

HEARING DISORDERS - COMPLICATIONS OF CYTOMEGALOVIRUS INFECTION IN CHILDREN

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REZUMAT

Introducere: Descoperit la începutul secolului XX, virusul citomegalic reprezintă cea mai frecventă cauză de infecție congenitală, cu o prevalență de 0,2-2,4%, precum și principala cauză a surdității neurosenzoriale în patologia pediatrică. **Scopul studiului:** Identificarea unor eventuali indici predictivi ai afectării auditive la copiii cu infecție congenitală cu CMV. **Material și metodă:** Lotul analizat a cuprins un număr de 45 de nou-născuți și sugari mici (1-3 luni), dintr-un număr total de 87 de cazuri investigate, internați în Clinica II Pediatrie Timișoara în perioada ianuarie 2004 - ianuarie 2007. Diagnosticul de infecție congenitală simptomatică suspiciunat clinic (hepatosplenomegalie, peteșii, trombocitopenie, microcefalie, convulsii etc.) a fost confirmat serologic în 17 cazuri prin dozarea anticorpilor specifici Ig G și IgM. Evaluarea audiometrică efectuată într-o manieră prospectivă a fost bianuală în primul an, iar apoi anuală, fiind aplicată la toți cei 45 de copii luați în studiu. Vârsta medie a ultimei examinări a fost 39 luni. **Rezultate:** Afectarea auzului a apărut la 21% (6 din 28) din copiii cu infecție congenitală asimptomatică și 53% (9 din 17) din cazuri în cadrul formei simptomatice de boală. De asemenea prezența peteșiilor, hepatosplenomegaliei și a retardului de creștere intrauterină au fost asociate cel mai frecvent cu pierderea auzului la copii în cadrul formei simptomatice de boală. **Concluzii:** Infecția congenitală simptomatică cu CMV constituie o cauză importantă a surdității neurosenzoriale în patologia pediatrică.

Cuvinte cheie: citomegalovirus, infecție congenitală, afectarea auzului

ABSTRACT

Introduction: Discovered at the beginning of the 20th century, the cytomegalic virus represents the most frequent cause of congenital infection, in 0.2-2.4% of the cases, as well as the main cause of neurosensory hearing loss in pediatric pathology. **Objective:** This study was performed in order to identify the possible predictive indices of the auditory impairment in children with congenital CMV infection. **Material and methods:** The study group consisted of 45 neonates and infants (1-3 months) out of a total number of 87 cases, hospitalized in the Pediatrics Clinic No. 2, from Timisoara, between January 2004 - January 2007, which were diagnosed with congenital CMV infection. The prospective audiometry, performed twice a year in the first year, then annually, applied to all the 45 children included in the study, the average age of the last examination being 39 months. **Results:** Hearing loss occurred in 21% (6 out of 28) of the children with the asymptomatic form of the disease and 53% (9 out of 17) of the children with the symptomatic form of the disease. Also, the petechias, hepatosplenomegaly and intrauterine growth retard have been associated most frequently with hearing loss in children, in the symptomatic form of the disease. **Conclusions:** The symptomatic congenital CMV infection represents a major factor in the neurosensory impairment, and especially the hearing loss in children.

Key Words: cytomegalovirus, congenital infection, sensorineural hearing loss

INTRODUCTION

The CMV infection represents the most frequent congenital infection and the recurrent fetopathy is on the first place among the maternal and fetal infections.¹⁻³

The prevalence of the congenital infection is of 0.2-2.4%, with a higher percent in developing countries and in countries with lower social and economical level, as compared to the developed countries. Also, according to the studies in field, the prevalence of the infection in the developed countries is of approximately 40%, as compared to 100% in the developing countries.⁴⁻⁶

The transmission is vertical, by transfer through the placenta, from the mother's blood. Between 30 to 40% of the women at the fertile age are untouched by the CMV infection, while in 1-3% of these the primary phase of the infection occurs during pregnancy. In case of the primary maternal infection, the infection risk in the newborn is 30%, compared to mother's recurrent infection, where the transmission risk of the

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virus is less than 1%. Among the children with CMV congenital infection, 10% develop a symptomatic form of disease, while 90% are born with asymptomatic infection.⁷⁻⁹

