Subpopulation Composition of Peripheral Blood Lymphocytes in Children with Infectious Mononucleosis

V. V. Novitskii, O. I. Urazova, I. O. Naslednikova, A. P. Pomogaeva, and L. V. Syusina

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 134, No. 7, pp. 66-68, July, 2002
Original article submitted June 28, 2001

In patients with viral and bacterial infectious mononucleosis during the acute period of disease and clinical convalescence blood content of $CD72^+$ and $CD16^+$ lymphocytes increased compared to normal. The count of $CD8^+$ cells increased in viral mononucleosis during convalescence and these changes persist in delayed periods after convalescence. In bacterial mononucleosis the content of $CD72^+$ lymphocytes return normal 18 months after convalescence.

Key Words: *infectious mononucleosis; lymphocytes; CD antigens*

Blood system is one of the most sensitive systems of the macroorganism to damage caused by infection agents. At the same time blood cells play the key role in the formation of antiinfectious immunity. Characteristic hematological changes observed in infectious mononucleosis (IM) (increased counts of mononuclears in the peripheral blood and their qualitative changes) are now regarded as a specific response of the immune system to the infection agent [2,3,9]. In 90% patients IM is caused by Epstein—Barr virus [4,10,11, 13,14]. Mononucleosis syndrome can also be caused by herpes simplex virus, cytomegalovirus, varicella, influenza, measles viruses, and the agents of diphtheria, pseudotuberculosis, toxoplasmosis, *etc.* [11,14].

The role of leukocytes in the pathogenesis of IM attracted much recent attention. Atypical mononuclears (AM) detected in the peripheral blood of patients with IM represent a morphologically heterogeneous population of transformed immunoblasts originating from both B and T cells. It is also known that T cells functioning as suppressors and natural killers regulate the growth of transformed lymphocytes by preventing malignization of the lymphoproliferative process [4,5,9,12]. On the other hand, the structure and function of lymphoid cells in IM are still little studied.

We investigated the subpopulation composition of peripheral blood lymphocytes in viral (VIM) and bacterial IM (BIM).

MATERIALS AND METHODS

Sixty-nine children aged 7-14 years with IM of medium severity running an acute smooth course were observed. The patients were examined during acute period (developed clinical hematological picture of the disease, group 1), during convalescence (group 2), and in delayed period (18 months) after the disease (group 3). IM was diagnosed on the basis of clinical and hematological signs [10]. The agent was identified by bacteriological and serological methods (enzyme immunoassay, indirect immunofluorescence). Epstein—Barr virus in the sera was detected by polymerase chain reaction (PCR). VIM group (n=35) included patients with mononucleosis caused by Epstein—Barr virus, cytomegalovirus, and herpes simplex virus. BIM group (n=34) consisted of patients with acute staphylococcal and streptococcal tonsillitis, oral diphtheria, and enteric pseudotuberculosis associated with the mononucleosis syndrome.

Control group consisted of 30 healthy children (IIA health group).

Department of Pathophysiology, Department of Childhood Infections, Siberian State Medical University, Tomsk. ***Address for correspondence:*** Urazov@mail2000.ru. Urazova O. I.

0007-4888/02/1341-057$27.00

Peripheral blood were analyzed by routine hematological methods [6]. Peripheral blood smears were prepared by the method of venous blood leukoconcentration (with Trilon B) [6].

Lymphoid cell subpopulations were studied using monoclonal antibodies (Sorbent Firm, Moscow) in the lymphocytotoxic test [8].

The results were statistically processed using Mann—Whitney nonparametric test [1,7].

RESULTS

All IM patients presented with typical combinations of clinical symptoms: fever, catarrhal inflammation of upper airways, enlarged lymph nodes, liver, and spleen.

Characteristic hematological changes were observed. The total leukocyte count increased by 70 and 62% in VIM and BIM, respectively, ($p<0.001$). This was associated with an increase in the absolute counts of lymphocytes, monocytes, and AM (by 78, 135%, and 15 times, respectively, in comparison with normal in VIM, $p<0.001$, and by 78, 61%, and 10-fold in BIM, $p<0.001$). During convalescence the count of monocytes returned to normal in both groups of patients, while the counts of AM and lymphocytes remained above the normal. These changes persisted 18 months after convalescence.

Study of the subpopulation composition of peripheral blood lymphocytes showed that the counts of $CD72^+$ and $CD16^+$ lymphocytes increased during the acute period of VIM, while the relative number of cells expressing CD3 antigen decreased compared to normal. The absolute count of lymphocytes remained virtually unchanged (Table 1). The count of $CD3^+$ cells returned to normal during convalescence.

