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CYTOMEGALOVIRUS INFECTION AT A NEWBORN – CASE REPORT

O. FALUP-PECURARIU[1,2] L. MUNTEAN[2]
R.I. LIXANDRU[2] C. FALUP-PECURARIU[1,3]

Abstract: *we present a case report of a newborn infant admitted for watery stools and failure to thrive that actually had active Cytomegalovirus infection (CMV infection). CMV is ubiquitous in the world and diagnosing this rare disease during the newborn period allows us as clinicians to administer treatment and also to screen for hearing deficits and brain anomalies. We also make a review of the recent literature regarding this issue.*

Key words: *newborn, cytomegalovirus infection, diagnostic challenges.*

1. Introduction

Cytomegalovirus (CMV) infection is a challenging diagnose at newborn.

CMV is the largest and the most complex member of the Herpesviridae family. Its DNA is composed of a 240 kilobases [14].

One of the particular findings regarding the virus itself is the lack of the enzyme tymidine kinase which makes it resistant to the antivirals that use this particular enzyme [20].

The incidence of the disease is between 0.2-2.5% of all live birth and it is more encountered in the underdeveloped regions or in lower economic class were crowding is prevalent [6].

We present a case report of a newborn girl diagnosed with congenital CMV infection.

2. Case report

We present a case report of a female infant admitted at the age of 5 weeks that had active CMV infection. She was admitted at the Childrens' Clinical Hospital Braşov, România between 11.06.2014-30.06.2014 at the Newborn Department Unit.

She was admitted because of watery stools, 7/day, poor general state, vomiting and loss of appetite.

She is the second child of the family, her older sister being 2 years old and going in a day care center.

Her mother was 21 years old and healthy, her father 22 years old, also healthy. The parents denied any cronical illnesses in the family. Both parents are nonsmokers.

[1] *Transilvania* University, Faculty of Medicine, Brasov
[2] Children's Clinical Hospital, Brasov
[3] County Clinical Emergency Hospital Brasov

She was born after a 39 weeks gestation, the whole pregnancy being followed up, with a birth weight of 3500gr., APGAR score 9 at 1 and 5 minuits, with normal development after birth. She was breast fed for 2 weeks and then she received cow milk. They are living in one bedroom.

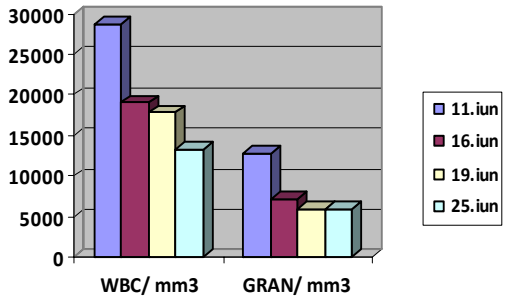
The diseases started 2 weeks before admittance, insidiously, with vomiting and 2-3 watery stools/day but later on vomiting started to be after each meal along with the watery stools. The general practitioner recommened admittance in the hospital.

At admittance her general state was poor she was 3700 gr, her rectal temperature was 38.5 °C, she was pale, had a mild hepatosplenomegaly and had 4 watery stools.

At this moment all the biochemical analysis were done and show leucocytosis 28.810 with a neutrophil predominance 12710, and 901000 thrombocytes, her ureea was 55 mg/dl (NV: 13-43mg/dl), a CRP of 4.43 mg/dl (NV:0-1 mg/dl), AST/ALT were 81/75, GGT of 121U/l, a normal Na/K normal alcaline fosfate level normal creatinine level, urine analysis positive for nitrits, but urine culture was negative.

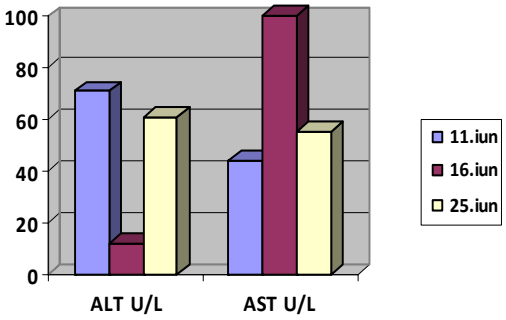
The ultrasound revealed only mild hepatomegaly and treatment was started with i.v. glucose and aminovenous solution along with 2 boluses and because of the watery stools and the high index of suspicion of bacterial diarrhea ceftazidim was started and probiotics were given.

