Srp Arh Celok Lek. 2016 Jan-Feb;144(1-2):56-62
ОРИГИНАЛНИ РАД / ORIGINAL ARTICLE
DOI: 10.2298/SARH1602056M
UDC: 616.98-079.4:578.825

Clinical and laboratory differences between Epstein–Barr and cytomegalovirus infectious mononucleosis in children

Raša Medović[1], Zoran Igrutinović[1,2], Ružica Radojević-Marjanović[3], Slavica Marković[1,2], Zorica Rašković[1,2], Aleksandra Simović[1,2], Jelena Tanasković-Nestorović[1,2], Marija Radovanović[1,2], Biljana Vuletić[1,2]

[1]Pediatric Clinic, Clinical Center, Kragujevac, Serbia;
[2]University of Kragujevac, Faculty of Medical Sciences, Kragujevac, Serbia;
[3]Clinic for Infectious Diseases, Clinical Center, Kragujevac, Serbia

SUMMARY

Introduction Infective mononucleosis is most commonly caused by Epstein–Barr virus (EBV), and in smaller percentage by cytomegalovirus (CMV).

Objective The aim of this paper was to determine the clinical and laboratory differences between EBV and CMV infectious mononucleosis in children.

Methods Cohort retrospective analytical research was conducted. We used data from medical history in six years period and monitored anamnestic data, frequency of inspection and palpation obtained data during physical examination, several laboratory tests, abdomen ultrasonography examination finding and emergence of disease complications. Statistical processing of data has been performed using SPSS 20.

Results Total number of examined children was 137, out of which 85.4% were with EBV and 14.6% with CMV infection. Affected children were most commonly younger than eight years. Boys were affected more often. There was no difference in frequency of high temperature, sore throat, bad breath, and respiratory symptomatology between examined children. Differences were discovered in frequency of stomachaches, eyelid swelling, skin rash and fatigue. Differences were not proven in the frequency of angina, lymphadenopathy and splenohepatomegaly between the groups. Values of transaminases and lactic dehydrogenases significantly decreased after seven days of hospitalization in both groups. In children with EBV, values of transaminases declined faster than in children with CMV. Anemia and bacterial superinfection of pharynx were most common disease complications. Thrombocytopenia was more common in children with CMV infection. Average duration of hospitalization was 6.7 days.

Conclusion In children with CMV abdominal pain, eyelid swelling, skin rash, fatigue and thrombocytopenia were more common. In children with EBV values of transaminases declined significantly faster.

Keywords: infectious mononucleosis; herpesvirus 4, human; children

INTRODUCTION

Infectious mononucleosis (IM) is an acute disease of reticuloendothelial and lymphatic system, that often affects persons in adolescence and childhood [1], and it is most commonly caused by the Epstein–Barr virus (EBV) and in smaller percentage by cytomegalovirus (CMV), between 7% and 16% [1-6], and extremely rarely can be caused by *Toxoplasma gondii*, viral hepatitis A, B, C or human herpes virus 6 [4].

According to dominant clinical signs, several different forms of IM are distinguished: pharyngeal, glandular, typhoid, septic and nervous. Regardless of the causing virus, incubating period most probably lasts 10–50 days [1, 2, 3]. Complications of IM are not common, but they can be very extreme and they can become dominant manifestations of the disease [7, 8, 9].

Diagnosis is made according to the characteristic clinical signs, hematologic changes in a complete blood count, the emergence of young lymphocytic forms – atypical lymphocytes (virocytes), increased value of transaminases during the first two to three weeks, often increased inflammation parameters, and additional help is provided by ultrasonographic abdomen examination. The most secure diagnosis confirmation is achieved by serological tests (IgM to EBV virus capsid antigen [EBV-VCA] and IgM to CMV) [1, 2, 3, 10, 11].

Apart from resting and performing a hygienic–dietary regimen, the affected children do not demand specific treatment [1, 2, 3, 10]. Certain researches have proved that application of antiviral medicines does not influence the clinical finding and the duration of the disease [12]. In case of bacterial superinfection of pharynx it is necessary to perform antibiotic therapy [10]. Mullarkey [13] proved positive effect of giving corticosteroids in the cases of severe clinical findings.

Domestic published studies about clinical and laboratory characteristics of IM in childhood are not common. There are publications for this particular disease symptom or complications of EBV infection [8, 14]. Such researches are much more common worldwide, but without focusing on attempts to find relevant differences between EBV and CMV infection [5, 6, 15-21]. Also, there is a need for permanent monitoring of disease characteristics,

Correspondence to:
Raša MEDOVIĆ
Klinika za pedijatriju
Klinički centar Kragujevac
Zmaj Jovina 30, 34000 Kragujevac
Serbia
rasamedovic@gmail.com

considering that it is a common clinical syndrome in childhood, with variable duration and clinical findings.