The counts of $CD72^+$ and $CD16^+$ lymphocytes remained above the control and the absolute count of $CD8^+$ cells increased. The counts of $CD72^+$, $CD16^+$, and $CD8^+$ lymphocytes remained high 18 months after VIM in comparison with those in healthy children (Table 1).

In BIM the counts of $CD72^+$ and $CD16^+$ cells increased compared to normal during the acute period of the disease (Table 1) and these changes persisted during convalescence. The content of $CD72^+$ cells returned to normal in these patients in delayed period after convalescence, while the count of $CD16^+$ cells remained above the control.

Hence, the counts of $CD72^+$ and $CD16^+$ lymphocytes increased in patients with VIM and BIM during the acute period and convalescence in comparison with the normal. In VIM the number of CD8 cells also increased and these changes persisted during the delayed period after convalescence. After BIM the count of $CD72^+$ lymphocytes returned to normal 18 months after convalescence.

TABLE 1. Subpopulation Composition of Peripheral Blood Lymphocytes in IM Patients ($\bar{X}\pm m$)

Groups	$CD72^+$		$CD3^+$		$CD8^+$		$CD16^+$	
	%	g/liter	%	g/liter	%	g/liter	%	g/liter
Healthy children (n=31)	17.45±1.76	0.47±0.05	31.71±3.31	0.94±0.12	13.72±1.72	0.37±0.06	15.08±2.90	0.39±0.09
Patients with VIM								
1 (n=17)	26.12±3.90***	1.22±0.18*	20.71±2.68***	0.91±0.11	15.41± 2.41	0.44±0.09	17.76±2.99	0.88±0.19***
2 (n=26)	22.62±2.98	0.82±0.09***+	30.71±3.25+	1.13±0.15	17.38±2.63	0.57±0.08***	16.00±2.05	0.65±0.11***
3 (n=9)	34.44±6.82***	1.12±0.26**	40.89±7.57	1.29±0.24	30.78±6.66***	1.11±0.03***	25.22±6.30	1.02±0.28***
Patients with BIM								
1 (n=28)	22.71±2.21	0.94±0.13**	26.36±3.06	1.15±0.16	12.14±1.83	0.50±0.10	14.07±2.30	0.60±0.10***
2 (n=10)	24.10±3.70	1.12±0.18*	27.60±5.12	1.20±0.24	20.20±8.07	0.47±0.06	11.40±1.57	0.57±0.10***
3 (n=6)	19.50±2.01	0.68±0.18	26.83±8.06	0.94±0.26	19.33±5.24	0.60±0.14	21.50±6.67	0.66±0.16***

Note. *$p<0.001$, **$p<0.01$, ***$p<0.05$ compared to healthy children, +$p<0.05$ compared to group 1.

REFERENCES

1. B. S. Bessmertnyi, *Mathematical Statistics in Clinical, Preventive, and Experimental Medicine* [in Russian], Moscow (1967).
2. A. G. Bukrinskaya and V. M. Zhdanov, *Molecular Bases of Virus Pathogenicity* [in Russian], Moscow (1991).
3. M. O. Gasparyan, *Infectious Mononucleosis in Children*, Abstract of Doct. Med. Sci. Dissertation, Moscow (1977).
4. V. V. Ivanova, O. V. Rodionova, A. A. Bukina, *et al.*, *Vestn. Perinatol. Pediatr.*, No. 1, 43-48 (2001).
5. V. A. Isakov, V. V. Borisova, and D. V. Isakov, *Herpes. Pathogenesis and Laboratory Diagnosis. Manual for Physicians*, St. Petersburg (1999).
6. *Laboratory Methods of Investigation in Clinical Practice. Handbook*, Ed. V. V. Men'shikov [in Russian], Moscow (1987).
7. G. F. Lakin, *Biometry* [in Russian], Moscow (1980).
8. R. V. Petrov, R. M. Khaitov, B. V. Pinegin, *et al.*, *Immunologiya*, No. 6, 51-62 (1992).
9. V. E. Polyakov, V. N. Lyalina, M. L. Vorob'ev, *et al.*, *Epidemiol. Infek. Bolezni*, No. 6, 50-54 (1998).
10. *Manual of Infectious Diseases of Children*, Ed. V. F. Uchaikin [in Russian], Moscow (1999).
11. J. Cozad, *Nurse Pract.*, **21**, No. 3, 14-16 (1996).
12. S. Imai, *Hokkaido Igaku Zasshi*, **65**, No. 5, 481-492 (1990).
13. H. Naher and D. Petzoldt, *Hautarzt,* **43**, No. 3, 114-119 (1992).
14. V. Shuster and N. W. Kreth, *Eur. J. Pediatr.*, **151**, No. 11, 794-798 (1992).