

## Case Report

**CMV (cytomegalovirus) infection in infants with leukocytosis without symptoms: A Case report**Arghavan Hosseinpouri<sup>1</sup> ■ Narges Obeidi<sup>2,3</sup> ■, GholamReza Fathpour<sup>1\*</sup> ■<sup>1</sup> Department of Cellular and Molecular Sciences, Faculty of Sciences, Persian Gulf University, Bushehr, Iran.<sup>2</sup> Department of Hematology, School of Paramedicine, Bushehr University of Medical Sciences, Bushehr, Iran.<sup>3</sup> Blood Transfusion Organization, Bushehr, Iran.<sup>4</sup> Department of Pediatric hematology and oncology, Bushehr University of Medical Sciences, Bushehr, Iran.**Article Information**

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**Abstract**

**Introduction:** CMV is an infectious disease usually transferred from pregnant women to the fetus or during breastfeeding. The symptoms include losing weight at birth, leukocytosis, and diarrhea.

**Case presentation:** In this case, the patient was a one-year-old girl. On initial examination, we did not observe swelling, tenderness, skin inflammation, or other symptoms such as splenomegaly or hepatomegaly, except in the CBC test that showed leukocytosis. The infant's mother did not have any disease during pregnancy. The experiments prescribed for diagnosing the causes of leukocytosis were CBC, urine analysis, immunoassay tests for EBV with the ELFA method, CMV with the CLIA method, serologic tests for COVID-19, wright and Widal agglutination, and 2ME tests for Brucella.

**Conclusions:** The results showed that the rate of IgM and IgG antibody were 27.688 and 228.761, respectively. There were no other signs and symptoms in the girl. Meanwhile, numerous papers indicated that CMV infection is normally associated with weight loss, diarrhea, and splenomegaly. However, in our case, the infant did not show any other signs, and in this sense, she was a specific case. Based on our findings, it is suggested that diagnosis carried out specifically on an infant should consider various aspects and assumptions along with what current findings describe.

**Keywords:** Cytomegalovirus Infections, Infectious Disease Transmission, Case Reports, Leukocytosis, Infant, Splenomegaly.

## 1. Introduction

CMV(cytomegalovirus) is a congenital infection (1). Ten to fifteen percent of newborns show symptomatic congenital infection. The most common effect is observed in patients with immune deficiency, children and the elderly (2). CMV infects different cells like the epithelial and endothelial cells (as retinal cells), fibroblast, smooth muscle cells, leukocytes and dendritic cells(2). Therefore, regarding the variety of infected sources, CMV infection shows signs like weight loss at birth, organ involvement, neurological disorders such as seizures, fever, enlargement of spleen and lymph nodes, diarrhea, and skin rash (3,4).

Research shows that 15% of infants with CMV suffer from loss of hearing, vision and nervous system. If treatment is not given in time, these complexities remain forever (5).

Important signs of CMV infection are leukocytosis, anemia, and thrombocytopenia. Lymphocytes cells are large and atypical (6). When naive T-cells are reduced, their diversity decreases (7). Since B-cells need T-cells for cytokine production and signaling, the fewer T-cells rate leads to fewer B-cells (8,9).

The immune response to CMV infection in the first days is IgM. After two to three weeks, IgG and T cells contribute to cellular immunity(10)(11)(12). The PCR technique is used for CMV. Elisa technique is used for detecting viral genome and infection in time and at late stages. Elisa shows antibody type and rate (13). What has been said so far about the signs and symptoms of

cytomegalovirus infection was not observed in this patient, thus going against the previous evidence.

The patient we studied was a one-year-old girl who showed no signs and symptoms other than leukocytosis after clinical and laboratory examination.

## 2. Case Presentation

The case was a one-year-old girl from Bushehr, Iran. The infant's mother had neither had disorders or infections during pregnancy, nor shown a history of infection during breastfeeding. The CBC test indicated a large number of white blood cells (leukocytosis, lymphocytosis with neutropenia) and thrombocytopenia as shown in Table 1. The smear of blood cells showed that red blood cells were microcytic and white blood cells were leukocytosis (cells were mature and blast cells were not observed). As shown in Table 1, ESR rate and ferritin was normal. The urine analysis test is also reported in Table 1. We traced WBC, RBC and epithelial cells in the urine sample. While the CBC test and urine analysis of the infant were signs of the disorder, the infant did not show other symptoms like diarrhea; organ involvement; impaired vision, hearing, or nervous system. In addition, ultrasonography did not report any disorder in the liver or the kidneys. Moreover, spleen abnormality and enlargement were not found.

Serologic and immunoassay tests are prescribed for infectious diseases like EBV, typhoid, COVID-19, and CMV. The results are described in Table 2. As shown in Table

1, considering leukocytosis in the CBC test, flowcytometry was recommended. As the girl had no other signs and symptoms, the researchers assumed the likelihood of leukemia. However, the flowcytometry results demonstrated that markers were normal or their size did not increase. The EBV immunoassay test was reported negative. The wright agglutination test, 2ME wright, and Widal agglutination test were negative. In addition, COVID19 antibody was reported negative. The result of the CMV immunoassay test was the missing link. The rate of IgM and IgG against CMV infection were very high. The results of the infectious test showed that the girl had CMV infection. IgG was 228.761 Au/ml. However, the reference range for the negative result is <10.0 with the CLIA method. For IgM CMV, the result showed 27.688 Au/ml, while for the negative CMV with the CLIA method, it should be <8.0. All the other tests, like clinical examinations, and abdominal and kidney ultrasonography were normal. No disorder, tissue degradation, or cyst was found in kidneys. According to the literature, CMV in infants could be associated with neurologic disorders and seizures(14). Nevertheless, our neurological examinations did not show any signs and the girl never had seizures. According to our results, the girl had CMV infection. As she had no sign and abnormality and her growth was normal, no drug was prescribed. If she had immune system deficiency or had undergone chemotherapy, she would have been recommended to use anti-viral medicine. We just followed up her condition for six months and checked her leukocytosis.

