CMV INFECTION, DIFFICULTY IN DIAGNOSIS AND TREATMENT IN THE NEWBORN AND IMMUNOCOMPETENT INFANT

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Abstract
Introduction. Cytomegalovirus (CMV) discovered in the early twentieth century has a ubiquitous distribution, being able to infect both human and several animal species. According to the literature, congenital infection prevalence is 0.2 to 2.4% and its subsequent fetal pathology ranks first in the maternal-fetal infections. Polymorphism manifestations of congenital infection is characterized by a wide range of asymptomatic starting point to various clinical symptoms. Regarding the treatment, scientific literature recommended “refraining” from the administering of antiviral therapy in mild and moderate clinical forms of CMV disease.

Methods. The study group was represented by a total of 186 children aged 0-18 acutely infected with CMV, hospitalized in Pediatrics II Clinic and Infectious Diseases Hospital "Victor Babes", Timisoara. The diagnosis was confirmed by serological determination of specific antibodies IgG and IgM type.

Results and conclusions. From the epidemiological point of view, the incidence of CMV disease, prevailed in infants, with a slight predominance in males, no significant difference on the environment of origin (rural / urban). The findings on clinical symptoms, laboratory investigations and, particularly the development of cases, determined the authors assert that, CMV infection is a major public health problem in the mother-child couple.

Keywords: CMV, infection, children

Introduction:
Cytomegalovirus (CMV) is a ubiquitous distribution, being able to infect both human and several animal species. The name of CMV, and its origins belongs to the family of herpes viruses which was proposed by Weller and Colab in 1960, is widely accepted in literature.1,2
Human herpes virus type 5 (HHV 5) or Cytomegalovirus belongs to the subfamily Beta-herpesviride, it has a spherical shape and a size between 160-200 nm, and it is considered the largest of human pathogenic viruses.
Due to the peculiarities of replication and cytopathogenic they possess, cytomegalovirus has the capacity to generate two types of infections namely: primary and recurrent.
The prevalence of congenital infection is 0.2 to 2.4%, with a higher rate in developing countries and those with weak socioeconomic level compared with developed ones. Thereby, according to studies from the literature, prevalence in developed countries is about 40% versus 100% in developing countries where the infection is acquired early in childhood.1,3 Clinical symptoms of cytomegalovirus infection varies by age, mode of transmission, infection type (primary or recurrent) and immunological status of the body (with special reference to the pediatric age).1,2,3

1. Congenital infection. It is produced by vertical contamination, transplacentar. It includes three forms:
   – The generalized form (septicemic, severe) appears at less than 5% of infected newborns and has clinical manifestations of a generalized infection.
   – The localized form (incomplete, average) usually occurs 6-8 weeks old or later, up to 4 months old. The most common form is neonatal hepatitis followed by neurological form.
   – The latent form (asymptomatic)it is asymptomatic, being diagnosed using serological investigations.

2. The perinatal infection.
   – It is produced by horizontal contamination of newborn and infant. Most cases are asymptomatic and symptomatic forms are the localized ones (pneumonia, hepatosplenomegaly syndrome, syndrome purple haemolytic anemia) or disabling (microcephaly, chorioretinitis, deafness).4

3. Postpartum infection.
   – It appears by horizontal contamination being asymptomatic in 95% of cases. When there are symptoms, they can manifest as prolonged febrile syndrome or mononucleosis-like syndrome.
   – Regarding the laboratory diagnosis of CMV infection in the last decade we have made remarkable progress. The infection’s laboratory diagnosis has 3 components: histopathological diagnosis, virological and serological.1,3
Histopathological diagnosis consists in highlighting the tissue biopsy of giant cells with large intranuclear inclusions, owl-like eyes.

Virologic diagnosis consists in isolating the virus in urine, blood, saliva, biopsy fragments. The most commonly used methods are: cultivation cytomegalovirus DEAFE (Detection of early antigen fluor escent foci), viral DNA by PCR and protein pp65.

Serological diagnosis consists in determination of antibodies specific for IgM or IgG. IgA anti-CMV using ELISA method.