The second hemogram showed a lowering of the leucocytes to a value of 19060 with a predominance of neutrophils (Graph 1), the value of hemoglobin was 10.4g/dl and hematocrit was 31.4% and thrombocytes were 646000. The general state remained poor the appetite was still poor, fever disapperead completely and stools started to normalise. Physical exam showed a mild hepatomegaly.

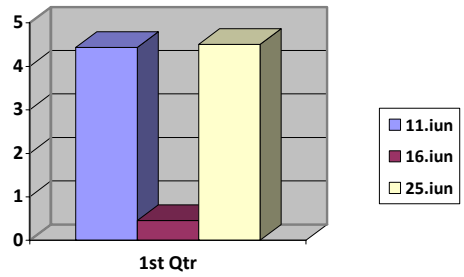


Graph 1. *Evolution of leucocytes and granulocytes during the admitted period*

On her 7th day of admittance the lab exams showed still leucocytosis with a predominance of neutrophils and thrombocytes 459000. The AST/ALT 116/100 U/l, bilirubin levels in normal range also the GGT remained high 125 U/l, urea and creatinine levels in normal range the same normal values for Na and K, Calcium and Chlor (Graph 2).



Graph 2. *Transaminase levels*



Graph 3. *CRP levels*

We have questioned at this moment the mother regarding her pregenancy history towards CMV infection and we performed the IgG and IgM for CMV along with those for toxoplasmosis and EBV.

We were taken into account the low socioeconomic status of the family, the older child going at day care center and also the perisitently high values of the AST/ALT.

Three days later results came and IgM was positive for CMV for the newborn baby. We performed viremia for CMV that showed over 700 copies normal values being under 100 copies.

CT brain scan was normal as showed in the picture, normal ophtalmological exam and eye fundus, again normal brain ultrasound and mild hepatomegaly (Fig 1).

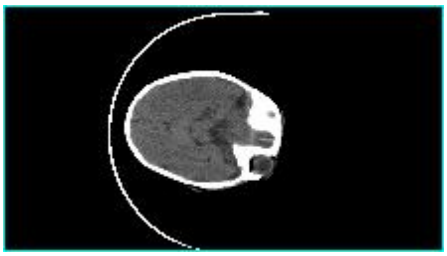


Fig 1. *Brain CT scan*

All the repeated values of AST/ALT remained constantly above 80 U/l value that is considered a sign of infection.

We started therapy with isoprinosine that was not well tolerated and reffered the child to the infectious disease unit were it started gancyclovir therapy.

At 12 weeks at her follow up visit her general state was good, she had a constant weight gain and her AST/ALT values were only 66/64 U/l, her ultrasound showed persistent mild hepatomegaly with no ophtalmological changes.

3. Discussion

We present a case report of a newborn infant that presented with watery stools, vomiting and loss of appetite but actually had active CMV infection.

However more than 90% of the newborns with congenital CMV are asymptomatic at birth [22], as was the case also with our infant that was admitted for acute diarrhea.

In the USA 30000 to 40000 newborns are yearly diagnosed with congenital CMV and from those around 9000 will have permanant sequelae [4]. The death rate of these patients is around 30% [16].

Epidemiological studies suggest that the timig of acquisition of the virus relative to the establishement of pregnancy is an important factor for the risk of transmission of the infection [18].

It has been recently described the fact that congenitally infected infants born from women with preconception immunity had a substantial risk for long term neurological sequelae [19].

However the highest risk pose mothers with primary infection. Humans are the only natural reservoir of the virus and both symptomatic and asymptomatic children shed the virus in their saliva and urine for many years we may easily understand why mothers usually are infected from their own children. This is also why simple teqniques like hand washing may reduce dramatically the risk of transmission [1].

Our infant had also a sister that was attending day care center and she may have been a reservoir of the disease. We have also to underline the fact that the infant was coming from a low income family which increases the risk of infection.