Although the possibility of evolution can vary in both forms of the disease, the possibility of mortality in the symptomatic forms (25-30% of the children) and the risk of developing severe sequelae (70-80% of the symptomatic forms and 15% of the asymptomatic forms, respectively) draw attention on this infection.^{4,5,10}

In this respect, studies in the specialty literature highlight the neurological/neurosensory impairment in these children (motor and cognitive disorders) with a specific reference to the auditory function: hypoacusia/deafness.¹¹⁻¹³

This study was performed in order to identify the possible predictive indices of the auditory impairment in children with congenital CMV infection. This fact will allow the rigorous monitoring of these children, a better counseling for parents and the elaboration of interventional strategies.

MATERIAL AND METHODS

The study group included 45 neonates and infants (1-3 months), from a total number of 87 cases, hospitalized in the Pediatric Clinic No. 2, from Timisoara, between January 2004 - January 2007, who were diagnosed with congenital CMV infection, first suspected by anamnesis and physical examination and then confirmed biologically, by determining antibodies anti-CMV of the type IgM and IgG, ELISSA method.

For each subject, we recorded: gender, background (urban, rural), the form of disease, from the clinical criteria point of view (symptomatic, asymptomatic). For all 45 children included, we also performed supplementary, targeted clinical investigations: prospective audiometry, performed twice a year in the first year, then annually, the average age of the last examination being 39 months. Audiometry was performed with the interdisciplinary collaboration with the Department of Otorhinolaryngology of the Victor Babes University of Medicine and Pharmacy, Timisoara.

The loss of neurosensory hearing has been defined as the air conduction threshold (>25 dB), with auditory brain stem response (ABR) >20 dB, on and audiogram correlated with the normal values for a child normally developed for the respective age. Progressive loss of hearing has been defined as neurosensory decrease of hearing with 10 dB or more, for any ABR

frequency or threshold, documented by two different evaluations.

According to these characteristics, the study group has been divided into two parts:

- Group I: 17 children with symptomatic form of the disease, suspected by presence of suggestive clinical signs, including: petechia and hepatosplenomegaly - 4, intra-uterine retarded development - 3, microcephaly - 4, convulsions - 6. (Fig. 1)

- Group II: 28 children with asymptomatic form of the disease.

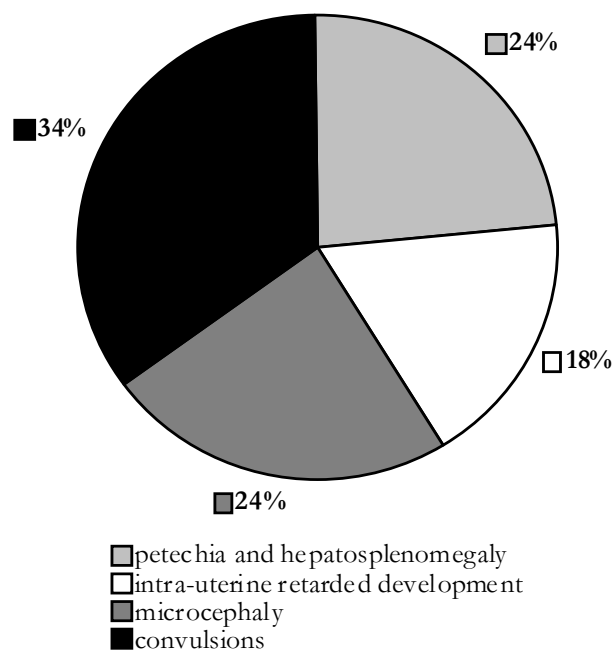


Figure 1. Symptomatic form of the disease.

RESULTS

During a three-year period, in the Pediatric Clinic No. 2, Timisoara, 45 cases of CMV infection were diagnosed, out of a total number of 87 cases investigated for this condition. The 87 cases have been investigated for the CMV infection because there were symptoms of microcephaly, petechias, prolonged icterus and hepatosplenomegaly. The diagnosis was confirmed by determining the CMV antibodies of the IgG and IgM type through the ELISA method. The age of the CMV-infected patients ranged between 6 weeks and 3 months.