OBJECTIVE

The aim of this study was to try to determine the clinical and laboratory differences between EBV and CMV infectious mononucleosis in children and to indicate the frequency of certain disease characteristics and laboratory findings.

METHODS

The study was designed as a cohort retrospective analytical research. We used data from the medical history of patients, both sexes, up to 16 years of age, who were hospitalized at the Pediatric Clinic, Clinical Centre Kragujevac, during a six-year period, from January 2009 until December 2014.

The examined patients were divided into two groups. The first group comprised patients in whom serologically acute EBV infection had been proven, they had an increased titer of antibodies in IgM class to EBV-VCA, while the second group contained patients with acute CMV infection, in whom an increased titer of antibodies in IgM class to CMV had been serologically proven. Antibodies to EBV-VCA and CMV in IgG class, as well as IgG antibodies to EBV nuclear antigen (EBNA) were not taken into consideration, considering that they mark a condition of an earlier infection. When proving specific EBV antibodies in serum, we used ELISA test (BIOKIT, Freiburg, Germany), and Abbott AxSYM CMV IgM test when proving IgM antibodies to CMV. We also interpreted the results of Monolatex test (Wampole Laboratories, Cranbury, NJ, USA) [10].

Using anamnestic data obtained personally from older children or heteroanamnestic data from parents on admission, we monitored the following parameters:

- duration of symptoms of the disease;
- body temperature of over 37.8°C (this cut-off value has been taken considering that a temperature up to 37.8°C can also be physiological) [22];
- complaints of sore throat, bad breath or difficulties when swallowing;
- presence of fatigue, eyelid swelling, skin rash;
- presence of stomach problems (stomachache, diarrhea, vomiting);
- presence of respiratory symptoms (coughing, heavy breathing, nose secretions);
- use of antibiotics before admission.

During physical examination of the children, the following were performed:

- inspection of pharynx and tonsils;
- by palpation, enlargement of reachable lymph glands of neck, axillary and inguinal areas;
- palpation of the abdomen when enlargement of the liver and/or spleen was suspected.

In our patients we monitored the following laboratory parameters:

- erythrocyte sedimentation (SE) values and C-reactive protein (CRP) – cut-off value of 15 mm/h for SE and 10 mg/l for CRP, and values of fibrinogen – normal 2–4 g/l [11];
- values of transaminases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) – cut-off value 40 μ/l and lactic dehydrogenase (LDH) – normal values up to 450 IU/l [10]. We noted the following on admission and on the seventh day of hospitalization:
- values of hemoglobin – cut-off value below two standard deviations, depending on the age and sex, and number of thrombocytes – normal 150–400×10^9/l [11, 23];
- number of leukocytes – normal 4–10×10^9/l and number of lymphocytes – normal 2–6×10^9/l [10, 11];
- presence of virocytes in the peripheral blood smear;
- direct and indirect Coombs test;
- findings of pharyngeal smear and values of antistreptolysin titer (ASOT) – normal values up to 250 IU/ml [11].

We followed the development of complications. Moreover, we monitored the findings of ultrasonography examination of the abdomen, and used tables for normal ultrasonography dimension of longitudinal diameter of the spleen and liver in childhood, according to the age and sex, as referential values [24].

Statistical analyses were performed using SPSS Statistics 20 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean values ± standard deviation, and categorial variables as percentage frequency of the categories. We used parametric methods (paired samples T-test and independent samples test) to calculate the significance of difference between the continuous variables. Chi square test is used to calculate the significance of difference between categorial variables. The value $p<0.05$ is considered statistically significant [25]. The results were shown in tables and graphics.

RESULTS

Total number of children hospitalized at the Pediatric Clinic, Clinical Centre Kragujevac in this period with confirmed diagnosis of IM was 137, out of which 80 (58.4%) were male and 57 (41.6%) female.

Acute EBV infection was diagnosed in 117 (85.4%) patients, and acute CMV infection in 20 (14.6%). In 39.3% of the patients with acute EBV infection simultaneously there was high titer of antibodies in IgM class to CMV. Such a finding is interpreted as acute EBV infection. There were no children with EBV/CMV co-infection. Monolatex test in our study showed specificity of 92.3%, and sensitivity of 70.8%.

