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Review Article

Clinical Aspect and Management of Human Cytomegalovirus infection

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Abstract

Cytomegalovirus infection considered one of the most important viruses that causes hearing loss, mental retardation, and cerebral palsy are all common side effects of infection person. Young children and personal connections are the most common causes of infection during pregnancy. As a result, it's a significant public-health issue. Congenital CMV (cCMV), the most public non-genetic cause of sensori-neural hearing loss, is linked to maternal infection. CMV can also induce cerebral palsy and cognitive impairment. CMV is spread through contact with body fluids from a viral carrier. After primary infection, Viruses are transmitted at higher level than other time of infection, and it increases with gestational age. When infection develops before 20 weeks, however, severe fetal consequences are more likely. Past infection does not provide the mother immunity or provide protection to the fetus. On ultrasonography, CMV can cause cerebral or extracerebral abnormalities, as well as fetal development limitation and loss. Seroconversion in pregnancy (de novo appearance of virus-specific immunoglobulin G (IgG) in the serum of previously seronegative pregnant women) or the detection of specific immunoglobulin M (IgM) and IgG antibodies in association with low IgG avidity should be used to diagnose primary maternal CMV in pregnancy. The effective method for preventing viral infection is to provide pregnant women with hygiene advice and education. Vaccines, antiviral medicines, and immunoglobulin have all had their roles expanded throughout time.

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Cytomegalovirus (CMV)

Human cytomegalovirus, belong to herpesviridae family, also known as (HHV-5). is a large virus with envelope that is hat is extensively spread in human populations. The viruses have double stranded DNA. Human Cytomegalovirus (HCMV), like other herpesviruses, becomes latent before reactivating to active viral replication in response to stimuli such as inflammation or immunological weakness caused by disease or medical therapy(El Helou *et al* ., 2019).

Cytomegalovirus (CMV) seroprevalence in the general population is 83 to 86% in women of reproductive age and 86% among organ or blood donors. The lowest seroprevalence was found in the WHO European zone (66%) for each of these three groups and the highest World Health Organization (WHO) Eastern Mediterranean region (90%)(Navt *et al* ., 2021) .Human herpesvirus type-5 (HHV-5) is not extremely contagious, young children's saliva and urine are important reservoirs of viruses, especially for those who work with youngsters. Cytomegalovirus is transmitted across the placenta, within the birth canal, and during breast feeding. In young children, it's transmitted via saliva. Later, it is transmitted sexually because it's present in both semen and cervical secretions, moreover can be transmitted during blood transfusion and organ transplants (Hasing *et al.*, 2021). HCMV infection normally causes no symptoms. This is due to the fact that a strong immune response to HCMV usually prevents the high viral loads that cause end-organ disease (EOD) in immunocompromised people (Styczyński *et al.*, 2021)

CMV seroprevalence is influenced by socioeconomic variables and ethnicity (higher in non-white). The question of whether immune responses to CMV can protect pregnant women from infection and virus transmission to their fetuses is a hot topic of debate. Because seropositive women might sometimes transmit CMV to their fetuses, some workers wonder if immunizing these women can help them protect their babies. The situation, however, is not black and white. (Griffiths and Reeves, 2021, Govender *et al.*, 2021) Exchange with children under the age of three years, particularly if they are in daycare, is another distinguishing factor that predicts a positive CMV (Ross and Kimberlin, 2021). Negative pregnant women exist in high seroprevalence zones are at higher risk for CMV infection(Avettand-Fenoël *et al.*, 2013,Balegamire *et al.*, 2021)

Congenital CMV

Neonatal HCMV infection can be congenital (from intrauterine infection), perinatal (from birth), or postnatal (through breast milk) (Angueyra et al., 2020). Congenital HCMV infection affects about 0.51% of live infants in developed nations and is caused by either a primary maternal infection received during pregnancy or a secondary maternal infection during pregnancy, from reactivation of HCMV in a previously infected mother. In a non-immunized pregnant women, the risk of primary maternal infection is roughly 1-40% chance of congenital infection (Maltezou *et al.*, 2020).When a seronegative mother contracts a primary infection during pregnancy, fetal infection is more likely to arise and be severe; because pre-existing maternal immunity reduces dissemination to the baby, the probability of symptomatic congenital infection following reactivation of maternal human herpesvirus type-5 (HHV-5) in pregnancy is decreased, but not eliminated(Coppola *et al.*, 2019). Approximately 52% of congenitally infected kids are symptomatic at birth; a high percentage of children are born to mothers with a primary infection. The symptoms of severe congenital HCMV infection are microcephaly, chorioretinitis, nerve deafness, hepatitis with jaundice and hepatosplenomegaly, and thrombocytopenia with petechiae, with a high mortality rate. About 80% of symptomatic infants who survive have major consequences such as mental, visual, or hearing impairment (Leung *et al.*, 2020).However, the majority of congenitally infected newborns remain asymptomatic at birth, with only 5±15% developing sequelae after a long period of observation. Isolated sensorineural deafness is the most frequent(Cannon *et al.*, 2021).

HCMV infects syncytiotrophoblast cells in vitro and in pregnancies complicated by CMV infection, implying that this could be a route of transfer from mother to babies (Cannon *et al.*, 2021).