There are several considerations about the mechanism by which CMV crosses the placenta but recent data showed that maternal antibodies may actually facilitate transmission of the CMV across the placenta. CMV uses IgG antibodies to cross the placenta via transcytosis as IgG virion complexes utilising the Fc receptor that expresses on the surface of syncitiothrophoblasts [2].

These low avidity complex antibodies are the ones that allow the virus to escape the macrophages and infect the fetus [12]. So this is why timing of pregnancy and the antibody avidity towards CMV are crucial factors for protection. The low avidity antibodies persist for about 20 weeks after infection and this we may regard as a window for infection [9].

Recently it was made a proposal regarding CMV congenital infection and its diagnoses. It is necessary to screen for maternal antibodies including their avidity index og CMV IgG, prenatal ultrasound for the assessment of any fetal malformations and amniocentesis with quantative PCR analysis for specific CMV DNA in the amniotic fluid [10].

The target organ for the CMV infection remains the brain but the cells that are involved are known only from animal experiments. The most affected cells are represented by the astrocytes [8], endothelial cells [11], neuronal cells, oligodendroglial cells, macrophages and neuronal cell stem [17].

Some possible mechanisms that may be involved in the pathogenesis of CMV infection are: loss of neuronal stem cells, or intermediate progenitors, these may affect the size of the brain and its maturation, ii) alteration in stem cell migration and fate of cell differentiation iii) infection of astroglia that may disrupt her normal function such as neuronal circuitary guidance, synaptic integration, and integration along with the functional mature neuron iv) alteration of the microcirculation due to the cytokines and other soluble factors from the glial cells that result in neurotoxicity along with altered neuronal physiology [7].

Main clinical signs of infection are intrauterine growth retardation, purpura, jaundice, microcephaly, hepato-splenomegaly, hearing impairmant and thrombocytopenia. There are also other signs that alert us in regard of the diagnose, such as failure to thrive and anemia [5], [21].

At our infant failure to thrive and hepatomegaly were the main clues that drove us to the final diagnoses.

However the main brain abnormalities that we find at children with congenital CMV are seen while examining them at the ultrasound, CT and/or MRI.

SNHL is encountered in 10-60% of children with congenital CMV [15].

Around 50% of the newborns with congenital CMV will present with intracranial calcifications on ultrasound.

The CT scan is able to describe ventriculomegaly with white matter changes, microgyria, cysts and encephalopathy. There are also often described lissencephaly, porencephaly due to CMV infection [23].

At this moment the best predictor of neurological impairment is given by the viral load. Over 1000 copies are predictors for fetal transmission while over 5000 copies are predictors for symptomatic infection [10].

There were no CT damages at the presented infant and also at brain ultrasound we found no cerebral lesions.

We were not able to perform a MRI.

There are some ways in which we may combat congenital CMV infection due to the fact that CMV vaccine remains far away from us.

Neonatal screening for hearing loss may be done on a routine basis. A prevalence of 65 per 100000 children may have a prelingual hearing deficit that may be attributed to CMV [13]. Screening for hearing deficits may improve language development and diminish intelectual deficit.

PCR DNA for CMV made to all newborns is sensitive specific and easliy appliable and may be taken into consideration as a prevention tool [3].

Handwashing is an important prevention tool.

4. Conclusion

We present a case report of cytomegalovirus infection at an asymptomatic infant at which the diagnoses was established on the values of AST/ALT and mild hepatomegaly. Her evolution was favorable.