Most of the children younger than four years of life (35.8%) and between four and eight years (38%), and lesser percentage belonged to the age categories of 8–12 years (15.3%), and 12–16 years (10.9%), with approximately equal distribution in relation to whether it was EBV or

CMV infection (p=0.772). There were no infected infants. It was noted that the youngest children had the most severe clinical findings in both groups, in terms of increased frequency of highly febrile children, children with splenomegaly, and more prominent cervical lymphadenopathy in the sense of agglomeration of nodes, but without differences in relation to other examined parameters (Table 1).

In 62.6% of patients with EBV and 65% with CMV infection, the disease lasted up to 10 days before hospitalization.

There was no significant difference in terms of our patients having temperature above 37.8°C before hospitalization, when we compared the EBV and CMV groups (Table 2) – 37.6% of children with EBV and 40% with CMV were highly febrile, with temperature over 39°C. The mean peak temperature was 38.5±0.7°C (range: 37.2–41.1°C) and the duration of fever was 7.6±3.2 days in the group with EBV, and 38.7±0.8°C (range: 37.3–40.9°C), with duration of 7.2±2.9 days in the group with CMV infection.

There was no significant difference between the groups when we compared anamnestic data about sore throat, bad breath and respiratory problems, but there was a difference when we observed incidence of fatigue, eyelid swelling, stomach problems and skin rash, and in considerably higher percentages in children with CMV infection (Table 2).

From anamnestic data we obtained the result that 72.6% of the patients with EBV and 75% of those with CMV received antibiotics before hospitalization.

Statistically valid difference in the frequency of angina, lymphadenopathy and splenohepatomegaly among the children was not found (Table 3).

There was no confirmed difference between the groups when frequency of increased values is considered, as well as difference in mean values of inflammation parameters: SE, CRP, fibrinogen, number of leucocytes and lymphocytes in CBC (Table 4).

In a peripheral blood smear in patients with EBV, in 82.9% we determined the presence of virocytes, and of that number most of the patients (41%) had 20% virocytes. It is similar with the patients with CMV – 78.9% had virocytes in peripheral smear and the highest percentage (38.8%) belong to the group that had 20% virocytes.

In terms of frequency of increased values, as well as in mean values of transaminases and LDH taken at the admission, statistically significant difference between the patients was not proven. It was confirmed that there is a significant decrease of values of all three markers that were repeated after seven days of hospitalization (Table 4). It has also been proven that there is a significant difference in the speed of decreasing of AST (p=0.000) and ALT (p=0.002) values after seven days, considerably faster in the patients with EBV infection (Graphs 1 and 2).

No patient affected by IM had positive direct and/or indirect Coombs test.

Analyzing the findings of ultrasonography examination of the abdomen, we determined that 74.8% of the children with EBV and 75% of them with CMV infection had splenomegaly, and 41.2% with EBV and 45% with CMV infection had hepatomegaly.

Table 1. Presence of disease symptoms and signs according to age categories

Disease symptoms/ signs	1–4 years		4–8 years		8–12 years		12–16 years		p-value
	n	%	n	%	n	%	n	%	
Highly febrile	34	65.4	10	19.2	5	9.6	3	5.8	0.001
Splenomegaly	42	46.1	25	27.5	18	19.8	6	6.6	0.013
Agglomeration of nodes	32	53.3	13	21.7	8	13.3	7	11.7	0.002

n – number of patients

Table 2. Presence of disease symptoms in the examined groups

Disease symptoms	EBV		CMV		p-value
	n	%	n	%	
High temperature	102	87.2	17	85	0.187
Sore throat	94	80.3	15	75	0.276
Bad breath	75	64.1	12	60	0.412
Respiratory symptoms	58	49.6	11	55	0.386
Fatigue	79	67.5	20	100	0.008
Eyelid swelling	27	23.1	17	85	0.000
Skin rash	28	23.9	12	60	0.003
Stomach problems	30	25.6	17	85	0.000

EBV – Epstein–Barr virus; CMV – cytomegalovirus

Table 3. Frequency of clinical manifestations in children with infectious mononucleosis

Clinical manifestations		EBV (%)	CMV (%)
Pharynx	Normal finding	6.8	5
	Hyperemic	93.2	95
Tonsils	Normal finding	27.3	25
	Hypertrophic	15.4	20
	Hypertrophic with plaques	57.3	55
Lymph nodes	Not enlarged	14.5	15
	Single up to 2 cm	15.4	20
	Single over 2 cm	22.2	20
	Agglomeration of nodes	44.4	40
	Nodes in several regions	3.4	5
Abdomen palpitation	Splenomegaly	66.7	65
	Hepatomegaly	33.2	35

