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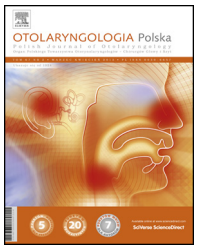

Original research article/Artykuł oryginalny

Congenital and acquired cytomegalovirus infection and hearing evaluation in children

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ABSTRACT

Objectives: Congenital cytomegalovirus (CMV) infection is one of the most common intrauterine diseases. In all, 1% of live births is affected by cytomegalovirus infection, while 90% neonates with perinatal infection do not show symptoms of disease. Symptomatic CMV is present in 5–10% of children. Typical clinical signs of CMV infection are microcephalia, mental retardation, progressive major amblyacousia, and neuromuscular infection. Hypoacusis is present in 30–60% of children with congenital symptomatic CMV – in most cases it is bilateral and applies to high frequency hearing loss. The purpose of this article is to emphasize the importance of hearing evaluation in children with congenital and acquired cytomegalovirus infection. **Patients and methods:** A group of 70 children had serological and genetic screening for CMV DNA, using PCR method, in urine and blood. In this group, 52 children were diagnosed with congenital CMV and 18 children had acquired CMV. Audiological examinations including PTA, ABR, TEOAE and immittance audiometry were performed. **Results:** Bilateral sensorineural hearing losses were found in 9 children, associated with mental and physical retardation, brain malformation and microcephalia, and unilateral losses in 3 children. In 40 cases, we did not observe hearing loss, although the level of bilirubin was high, and splenomegaly, hepatomegaly and paralysis of facial nerve were present. In the group of children with acquired CMV, we did not notice hearing loss. **Conclusions:** This research proved that CMV infection often caused hearing loss. In spite of this, all children with congenital and acquired CMV should be monitored and assessed throughout their lifetime by an audiologist.

Introduction

Congenital cytomegalovirus (CMV) infection is one of the most common intrauterine diseases. It is estimated that the disease may affect from 0.64% to 0.70% of newborns worldwide [1]. Sensorineural hearing loss (SNHL) is the most common sequela of congenital CMV infection, occurring in 10–15% of all infected children. Hearing loss reportedly occurs

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in 30–40% of children who have clinically apparent (symptomatic) disease at birth and in 5–10% of children with clinically silent (asymptomatic) infections. In USA, 15–21% of all congenital hearing losses may be caused by this infection [2, 3].

At the beginning of the 20th century, the CMV infection was described as an insertion disease due to the discovery of large cells with insertions inside the nucleus and cytoplasm in the necropsy material collected from salivary glands. Weller coined the term ''cytomegalovirus'' in 1960, based on histopathological examination [4]. The cytomegalovirus is the herpes virus with double-stranded DNA, the nucleocapsid of which is surrounded by a lipid-protein layer. Cytomegalovirus infection affects 40–100% of the population and is more frequent in the developing countries and in the part of society with lower economic status [5]. In our country, the percentage of seropositive patients can be estimated as 70% of the population. Multiplication of the virus can cause active infection with a number of clinical effects, or may produce no side effects and become latent. When the infection affects people with efficient immune system, it is usually asymptomatic or produces mild, mononucleosis-like symptoms. CMV infections are classified into primary and secondary types. The primary type can be characterized by the presence of IgM anti-CMV antibodies in the blood serum of previously seronegative patients. The secondary type involves reactivation of hidden infection or the secondary infection caused by another virus type in a person with anti-CMV antibodies. The direct impact of the virus on cells is not the only key factor in the pathomechanism of changes – the typical inflammatory reaction of blood vessels with leukocyte infiltrations is also very important. In USA, cytomegalovirus is the most common cause of congenital infections, SNHL, mental retardation and cerebral palsy. It is estimated that symptomatic CMV is 90% associated with the risk of ophthalmic and audiological damages of varied intensity. However, children with delitescent infection are at a 10–15% risk of hearing loss [5–8].

The purpose of this work is to emphasize the importance of hearing evaluation in children with congenital and acquired cytomegalovirus infections.

Materials and methods

The study group comprised 70 children, 39 boys and 31 girls at the age of 2–12 years (average age: 6 years), with diagnosed congenital and acquired cytomegalovirus infection.

The cytomegalovirus infection was diagnosed from clinical records and by serological and molecular screening. The characteristic anti-CMV antibodies were determined by enzyme-linked immunoassay (ELISA). The presence of the viral DNA (CMV DNA) in urine and blood was checked by using polymerase chain reaction (PCR). Congenital infection was considered the consequence of a primary maternal infection during pregnancy. Maternal CMV infection was considered as primary when a maternal seroconversion of CMV IgG occurred during pregnancy, or when the initial CMV serology was highly suggestive of a primary CMV infection. Serology was assumed to be highly suggestive of primary infection when very high IgM and very low IgG antibodies were detected in the serum sample collected in the first trimester.

All children went through a full laryngological examination in order to exclude ear, nose and throat abnormalities. The next step was an audiological examination to determine the degree and localization of hearing loss.

Hearing examination was conducted in 70 children. The audiological examination consisted of pure tone audiometry (PTA) (using Madsen 622 audiometer and TDH 39 headphones) to determine air conduction at the frequency of 125–8000 Hz and bone conduction at the frequency of 250–4000 Hz. The impedance audiometry test (Zodiak 901P immittance audiometer, Madsen) was conducted by recording the tympanogram and the reflex of the stapes muscle. Ipsi- and contralateral stimulation was performed with a probe trial tone at 226 Hz. The recording of transiently evoked otoacoustic emission (TEOAE) was performed using an Echocheck probe, and the responses from the brain stem (ABR) were examined using a Racia instrument; the click-evoked response was repeated 1600 times (one patient was in pharmacological coma).

Additionally, all parents were thoroughly interviewed regarding the course of pregnancy, the childbirth and infancy and the current health condition of their children.

Results

CMV infection was diagnosed in 52 children and acquired CMV in 18 children.

Nine children (5 girls and 4 boys – above 3 y.o.) among the patients with congenital CMV (17% of the group) were diagnosed with profound bilateral SNHL (average PTA 85–90 dB), while a similar unilateral hearing loss was diagnosed in 3 children (two in the left and one in the right ear).

In the group of nine children with severe bilateral SNHL, mental and physical retardation, enlargement of ventricular system and microcephalia (two children) and heart defect (one child) were diagnosed at infancy in addition to CMV. Three children with unilateral hearing loss did not have any additional abnormalities.

The PTA of all children with hearing loss showed similar air and bone conduction at low and middle frequencies at the level of 70 dB, while at the frequency above 2000 Hz the level was 90 dB (Table I).

Table I – Average pure-tone audiometry in children with hearing loss caused by congenital CMV

Frequency	kHz	0.125	0.25	0.5	1	2	3	4	6	8
Right ear *n*-10	dB	75	80	75	80	85	90	90	95	90
Left ear *n*-11	dB	75	75	75	85	80	95	90	95	95
SD +–	dB	4.0	3.0	2.0	5.0	5.0	4.5	3.0	3.0	4.0

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