Transference

Maternal viraemia causes placental infection, which is after that virus spread to the fetus over the placenta. Human herpesvirus type-5 (HHV-5) replication is tolerated by placental cytotrophoblasts. When the virus attacks an embryo or a fetus, it replicates in a variety of organs, including the renal tubular epithelium. Human herpesvirus type-5 (HHV-5) is spread to disabled people by contact with body fluids such as saliva, urine, or sperm from someone who is actively shedding the virus. Contact with the urine or saliva of small children poses the greatest risk of harm for women of reproductive age. The rate of transfer to the fetus appears to rise. The less severe the signals in progeny appear to be the later in gestation the spread occurs. It has also been revealed that term infants with no underlying immunodeficiency who contract CMV from breast milk do not have clinical signal(Enders *et al.*, 2011)

Passive immunization and adoptive T-cell transfer

Although CMV hyperimmune globulin has been shown to minimize the incidence of HCMV infection in kidney transplant recipients, it is costly and rarely used in practice (Navarro *et al.*, 2019) .Riddell and colleagues in Seattle have demonstrated that transfer of virues specific cytotoxic T lymphocyte (CTL) clones can restore cellular immunity against CMV in Bone marrow transplantation recipients: CTL clones from immune BMT donors were generated in vitro and injected into recipients, with the ability to remain in the circulatory system (Barrett and Bollard, 2015). Although a randomized controlled trial has yet to establish that this technique reduces the frequency of CMV illness in BMT recipients, the perception is that the disease is less in CTL recipients. This work has already been reviewed elsewhere. In reality, if a CTL clone is composed of a few enlarged clones. Re-formation by adoptive transfer of a CTL clone may be equivalent to the usual CTL response. However, it will be fascinating to see if donor copies produced directly from the transplant reconstitute in the recipient to supply the same proportion of the CTL response as they did in the donor, as this could provide insight into CTL response homoeostatic regulation. It has been discovered that donor CMV specific CD4 cells are also required for adoptively transferred CD8 CTL to be retained and expanded in the recipient following the transfer, presumably to give 'assistance' via their secreted cytokines or other mechanisms (Pei *et al.*, 2022).

Vaccines

Seronegative pregnant women should avoid contact with potentially infected children in daycare settings, though this may be impossible. If vaccination were available, this group of seronegative women of reproductive age would be the target. GCV should never be used during pregnancy (Pembrey *et al.*, 2017;Leruez-Ville *et al.*, 2020)

However, For CMV, no approved vaccination is currently available (indeed the Oka strain vaccine for VZV is the only currently available licensed vaccine for any human herpesvirus).Many years ago, an experimental candidate vaccine based on a live laboratory (Towne) strain of HCMV was evaluated in kidney transplant patients with some evidence of protective protection, maybe equivalent to having previously had spontaneous HCMV infection (Gerna and Lilleri, 2019). However, there is considerable interest in developing a CMV vaccine, and a recent Institute of Medicine vaccine review panel concluded that CMV was the most important vaccine need in developed countries after HIV this was due in part to their use of a formula that weighted the number of quality years of life saved by a potential vaccine, and thus the weighting of preventing congenital CMV infection (Zhou *et al.* , 2021).Several contenders are still in the early stages of development. These are based on a variety of strategies: Glycoprotein B (to induce neutralizing antibodies) and the pp65 tegument protein are two single

potential proteins (with the aim of inducing CTL)(Limaye *et al* ., 2020). Because the majority of the ordinary reaction to HCMV seems to be intensive on a few proteins, these proteins may be targets for vaccine development. In this respect, it's worth noting that pure MCMV dense bodies, which are composed of tegument proteins but lack DNA, cause a CTL response in the human that is nearly identical to that induced by intact MCMV(Gergely *et al.*, 2021).A full live virus vaccine is also being developed, employing recombinant virus derived from AD169 and the Toledo isolate, which has a tropism and genetic structure similar to a clinical isolate(Wang *et al.*, 2021)HCMV is a difficult but intriguing clinical problem with a lot to teach us about how to live with persistent viruses and how to deal with the clinical repercussions when the virus-host connection breaks down (Sufiawati *et al.*, 2021).

Prevention and Control

Because of the challenge that HCMV poses in immunocompromised patients, numerous prophylactic strategies have been developed. Because HCMV can be transmitted through the blood and blood products of hospital patients, transfusion recipients at risk of HCMV infection now get screened seronegative blood; otherwise, the risk of transfusion-related HCMV infection was (2.5%)percent per unit of blood (Wu *et al.*, 2017). Transmission occurs when the virus infects leucocytes and the blood is depleted of leucocytes (a practice that is now commonly used in the medical community). Finally, seropositive donors' solid organ and bone marrow transplants can transfer HCMV, causing very severe illness in seronegative recipients (Griffiths and Reeves, 2021)

Conclusion

The most public pathogen answerable for teratogenic congenital infection is CMV. Pregnant women's hygiene information and education are presently the most effective preventative technique for CMV infection. Vaccines, antiviral medicines, and immunoglobulins have yet to be demonstrated. Counseling parents is tough since precise prognosis prediction has proven difficult due to the lack of reliable prognostic signs and effective remedies. Pregnancy termination should be explored as a treatment option.

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