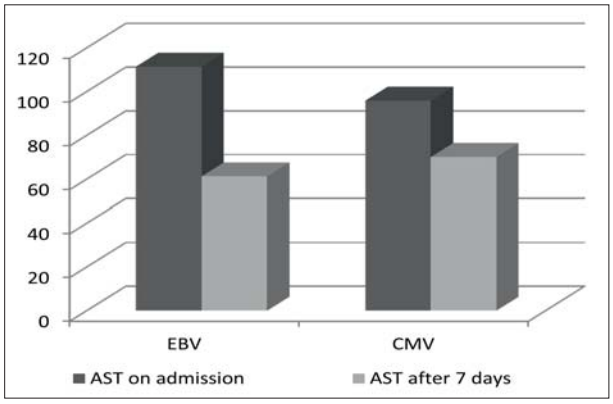
p>0.05

Table 4. Percentage of increased values and mean values of laboratory parameters in the examined groups

Laboratory parameters	EBV		CMV	
	%	Mean value	%	Mean value
Erythrocyte sedimentation rate	60.4	25.4 mm/h	65	28.1 mm/h
CRP	53.7	26.6 mg/l	50	22.2 mg/l
Fibrinogen	9.7	3.101 g/l	10.5	2.996 g/l
Number of leukocytes	65	15.2×10^9/l	60	14.9×10^9/l
Number of lymphocytes	74.7	10.7×10^9/l	70	10.1×10^9/l
AST on admission	74.4	111.4 µ/l	70	95.9 µ/l
AST after seven days	/	61.2 µ/l	/	70.1 µ/l
ALT on admission	66.7	126.4 µ/l	65	119.8 µ/l
ALT after seven days	/	70.1 µ/l	/	85.5 µ/l
LDH on admission	96.3	796.5 IU/l	95	835.1 IU/l
LDH after seven days	/	629.4 IU/l	/	591.3 IU/l

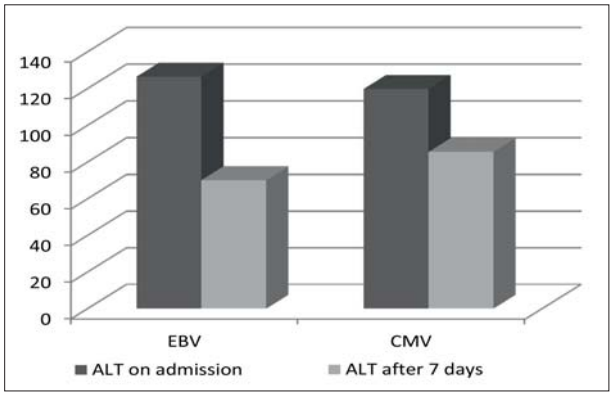
CRP – C-reactive protein; AST – aspartate aminotransferase; ALT – alanine aminotransferase; LDH – lactic dehydrogenase

doi: 10.2298/SARH1602056M



Graph 1. Values of AST on admission and after seven days in the examined groups

AST – aspartate aminotransferase; EBV – Epstein–Barr virus; CMV – cytomegalovirus



Graph 2. Values of ALT on admission and after seven days in the examined groups

ALT – alanine aminotransferase

Table 5. Presence of disease complications in the examined groups

Disease complications	EBV		CMV		p-value
	n	%	n	%	
Bacterial superinfection	22	18.8	4	20	0.257
Anemia	63	53.8	11	55	1.432
Thrombocytopenia	51	43.6	14	70	0.029
Leukopenia	5	4.3	1	5	2.189
Hepatitis	1	0.008	0	0	/
Spleen rupture	0	0	0	0	/
Secondary hemophagocytic lymphohistiocytosis	1	0.008	0	0	/
Respiratory complications	0	0	0	0	/
Cardiologic complications	0	0	0	0	/
Neurological complications	0	0	0	0	/

When considering IM complications, a significant difference between the patients was not proven, except that higher percentage of children with CMV had thrombocytopenia (Table 5), but in most cases this was a mild form of thrombocytopenia.

The ASOT was increased in 10.3% of the patients with EBV, and in 10% of those with CMV infection.

Average duration of hospitalization in both groups was 6.7±0.8 days.

DISCUSSION

According to our results, there was a higher number of infected boys (ratio M:F=1.4:1), which is in correlation to other studies that have dealt with this disease [5, 6, 15-21].