### 3.Discussion

As described in the introduction, numerous papers report neurodegeneration, impaired hearing, vision and organ involvement, diarrhea, anemia, leukocytosis in CMV infection. To diagnose CMV infection, we need to check for anemia, gastrointestinal(15), CMV cyst in kidney(16), and urine culture (17)(18). With no disease history, congenital infection, or any other signs and symptoms, this case was very ambiguous. According to our results, in CMV infection particularly in infants, specific attention should be paid to common signs like leukocytosis although leukocytosis is a common symptom in leukemia (ALL)(19). Leukemia is very rare among children and only .5% of infants with leukocytosis may have leukemia type ALL. However, CMV infection among infants is minimal (.6–.7%) (10). Differentiating between an infectious disease and leukemia without any other signs and symptoms is questionable. However, it seems that serologic and immunoassay tests for detecting infectious diseases should be given priority over prescribing cancer tests like flowcytometry, particularly because of the costs associated with it. Various papers reported congenital CMV and possible effects on fetus during and after pregnancy. Having found that, we need to consider a small percent of infants (only .64 %) who have CMV with infection during the embryonic period (20)(21)(22). The researchers suggest that more attention be paid to microbial tests specifically in infants as their signs and symptoms were very different from what had been reported in the literature. According to our reports, the symptoms seem unique in some infants.

The spleen of an infant won't be completely mature until two years and they have naive immune systems. Therefore, they cannot respond to microbes and viruses like adults.

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## Conflicts of interest

The authors declare no conflict of interest.

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Hematology			
Test	Result	Unit	Reference Range
ESR 1hr	9	mm/h	0-10
CBC			
W.B.C.	H 23560	Cell/ $\mu$ L	4000-11000
Differential			
Neutrophil	(L) 11.9%	-	-
Lymphocyte	(H) 82.4 %	-	-
Monocyte	5.6%	-	-
Eosinophil	----%	-	-
Basophil	0.1 %	-	-
R.B.C.	4.96	$10^{*6}\mu$ L	4-5.4
HGB	11.3	g/dL	12.3- 15.3
HCT	L 34.4	%	34.5- 44.6
M.C.V.	L 69.4	fL	80-100
M.C.H.	L 22.8	pg	26-34
M.C.H.C.	32.8	g/dL	30-36
Platelets	266000	Cell/ $\mu$ L	140000-450000
RDW-CV	14.4	%	11.6-14.5
MPV	10.2	fL	7-11
Hormone			
Ferritin	22.21	ng/mL	Female: 5.0- 223.5
Urine Analysis			
Macroscopic			
Color	Yellow		
Appearance	Clear		
Specific Gravity	1.005		
pH	7		
U.Protein	Negative		
Glucose	Negative		
Urine Ketone	Negative		
Bilirubin	Negative		
Urobilinogen	Negative		
W.B.C.	1-2		
R.B.C	0-1		
Epithelial Cells	3-4		
Bacteria	Negative		
Mucus	Negative		
Casts	Negative		
Crystals	Negative		
Leukocyte esterase	Negative		
Yeasts	Negative		
Nitrite	Negative		
H: High			
L: Low			
Urine culture: No growth after 24 hrs			

**Table1.** The hematology test was show anemia and lymphocytosis and thrombocytosis. The rate of ferritin with CLIA method was reported normal. The urine analysis test was reported with a trace RBC and WBC and Epithelial cell.

<b>Serology</b>			
Test	Results	Unit	Reference Range
Wright Agglutinin	Negative	-	Positive: $\geq 1/80$
2ME Wright	Negative	-	-
Widal Agglutination Test	Negative		O Ag Positive: $\geq 1.80$ H Ag Positive: $\geq 1.40$
Covid19 IgM	0.01	Index	Negative: $< 0.9$ Equivocal: $0.9- 1.1$ Positive: $> 1.1$ Diagnostic Sensitivity: 79.4% Diagnostic Specificity: 97.3 %
Covid19 IgG	0.01	Index	Negative: $< 0.9$ Equivocal: $0.9- 1.1$ Positive: $> 1.1$ Diagnostic Sensitivity: 94.1 % Diagnostic Specificity: 98.3 %
<b>Immunoassay- Infectious Disease</b>			
Test	Result	Unit	Reference Range
CMV Antibody (IgG)	228.761	Au/mL	Negative: $< 10.0$ Equivocal: $10.0 = < \text{Titer} < 14.0$ Positive: $\geq 14.0$
CMV Antibody(IgM)	27.688	Au/mL	Negative: $< 8.0$ Equivocal: $8.0 = < \text{Titer} < 12.0$ Positive: $\geq 12.0$
EBV (VCA) (IgM)	0.01	IU	Negative: $< 0.12$ Equivocal: $\geq 0.12$ to $< 0.19$ Positive: $\geq 0.19$

**Table2.** The serologic analysis for covid19 and typhoid serologic test was reported normal without increase in IgM antibody for first days' infection and IgG antibody for infection in the past. The immunoassay test for EBV with elisa method reported negative but immunoassay test for CMV with CLIA method was show increase high in IgM and IgG, that this show the infant has CMV infection.