SERUM ADENOSINE DEAMINASE LEVELS IN INFANTS WITH CYTOMEGALOVIRUS INFECTION

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Abstract

Background: Human cytomegalovirus (HCMV) is the most common cause of congenital and perinatal infections. Adenosine deaminase (ADA) deficiency leads to B and T cell dysfunction resulting in immunosuppression thereby enhancing susceptibility to infections.

Objective: To investigate serum levels of ADA among infants infected with HCMV.

Patients & Methods: HCMV infection was diagnosed based on the detection of HCMV-specific IgM using ELISA among 62 symptomatic and 50 healthy looking infants. Then HCMV specific IgM positive sera and negative sera were subjected to measurement of ADA level.

Results: The mean serum ADA level of symptomatic infants infected with HCMV (3.16 ± 3.34 U/L) was found to be of significant difference when compared with that of both symptomatic and asymptomatic infants who were sero-negative for HCMV specific IgM (7.78 ± 4.71 U/L, $P < 0.05$) and (10.38 ± 5.54 U/L, $P < 0.05$) respectively.

Conclusion: Infants with serum ADA deficiency are susceptible to HCMV infection.

Key words: Human cytomegalovirus, adenosine deaminase, infants.

Iraqi J Med Sci 2004; Vol.3(2): 148-150

Introduction

HCMV is the most common cause of congenital and perinatal infections throughout the world[1]. The most severe forms of this viral disease develop in 5-10% of infants infected *in utero* and these infants have signs of severe generalized infections involving the liver and CNS. Both humoral and cellular immune responses are important in protective immunity against HCMV infection[2].

Deficiency of ADA is severe combined immunodeficiency (SCID) that is inherited as an autosomal trait. The patient is presented in infancy with recurrent infections[3]. This deficiency is also responsible for enhancing susceptibility to congenital infections[4]. Immune deficiency is thought to occur by lymphoid cells that are particularly sensitive to the toxic effects of adenosine and 2-deoxyadenosine that accumulate due to ADA deficiency[5]. Hence, the aim of this study was to investigate the deficiency of ADA among HCMV infected infants.

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Received 10th January2004: Accepted 30th March 2004.

Patients & Methods

A total of 112 cases (from Al-Kadymia teaching hospital) were included in this study. They were divided into two groups; group A included 62 symptomatic babies clinically suspected to be infected with HCMV, those include babies born with various manifestations like jaundice, rash, hepatomegaly, neurological manifestations (like microcephaly, hydrocephaly, intracerebral calcification, meningocele), intrauterine growth retardation and eye abnormalities (like chorioretinitis, cataract, absence of eye). However, all the cases were presented with various combinations of symptoms. Their ages ranged between one and sixty days. Group B included 50 healthy looking newborns as indicated by general clinical examination in the labor room from which cord blood was collected.

Blood samples were collected from each individual included in this study. Serum was then separated and dispensed into tightly closed capped tubes in 0.2ml aliquots and stored at -20°C until use. All sera were screened for HCMV specific IgM using ELISA (Biokit-Spain). Procedures and interpretation of the results were followed as written in the instructions supplied with the kit.

Total ADA levels were measured [(6)] in the sera of each individual which were grouped as

follows according to the HCMV specific IgM results: Group 1 (G1): includes all sera found to be positive for HCMV specific IgM using the ELISA technique (N=9). Group 2 (G2): includes randomly chosen sera from symptomatic infants found to be negative for HCMV specific IgM using ELISA technique (N=8). Group3 (G3): includes randomly chosen sera from healthy looking newborns (group B) and all were negative for HCMV specific IgM using ELISA technique (N=22).

Results

HCMV infection, as indicated by specific IgM measured by ELISA was detected in 9 out of 62 (14.52%) symptomatic infants. None of the cord sera obtained from healthy looking newborns was infected with HCMV as evidenced by the negative result by ELISA for specific IgM.

The mean value of serum ADA of symptomatic HCMV infected infants (G1) was found to be of statistically significant difference ($P < 0.05$) when compared with that of both symptomatic non HCMV infected ones (G2) (Tables 1, 2) and asymptomatic non HCMV infected infants (G3). However, no significant difference ($P > 0.05$) was found regarding the mean value of serum ADA of symptomatic and asymptomatic non HCMV infected infants (Table 3).

Table 1: Mean ± SD of serum adenosine deaminase (ADA) level in U/L among symptomatic infants with or without human cytomegalovirus (HCMV)

Symptomatic infants	Number of cases No. (%)	Mean ADA ± SD
HCMV infected	9 (52.94%)	3.16±3.34
non HCMV infected	8 (47.06%)	7.78±4.71
Total	17	

t = -2.31, P< 0.05, SD= standard deviation

Table 2: Mean ± SD of serum adenosine deaminase (ADA) level in U/L among symptomatic human cytomegalovirus (HCMV) infected and asymptomatic non HCMV infected infants

Group of infants	Number of cases No. (%)	Mean ADA ± SD
Symptomatic, HCMV infected	9 (29.03%)	3.16 ± 3.34
Asymptomatic, Non HCMV infected	22 (70.96%)	10.38 ± 5.54
Total	31	

t= 4.46, P< 0.05, SD= standard deviation

Table 3: Mean ± SD of serum adenosine deaminase (ADA) level in U/L among symptomatic non human cytomegalovirus (HCMV) infected and asymptomatic non HCMV infected infants

Group of infants	Number of cases No. (%)	Mean ADA ± SD
Symptomatic, Non HCMV infected	8(26.66%)	7.78 ± 4.71
Asymptomatic non HCMV infected	22(73.33%)	10.38 ± 5.54
Total	30	

t= 1.27, P > 0.05, SD= standard deviation

Discussion

HCMV is the most common cause of congenital infections, affecting 0.2% of all live births in industrialized countries and up to 3% in developed countries[7]. Specific as well as non specific immune surveillance mechanisms play a role in controlling HCMV infection[8]. Cell mediated immunity is important for the recovery from HCMV infection[9]. Although HCMV infection causes few symptoms in immunocompromized adults, about 10% of newborns with congenital infections develop symptoms[7]. It is generally accepted that the fetus and infants have a high susceptibility to viral infections related to the immaturity of the immune system. However, the mechanisms involved remain poorly understood[10].

ADA deficiency is an autosomal recessive character that leads to SCID. The pathophysiology and molecular biology vary, however, the lack of T and B cell function is the common end point in all forms of SCID. In this study, a significant difference was found regarding the mean value of serum ADA among HCMV infected infants when compared with the control groups. It seems likely that such findings agree with others who documented that patients with ADA deficiency are susceptible to TORCH, as the enzyme deficiency results in B and T cell dysfunction resulting in a state of immunosuppression[4]. In addition, such children usually succumb to infection early in life[11, 12].

It will be of both interest and importance to screen cord sera for the prevalence of this type of SCID, for these children should not receive live vaccines especially OPV and BCG. It is also of interest to perform molecular studies to identify any specific genetic defects regarding this type of immune deficiency.

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