Also, Epstien–Barr virus stands out as the main cause of IM, and the percentage of patients affected by cytomegalovirus in our study is on the higher limit, which is described in the literature (about 15%) [1-6]. We reached an interesting result that almost 40% of the patients with acute EBV infection had an increased titer of antibodies in IgM class to CMV. In these cases we determined avidity to IgG antibody to CMV. In the case of recent CMV infection, the avidity is lower, whereas in the case of an old infection or virus reactivation, the avidity is higher. In all our patients with positive IgM antibodies to both viruses, avidity to IgG antibody to CMV was higher, so these results were interpreted as acute EBV infection. Additional help in these situations represented positive Monolatex test. It should be considered that IgM antibodies to CMV in 20–40% of patients can remain increased up to a year and even longer from acute infection, as well as from manufacturer's reagents of and the method of work with ELISA tests [3, 10, 11, 26]. Nevertheless, this high percentage of coinciding positive IgM antibodies to both viruses should represent a basis for some following researches. Fortunately, we did not have children with EBV/CMV co-infection, which usually has severe clinical presentations and in most cases requires treatment with antiviral drugs [4].

In our study, affected children were most commonly younger than eight years, which corresponds to comparative studies from different geographical areas [5, 6, 15-21]. Data from the literature show that the greatest incidence of infection is in the range of 16–25 years of life, and we included only children up to the age of 16 [1, 2, 3, 16]. Regardless of the fact that we did not have any infants with IM, the youngest patients have had most prominent typical symptoms of the disease (high fever, splenomegaly and lymphadenopathy), but without differences in other symptoms and laboratory analysis toward other age groups. These age differences are described in much of relevant literature [1, 2, 3].

When increased temperature and sore throat, the two most common symptoms, are considered, our results correlate with comparative studies [5, 6, 15-21]. What is rarely mentioned in literature is complaint to bad breath. The percentage of children with this problem in both groups was very high, and amounted to about 60%.

Data that are also rarely mentioned in the literature are presence of stomach pain due to the enlarged mesenterial lymph nodes and/or spleen/liver enlargement, as well as eyelid swelling due to difficult lymph drainage from the facial and eye area. For both symptoms we found a difference between the groups – greater percentage of children that had these symptoms were infected with CMV. Grotto et al. [16] have determined that 40% of the patients have abdominal pain, although they focused exclusively on patients with EBV infection.

For two more symptoms of the disease a difference between the groups was determined in favor of CMV. The first one is skin rash, which can arise from the basic infection, but it can also appear due to the interaction between heterophil antibodies with antibiotics [7, 14]. The other symptom is the feeling of fatigue. Despite the fact that it is a subjective feeling, our results correspond to several other studies [5, 19]. Data from literature state that the feeling of tiredness and reduced physical activity can be present up to six months after infection [1, 2, 3, 9].

Jenson [7] and Wang et al. [4] showed that EBV and CMV in childhood can lead to immunosuppression and secondary viral infection with some of respiratory viruses. During the course of the disease, about 50% of infected children had some of the respiratory symptoms.

These viruses, especially EBV, have shown negative impact on the immune system and the later development of various lymphoproliferative diseases [27]. On the other hand, they may have influence on the differentiation of NK and $CD8^+$ T lymphocytes, which can later participate in defense against viral infections [28]. Also, it was shown that early-life IM protects against persistent IgE sensitization and development of allergic diseases [29].

After analyzing the results of other researchers, it can be concluded that frequency of classical clinical signs of angina, hyperemic pharynx and hypertrophic tonsils with purulent plaques is in correlation to our own [5, 6, 15-21]. It is similar with lymphadenopathy. Discrepancy in the results occurs when frequency of spleno/hepatomegaly is concerned. Saldana et al. [19] determined splenomegaly in only 16.5% of their cases, while Balasubramanian et al. [6] in 81% of their patients. In researches of Son and Shin [20] and Cengiz et al. [5] frequency of hepatomegaly is 25%, and up to 58.1% in the study taken by Gao et al. [15].

Inflammation parameters were increased in a large number of patients in both groups. Wang et al. [4] state similar percentage of children with increased CRP, while the value of SE was monitored only by colleagues from Turkey, who found elevated levels in 26.4% of their cases [5]. It was noticed that mean value for SE is about 25 mm/h and about 25 mg/l for CRP, the values not considerably high, considering that these are viral infections [11].

Only in 10% of the patients fibrinogen values were elevated, and these 10% most likely represent patients with bacterial superinfection. In contrast, about 55% of affected children have values of fibrinogen below 2 g/l, which is another proof of weakened secretory function of an affected liver.

Total number of leukocytes and lymphocytes, with slightly increased mean values that are around 15×10^9/l for leukocytes, and around 10×10^9/l for lymphocytes, and with a percentage of virocytes of about 20% in most cases, is concurrent with the data from literature [1, 2, 3, 5, 6, 15-21].

