7% of cases of nonimmune hydrops, with a prevalence of congenital cytomegalovirus (CMV) infection of 0.64% (4).

IT is important to remember that NIHF represent almost 85% of all cases of hydrops fetalis. (3) The current case study is to present a case of non-immune hydrops due to CMV which was reversed by antiviral treatment.

# Case Report

A 28 years old primigravida 19 weeks pregnant carrying Diamniotic dichorionic twin pregnancy was admitted to the hospital suffering from jaundice. She did investigations in the form of liver enzymes which were elevated, (magnetic resonance cholangio-pancreatography) which was normal. The virology studies revealed high levels of

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Ashraf Sobhi Abolouz Obstetrics and Gynbecology department, October 6th University IgG & IgM for cytomegalovirus (CMV), but negative PCR results.

Obstetric US didn't reveal fetal anomalies, so she was discharged and instructed to followup in the outpatient clinic.

During follow-up four days later there was mild ascites in the first twin and severe ascites in the second twin as shown by ultrasound (figure 1). She started to have intravenous Ganciclovir twice daily for two weeks. Two weeks later there was marked improvement in the condition of both fetuses so oral acyclovir was continued for further 3 weeks with close follow-up by obstetric ultrasound, which showed disappearance of ascites in both fetuses (figure 2). Pregnancy carried on uneventful and delivery of two normal twins by cesarean section at 37 Weeks. Seven months follow up of both babies showed no CNS affection or sensory or hearing affection.

# **Discussion**

Congenital CMV is the most frequent congenital infection complicating almost up to 2% of all pregnancies throughout the world. It is one of the leading causes of hearing loss and neurological deficits during infancy and childhood (6). Congenital CMV infection may also result intrauterine fetal death, cytomegalic inclusion disease, and pneumonia (6). Putting in mind that the congenital infection will mostly pass unnoticed as it is asymptomatic in 90% of the cases. (4) Also it is important to remember that the trans-fetal infection represent from 0.1% to 1% in cases of recurrent maternal infection with CMV. (7)

Sonographical signs intrauterine of CMV infection were reported as cerebral calcifications, cerebellar hemorrhage, hyperechogenic bowel. fetal hydrops, effusion. pericardial cardiomegaly, placentomegaly, and oligohydramnios (8).

To the best of our knowledge not many cases

with congenital CMV infection had prolonged survival whether due to cerebral affection or due to multiple congenital anomalies. (7) In the current case not only did both fetuses survive, but also features of hydrops present in the ultrasound were reverted by Ganciclovir treatment suggesting that treatment may reverse the problem especially in early cases (the difference between the ultrasound done in the hospital and the follow-up ultrasound was about 4 days).

The diagnosis of CMV infection as a cause of fetal hydrops is challenging since the laboratory tests are not highly sensitive, also the rarity of the cases and the evidence of neonatal infection, putting in consideration the importance of early administration of treatment, so high index of suspicion is needed (7). Neither the less the infection is mostly recurrent infection as the CMV IgG titer was high which may explain also the mild form of fetal symptoms and the good response to the antiviral treatment. That is why the maternal immunity response during primary or recurrent viral infestation should be considered as one of the important items to explain the severity of the fetal infection.

F. D'Antonio et al after revising eight studies (618 women) concluded that prenatal valacyclovir administration in pregnancies with maternal CMV infection can reduce the risk of congenital CMV infection (9). Valacyclovir is an acceptable, tolerable and effective line of treatment in management of intrauterine vertical transmission of CMV (10).

### **Conclusion**

CMV infection should be considered as one of the causes of fetal hydrops with a high index of suspicion, although the laboratory tests are not highly sensitive, YET early initiation of IV antiviral treatment would have a good response with good prognosis for the outcoming babies.

#### **References**

- 1. Holzgreve W, Holzgreve B, Curry CJR. Non-immune hydrops fetalis-diagnosis and management. Semin Perinatol. 1985;9:52–67.
- Gough JD, Keeling JW, Castle B, Illiff PJ. The obstetric management of nonimmune Hydrops. Br J Obstet Gynaecol. 1986;93:226–234.
- Barron SD, Pass RF. Infectious causes of hydrops fetalis. Semin Perinatol. 1995;19 (6):493–501.
- 4. Desilets V, Audibert F, Society of O, Gynaecologists of C. Investigation and management of non-immune fetal hydrops. J Obstet Gynaecol Can. 2013;35 (10):923–38.f
- Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol. 2007;17 (4):253–76.
- Ko HM, Kim KS, Park JW, Lee YJ, Lee MY, Lee MC, et al. Congenital cytomegalovirus infection: three autopsy case reports. J Korean Med Sci. 2000;15 (3):337–42.

- S Y Semerci, Aslan Babayigit, Burcu Cebeci, Gokhan Buyukkale, and Merih Cetinkaya; CMV as a Seldom Cause of Non-Immune Hydrops Fetalis: Case Report and Review of the Literature. Iran Red Crescent Med J. 2017 August; 19 (8):e55570.
- Ross SA, Ahmed A, Palmer AL, Michaels MG, Sanchez PJ, Bernstein DI, et al. Detection of congenital cytomegalovirus infection by realtime polymerase chain reaction analysis of saliva or urine specimens. J Infect Dis. 2014; 210 (9):1415–8.
- F. D'Antonio, D. Marinceu, S. Prasad and A. Khalil, Effectiveness and safety of prenatal valacyclovir for congenital cytomegalovirus infection: systematic review and meta-analysis / 09 December 2022 doi: 10.1002/uog.26136
- V. FAURE-BARDON, J. FOURGEAUD, J. STIRNEMANN, M. LERUEZ-VILLE and Y. VILLE, Secondary prevention of congenital cytomegalovirus infection with valacyclovir following maternal primary infection: Ultrasound Obstet Gynecol 2021; 58: 576–581