According to the audiometric evaluations, the hearing loss occurred in 21% (6 out of 28) of the children with the asymptomatic form of the disease and 53% (9 out of 17) of the children with the symptomatic form of the disease.

For the symptomatic form of the CMV infection, the hearing loss during the study period occurred in all children with petechia and hepatosplenomegaly

(4 cases), all children with intra-uterine retarded development (3 cases), in one child with microcephaly and in one child with convulsions. (Fig. 2) The results of the study also revealed that, in the case of children with intrauterine growth retard, petechias and hepatosplenomegaly, the risk to develop hearing loss is twice that of children with normal intrauterine growth and without hepatosplenomegaly.

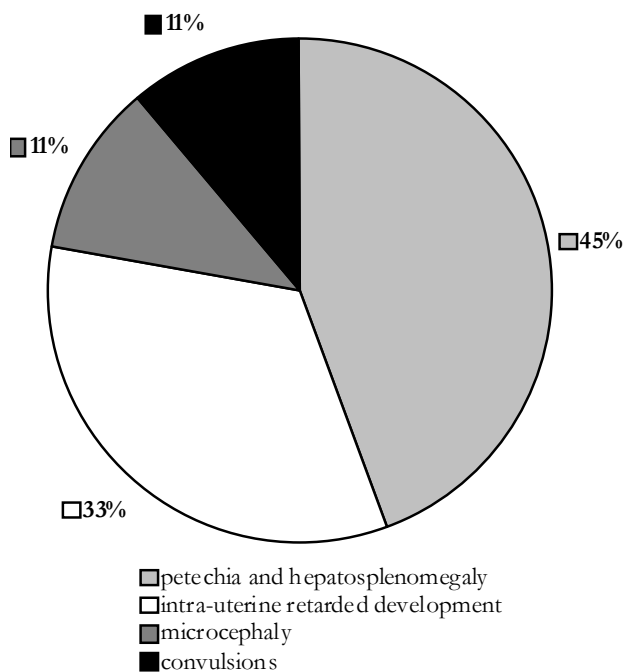


Figure 2. Hearing loss in the symptomatic form.

As for the background and gender distribution, we have noticed an equal incidence of the disease among the children coming from the rural and urban areas, as well as among males and females, similar to data reported by other authors.

DISCUSSIONS

The CMV infection represents a public health problem, due to the high incidence of congenital infection, the character of persistent viral infection with possibilities of reactivation in the immunosuppressant stages, as well as the important complications it entails. The positive diagnosis, besides the clinical observations (microcephaly, petechias and convulsions), requires laboratory exams: serological and viral. For the studied group we applied serological tests, used for the usual diagnosis: The ELISA tests pointed out quantities of antibodies and detected the different classes of immunoglobulins (IgG, IgM). During the congenital infection, the evolution can be lethal, while survival is associated important sequelae. Hearing loss is the most frequent among these sequelae, therefore in all

children included in the study we have additionally performed a prospective audiometric test, twice a year in the first year of life, then once a year.

The results of this long-term study on children with symptomatic and asymptomatic congenital infection demonstrate that the symptomatic congenital CMV infection, manifested in intrauterine growth retard, petechias, microcephaly and convulsions leads to important neurosensorial damage, especially related to the hearing loss.

Previous studies have demonstrated that evidence of SNC involvement at birth is a strong predictor of cognitive and motor deficits in children with symptomatic congenital CMV infection.^{5,14} Although a significant proportion of infants with microcephaly at birth develop hearing loss, this finding was not predictive of hearing loss in our study.

Because most infants with congenital CMV infection are without symptoms at birth, these children are unlikely to be recognized as being at risk for hearing loss and will not receive further hearing evaluations to detect late-onset hearing loss.

CONCLUSIONS

1. The symptomatic congenital CMV infection represents a major risk factor for neurosensorial impairment, and especially for hearing loss in children.
2. The clinical data of CNS damage at birth (microcephaly, convulsions) did not represent, in our study, predictive factors for the hearing loss, as compared to other symptoms of the infection (intrauterine growth retard, hepatosplenomegaly).
3. Taking into consideration the results of this study, we think it is essential to monitor, using audiometric prospective tests, all the children with CMV congenital infection.

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