References

1. Adler, S.P., Finney, J.W., Manganello, A.M., et al.: *Prevention of child to mother transmission of cytomagalovirus among pregnant women*. In: J Pediatr, 2004; 145: 485-491.
2. Ashkenazi, A.: *Targeting death and decoy receptors of the tumor necrosis factor superfamily*. In: Nature Rev Cancer., 2002;2: 420-430.
3. Barbi, M., Binda, S., Caroppo, S. et al.: *Neonatal screening for congenital cytomegalovirus infection and hearing loss.* In: J Clin Virol., 2006; 35:206-209.
4. Damato, E.G., Winnen, C.W.: *Cytomegalovirus infection: perinatal implications.* In: J Obstet Gynecol Neonatal Nurs., 2002;31: 86-92.
5. Dworsky, M.E., Welch, K., Cassady, G., et al.: *Occupational risk for primary cytomegalovirus infection among pediatric health care workers*. In: N Engl J Med., 1983;309: 950-953.
6. Hicks, T, Fowler K, Richardson M et al. *Congenital cytomegalovirus infection and neonatal auditory screening.* In: J.Pediatr., 1993; 123: 779-782.
7. Ho, S.W., van den Pol, A.N.: *Bystander attenuation of neuronal and astrocytes intracellular communication by murine cytomegalovirus infection of the glia.* In: J Virol., 2007;81: 7286-7292.
8. Lathey, J.L., Spector, S.A.: *Unrestricted replication of human cytomegalovirus in hydrocortisone treated macrophages*. In: J Virol.,1991; 65:6371-6375.
9. Lazzarotto, T., Spezzacatena, P., Pradelli, P., et al.: *Avidity of immunglobulin G directed against human cytomegalovirus during primary and secondary infections in immunocompetent and immunocompromised subjects*. In: Clin Diagn Lab Immunol., 1997; 4: 469-473.
10. Lazzarotto, T., Varani, S., Guerra, B., et al.: *Prenatal indicators of congenital cytomegalovirus infection.* In: J Pediatr., 2000; 137:90-95.
11. Loksengard, J.R., Cheeran, M.C., Gekker, G., et al.: *Human cytomegalovirus replication and modulation of apoptosis in astrocytes* In: J Hum Virol., 1999; 2:91-101.
12. Maidji, E., McDonagh, S., Genbacev, O., et al.: *Maternal antibodies enhance or prevent cytomegalovirus infection in the placenta by neonatal Fc*

receptor mediator transcytosis. In: Am J pathol., 2006; 168: 1210-1226.
13. Nance, W.E., Lim, B.G., Dodson, K.M.: *Importance of congenital cytomegalovirus infections as a cause of pre-lingual hearing loss.* In: J Clin Virol., 2006; 35: 221-225.
14. Nelson, C.T., Demmler, C.J.: *Cytomegalovirus infection in pregnant mother, fetus and newborn infant*. In: Clin Perinatol., 1997; 24:151-160.
15. Pass, R.F.: *Congenital cytomegalovirus infection and hearing loss.* In: Herpes, 2005; 12:50-55.
16. Peckham, C., Tookey, P., Logan, S., et al.: *Screening options for prevention of cytomegalovirus infection.* In: J Med Screen., 2001; 8:119-124.
17. Poland, S.D., Costello, P., Dekaban, G.A., et al.: *Cytomegalovirus in the brain: in vitro infection of human brain derived cells*. In: J Infect Dis., 1990; 162: 1252-1262.
18. Revello, M.G., Zavattoni, M., Furione, E., et al.: *Preconceptional primary human cytomegalovirus infection and risk of congenital infection*. In: J Infect Dis., 2006; 193: 783-787.
19. Ross, S.A., Fowler, K.B., Ashrith, G. et al.: *Hearing loss in children with congenital cytomegalovirus infection born to mothers with preexisting immunity.* In: J Pediatr., 2006; 148: 332-336.
20. Stagno, S.: *Cytomegalovirus*. In: *Nelson Textbook of Pediatrics,* Behrman R.E., Kliegman, R.M., Jenson, H.B. (eds.). W.B. Saunders co. Philadelphia, 1999, p.981-983.
21. Tanaka-Kitajima, N., Sugaya, N., Futatani, T. et al.: *Ganciclovir therapy for congenital cytomegalovirus infection in six infants*. In: Pediatr Inf Dis J., 2005; 24:782-785.
22. Trincado, D.E., Rawlinson, W.D.: *Congenital and perinatal infections with cytomegalovirus.* In: J Pediatr Child Health*.,* 2001;37: 187-92.
23. Yamamoto, A.Y., Mussi-Pinhata, M.M., Cristina, P. et al.: *Congenital cytomegalovirus infection in preterm and full-term newborn infants from a population with high seroprevalence rate*. In: Pediatr Inf Dis J., 2001; 20:188-192.