Also, frequency of increased values of transaminases in both groups correlate with the results of other researchers and literature [1, 2, 3, 5, 6, 15-21]. Mean values of about 100 μ/l for AST and somewhat higher, about 115 μ/l, for ALT indicate a mild lesion of the liver [11].

Parameter that is rarely mentioned in literature is LDH, which was increased in about 95% of examined children in our study, so that even though it is a non-specific parameter, it can still be considered reliable as a helpful diagnostic tool.

We used these three analyses as the parameters of laboratory recovery, and after seven days determined that there was significant decrease in most of the cases. An interesting difference that was noticed between the groups is the time of normalisation of the values of transaminases. In children with EBV there is faster decrease of values than in children with CMV infection, which can be used in practical work. This difference was not noticed in terms of LDH values.

When disease complications are concerned, the highest number of patients had anemia as the most common complication, which is similar with the result of Cengiz et al. [5] and Grotto et al. [16]. However, this finding must be carefully interpreted considering the lack of information about other factors that influence the emergence of anemia (diet, age of life, menstruations, growth, etc). None of the patients had a positive Coombs test, which supports the fact that anemia is entirely a consequence of infection or other mentioned factors, and not hemolysis of erythrocytes in an enlarged spleen.

A small percentage of patients had leukopenia, about 4% in both groups. Slightly higher percentage, about 6%, was determined by Son and Shin [20], and slightly lower, 2.2%, by Cengiz et al. [5], while in other comparative studies leukopenia was not mentioned as a disease complication.

It is interesting that thrombocytopenia was a more frequent complication in our patients (47%), while in research of Son and Shin [20], that percentage is considerably lower, 13.2%, and in research of Saldana et al. [19] it is present in only 7.3%. It is also interesting that thrombocytopenia in our respondents is more often presented with CMV mononucleosis.

About 20% of patients in both groups had bacterial superinfection of pharynx, with the highest number of those affected by β-hemolytic streptococcus, which was proven by determining ASOT.

Average duration of hospitalization of our patients was about a week. However, loss of time in waiting for the results of virusologic analyses must be taken into account, so that real time would have been shorter. In comparative studies average duration of hospitalization is in the range of 3.5–9 days [4, 5, 15, 20].

It is important to indicate the application of antibiotics during the disease. We have determined that a percentage of children who take antibiotics before hospitalization in both groups is about 70–75%, which is rarely mentioned in the literature.

CONCLUSION

EBV is a more common cause of IM than CMV. Valid differences in the frequency of high temperature, sore throat, bad breath, respiratory symptomatology and an-

doi: 10.2298/SARH1602056M

gina, lymphadenopathy and spleen/hepatomegaly in the groups was not discovered. Abdominal pain, eyelid swelling, skin rash, and fatigue were more common in children with CMV. Values of transaminases and LDH significantly decreased after seven days of hospitalization. In children with EBV, values of transaminases decline significantly faster. Anemia and bacterial superinfection of pharynx are the most common disease complications. Thrombocytopenia is more common in children with CMV infection.