IgM antibodies appear in about 3-4 weeks after the exposure to infection and persists in the body for 3-4 months. Thereby, the presence of IgM antibodies in a newborn means congenital infection.

IgG antibodies show an upward titer during active infection, which then stabilizes. Thereby, a person who has been exposed to CMV infection will remain, for the rest of the life, with stable IgG titers, which means that the virus has become inactive.

Etiological therapy for CMV infection is the use of antiviral medication. Severe forms "life-threatening" and those targeting eye damage (chorioretinitis) will benefit from this therapy represented by Ganciclovir, Valganciclovir, Cidofovir and Foscarnet.

Regarding infection prophylaxis, anti-CMV therapy has not proved useful in preventing CMV infection in the fetus and neither to decrease the frequency or severity of any fetal visceral damage. Currently there is no effective anti-CMV vaccine nor other specific and efficient methods for the prophylaxis of CMV infection in pregnant women.

Material and Methods
The study group was represented by a total of 186 children - 115 boys and 71 girls - aged between 0-18 years old hospitalized in Pediatrics II Clinic and Infectious Diseases Hospital "Victor Babes", Timisoara during January 2009 - January 2012. The study method used was actively investigation of the selected persons. Demographic, clinical and paraclinical parameters were registered.

The infection was confirmed by serological determination of specific antibodies IgG and IgM type. The study included all patients tested positive for IgM antibodies to cytomegalovirus, regardless of age, gender, home.

Results and conclusions:
In the studied group was a slight predominance of males versus females in all years of study. (fig.1) Knowing that in the general population there is a predominance of females, it is likely that this reversal of the relations between the genders indicate either a male predisposition for contracting infections or more likely that they will develop more severe clinical forms that require hospitalization.

![Fig. 1. Sex distribution](image)

![Fig 2. Age group](image)

The obtained data in this study are overlapping with those specified in the literature, mentioning a slight prevalence of males in acquiring cytomegalovirus infection.

By age group it is noted that a percentage between 30 and 40% of patients treated for CMV disease represents children under 6 months. Over 80% of each year's illnesses are children aged under 6 years.

Another parameter taken into consideration was the area of origin.

During those 4 years the percentage distribution is relatively similar, with the exception of 2010 when it was higher proportion of patients in urban areas. With all these variations, the differences are not statistically significant ($\chi^2 = 2.75$, $p = 0.431$), so we can not say the lack of homogeneity of the lot on this feature.

Clinical forms found in patients enrolled in this study were polymorphic, dependent on their age. We note that the most common clinical form encountered is hepatitis (almost 50% of cases), followed by mononucleosis (22% of cases) and
febrile syndrome (16% of cases). (Fig. 3) It is noted a predominance of hepatic form at patients under 1 year old; in other age groups this form decreases as frequency to increase the forms manifested as mononucleosis, prolonged febrile syndrome.

Fig 3. Clinical forms in CMV infection

In acute infections, the number of cases that presented complications are relatively few, the complication rate was of 9.14%. It is noted that hearing loss is the most common complication, followed by periventricular calcifications.

From the studied lot, 49 cases (26.44% of cases) received antiviral treatment, represented by Ganciclovir, mainly orally administered for 7 to 30 days. The significant factors that influenced the decision to adopt antiviral therapy were represented by clinical form of the disease and age. The antiviral treatment was given especially to very young patients (0-6 months old and 6-12 months old). The clinical forms which have been treated with antiviral therapy are: hepatitis (44.44% of cases), pneumonia (100% of cases) and gastroenteritis (75% of cases).

Conclusions:
1. Most likely, males have a higher vulnerability to develop more severe forms of infection with cytomegalovirus.
2. The most common clinical forms of CMV disease in hospitalized patients, in descending order, are: hepatitis (50%), mononucleosis (21%) and prolonged febrile syndrome (16%).
3. The most common complication is the hearing loss, followed by periventricular calcifications.
4. Antiviral treatment is indicated especially at very young age groups (1-12 months) and severe clinical forms (hepatitis, pneumonia and gastroenteritis).
5. There is no difference in prevalence between gender and residence.
6. In terms of age groups, there is an increased prevalence of infection in the age group of 0-6 years and 6-12 years.

References:

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