REFERENCES

1. Luzuriaga K, Sullivan JL. Infectious mononucleosis. N Engl J Med. 2010; 362(21):1993-2000. [DOI: 10.1056/NEJMcp1001116] [PMID: 20505178]
2. Jenson BH. Epstein–Barr virus. In: Behrman ER, Kliegman MR, Jenson BH. Nelson Textbook of Pediatrics, Vol. 1. 17th ed. Belgrade: Saunders, Bard–Fin, 2009. p.1062-66.
3. Stagno S. Cytomegalovirus. In: Behrman ER, Kliegman MR, Jenson BH. Nelson Textbook of Pediatrics, Vol. 1. 17th ed. Belgrade: Saunders, Bard–Fin, 2009. p.1066-69.
4. Wang X, Yang K, Wei C, Huang Y, Zhao D. Coinfection with EBV/CMV and other respiratory agents in children with suspected infectious mononucleosis. Virol J. 2010; 7:247. [DOI: 10.1186/1743-422X-7-247] [PMID: 20858235]
5. Cengiz AB, Cultu-Kantaroğlu O, Seçmeer G, Ceyhan M, Kara A, Gürgey A. Infectious mononucleosis in Turkish children. Turk J Pediatr. 2010; 52(3):245-54. [PMID: 20718181]
6. Balasubramanian S, Ganesh R, Kumar JR. Profile of EBV associated infectious mononucleosis. Indian Pediatr. 2012; 49(10):837-8. [PMID: 23144105]
7. Jenson HB. Acute complications of Epstein–Barr virus infectious mononucleosis. Curr Opin Pediatr. 2000; 12(3):263-8. [PMID: 10836164]
8. Mijailović Z, Canović P, Gajović O, Tomašević S. Myopericarditis during acute Epstein–Barr virus infection: a case report. Med Pregl. 2006; 59(9-10):490-3. [DOI: 10.2298/MPNS0610490M] [PMID: 17345829]
9. Huang Y, Katz BZ, Mears C, Kielhofner GW, Taylor R. Postinfectious fatigue in adolescents and physical activity. Arch Pediatr Adolesc Med. 2010; 164(9):803-9. [DOI: 10.1001/archpediatrics.2010.144] [PMID: 20819961]
10. Vouloumanou EK, Rafailidis PI, Falagas ME. Current diagnosis and management of infectious mononucleosis. Curr Opin Hematol. 2012; 19(1):14-20. [DOI: 10.1097/MOH.0b013e32834daa08] [PMID: 22123662]
11. Van den Bruel A, Thompson MJ, Haj-Hassan T, Stevens R, Moll H, Lakhanpaul M, et al. Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review. BMJ. 2011; 342:d3082. [DOI: 10.1136/bmj.d3082] [PMID: 21653621]
12. Zhu MH, Liang M, Wang ZJ, Wen HY. Value of antiviral therapy for infectious monocytosis in children. Zhongguo Dang Dai Er Ke Za Zhi. 2012; 14(3):198-201. [PMID: 22433408]
13. Mullarkey C. Soothing a sore throat: the efficacy and safety of steroids in acute pharyngitis. Ir J Med Sci. 2011; 180(4):837-40. [DOI: 10.1007/s11845-011-0719-z] [PMID: 21618052]
14. Lendak D, Mihajlović D, Turkulov V, Stefan-Mikić S, Tomić S. Rash in primary Epstein–Barr virus infection. Med Pregl. 2012; 65(3-4):138-41. [DOI: 10.2298/MPNS1204138L] [PMID: 22788063]
15. Gao LW, Xie ZD, Liu YY, Wang Y, Shen KL. Epidemiologic and clinical characteristics of infectious mononucleosis associated with Epstein–Barr virus infection in children in Beijing, China. World J Pediatr. 2011; 7(1):45-9. [DOI: 10.1007/s12519-011-0244-1] [PMID: 21191775]
16. Grotto I, Mimouni D, Huerta M, Mimouni M, Cohen D, Robin G, et al. Clinical and laboratory presentation of EBV positive infectious mononucleosis in young adults. Epidemiol Infect. 2003; 131(1):683-9. [DOI: 10.1017/S0950268803008550] [PMID: 12948368]
17. Cheng CC, Chang LY, Shao PL, Lee PI, Chen JM, Lu CY, et al. Clinical manifestations and quantitative analysis of virus load in Taiwanese children with Epstein–Barr virus-associated infectious mononucleosis. J Microbiol Immunol Infect. 2007; 40(3):216-21. [PMID: 17639161]
18. Chan CW, Chiang AK, Chan KH, Lau AS. Epstein–Barr virus-associated infectious mononucleosis in Chinese children. Pediatr Infect Dis J. 2003; 22(11): 974-8. [PMID: 14614370]
19. González Saldaña N, Monroy Colín VA, Piña Ruiz G, Juárez Olguín H. Clinical and laboratory characteristics of infectious mononucleosis by Epstein–Barr virus in Mexican children. BMC Res Notes. 2012; 5:361. [DOI: 10.1186/1756-0500-5-361] [PMID: 22818256]
20. Son KH, Shin MY. Clinical features of Epstein–Barr virus-associated infectious mononucleosis in hospitalized Korean children. Korean J Pediatr. 2011; 54(10):409-13. [DOI: 10.3345/kjp.2011.54.10.409] [PMID: 22232623]
21. Evci C, Akalin H, Heper Y, Yilmaz E, Bakir Ozbey S, Mistik R, et al. Retrospective evaluation of patients who were diagnosed as infectious mononucleosis between 1984-2005. Mikrobiyol Bul. 2007; 41(1):95-100. [PMID: 17427557]
22. Powell KR. Fever and fever without focus. In: Behrman ER, Kliegman MR, Jenson BH. Nelson Textbook of Pediatrics, Vol. 1. 17th ed. Belgrade: Saunders, Bard-Fin; 2009. p.839-46.
23. Ballin A, Senecky Y, Rubinstein U, Schaefer E, Peri R, Amsel S, et al. Anemia associated with acute infection in children. Isr Med Assoc J. 2012; 14(8):484-7. [PMID: 22977967]
24. Konuş OL, Ozdemir A, Akkaya A, Erbaş G, Celik H, Işik S. Normal liver, spleen and kidney dimensions in neonates, infants, and children: evaluation with sonography. AJR Am J Roentgenol. 1998; 171(6):1693-8. [DOI: 10.2214/ajr.171.6.9843315] [PMID: 9843315]
25. Dunn JO, Clark AV. Basic Statistics: A Primer for the Biomedical Sciences. 4th ed. Hoboken: John Wiley & Sons; 2009.
26. Park JM, Shin JI, Lee JS, Jang YH, Kim SH, Lee KH, et al. False positive immunoglobulin M antibody to Cytomegalovirus in child with infectious mononucleosis caused by Epstein Barr virus infection. Yonsei Med J. 2009; 50(5):713-6. [DOI: 10.3349/ymj.2009.50.5.713] [PMID: 19881978]
27. Azzi T, Lünemann A, Murer A, Ueda S, Béziat V, Malmberg KJ, et al. Role for early-differentiated natural killer cells in infectious mononucleosis. Blood. 2014; 124(16):2533-43. [DOI: 10.1182/blood-2014-01-553024] [PMID: 25205117]
28. Kimura H, Kawada J, Ito Y. Epstein–Barr virus-associated lymphoid malignancies: the expanding spectrum of hematopoietic neoplasms. Nagoya J Med Sci. 2013; 75(3-4):169-79. [PMID: 24640173]
29. Saghafian-Hedengren S, Sverremark-Ekström E, Linde A, Lilja G, Nilsson C. Early-life EBV infection protects against persistent IgE sensitization. J Allergy Clin Immunol. 2010; 125(2):433-8. [DOI: 10.1016/j.jaci.2009.09.033] [PMID: 19963258]

Клиничке и лабораторијске разлике између Епстин–Бар и цитомегаловирусне инфективне мононуклеозе код деце

Раша Медовић[1], Зоран Игрутиновић[1,2], Ружица Радојевић-Марјановић[3], Славица Марковић[1,2], Зорица Рашковић[1,2], Александра Симовић[1,2], Јелена Танасковић-Несторовић[1,2], Марија Радовановић[1,2], Биљана Вулетић[1,2]

[1]Педијатријска клиника, Клинички центар, Крагујевац, Србија;
[2]Универзитет у Крагујевцу, Факултет медицинских наука, Крагујевац, Србија;
[3]Клиника за инфективне болести, Клинички центар, Крагујевац, Србија

КРАТАК САДРЖАЈ

Увод Инфективна мононуклеоза најчешће је узрокована Епстин–Бар (*Epstein–Barr*) вирусом (ЕБВ), а у мањем проценту цитомегаловирусом (ЦМВ).

Циљ рада Циљ рада је био да се утврде клиничке и лабораторијске разлике између ЕБВ и ЦМВ инфективне мононуклеозе код деце.

Методе рада Урађено је кохортно ретроспективно аналитичко истраживање. Коришћени су подаци из историја болести током шестогодишњег периода и праћени анамнестички подаци, учесталост инспекцијски и палпаторно добијених налаза при физикалном прегледу, неколики лабораторијски тестови, налази ехосонографског прегледа абдомена и појава компликација болести. Статистичка обрада података урађена је у програму *SPSS 20*.

Резултати Укупно је испитано 137 деце, од којих 85,4% са ЕБВ и 14,6% са ЦМВ инфекцијом. Инфицирана деца су најчешће била млађа од осам година. Чешће су оболевали дечаци. Није било разлике у учесталости повишене температуре, гушобоље, задаха из уста и респираторне симптоматологије између испитиване деце. Пронађена је разлика у учесталости стомачног бола, отока очних капака, оспе по кожи и малаксалости. Није доказана разлика у учесталости ангине, лимфаденопатије и спленохепатомегалије између група. Вредности трансаминаза и лактичне дехидрогеназе значајно су се смањивале после седам дана болничког лечења у обе групе испитаника. Код деце са ЕБВ вредности трансаминаза су се нормализовале брже него код деце са ЦМВ. Анемија и бактеријска суперинфекција ждрела су биле најчешће компликације болести. Тромбоцитопенија је била чешћа код деце са ЦМВ. Хоспитализација је у просеку трајала 6,7 дана.

Закључак Код деце са ЦМВ чешће се јављају бол у стомаку, оток очних капака, оспа по кожи, малаксалост и тромбоцитопенија. Код деце са ЕБВ вредности трансаминаза се смањују знатно брже.

Кључне речи: инфективна мононуклеоза; хумани херпесвирус 4; деца

Примљен • Received: 25/03/2015 **Прихваћен • Accepted:** 03/06/2015