EFFECT OF PERTUSSIS ANTIBODIES ON INDUCTION OF SUPPRESSOR CELLS OF HUMORAL IMMUNITY OF MICE

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The corpuscular pertussis vaccine used nowadays is known to be the source of serious postvaccinal complications, including autoimmune and encephalic manifestations. In recent years, in order to explain the side effects of vaccine preparations, great importance has been attached to the presence of antigenic determinants, common with the antigenic structures of the host, in them [3]. In relation to pertussis vaccine, the antigenic similarity of bacterial subtances with mammalian brain substance, which in turn, contains the Thy-1 antigen, a marker of T lymphocytes, is an interesting fact [1, 2]. Assuming the presence of common antigenic determinants, the investigation described below was carried out in order to study the action of pertussis antibodies on Thy-1-positive cells, to which are ascribed a very important role in the regulation of the immune response of the organisms.

EXPERIMENTAL METHODS

The following substances were used: 1) standard pertussis agglutinating serum, batch 192, produced by the N. F. Gamaleya Research Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR; 2) antibodies against ultrasonic pertussis antigen and dialyzate antigen [4], purified by immunosorption [6]; 3) antitoxic staphylococcal serum, produced by the N.F. Gamaleya Institute. Optimal doses of the serum preparations were determined by preliminary experiments; they were 0.2 ml for the standard pertussis agglutinating serum and 700 μg as protein for the pure antibodies against these antigens isolated from it. Antitoxic staphylococcal serum was used in a dose of 0.2 ml per mouse.

The effect of pertussis antibodies on T suppressor cells was studied on a model of induction of specific suppression in an adoptive transfer system [7] on male (CBA × C57Bl/6)F_1 mice

TABLE 1. Effect of Pertussis Antisera on Ability of Spleen Cells from Donors with Induced Suppressive Activity to Suppress Humoral Activity to Sheep Red Blood Cells in Recipients

Type of serum preparation	Time of injection of prepn., days	Number of AFC per spleen*			p (expt. – control of immune response
		control of immune response	control of suppression of immune response	expt.	
Pertussis agglutinating serum (0.2 ml)	1	74100 (4,83±0,03)	4565 (3,75±0,03)	77490 (4,89±0,04)	>0,1
	13	74100 (4,83±0,03)	4565 (3,65±0,03)	36440 (4,56±0,05)	<0,01
Antibodies to ultrasonically treated antigen (700 μg)	1	76050 (4,88±0,20)	4040 (3,60±0,06)	66340 (4,82±0,10)	>0,1
	13	76050 (4,88±0,20)	4040 (3,60±0,06)	27434 (4,44±0,08)	<0,01
Antibodies to dialyzate antigen (700 μg)	1	57825 (4,76±0,07)	3650 (3,56±0,04)	24740 (4,39±0,05)	<0,01
	13	57825 (4,76±0,07)	3650 (3,56±0,04)	4673 (3,67±0,04)	<0,01
Antitoxic staphylococcal serum (0.2 ml)	1	57825 (4,76±0,07)	3650 (3,56±0,04)	4562 (3,66±0,05)	<0,01

Legend. *Absolute values of number of AFC, log of number of AFC and mean error in parentheses.

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weighing 18-20 g (from the Rappolovo Nursery), which were incubated intraperitoneally with the test serum preparations in optimal doses in a volume of 0.5 ml, 24 h or 13 days after injection of a dose of sheep red blood cells (SRBC) inducing T suppressor cells.

EXPERIMENTAL RESULTS

The results are given in Table 1. Injection of $5 \cdot 10^7$ splenocytes from donors dying on the 14th day after immunization with SRBC in a dose of $5 \cdot 10^9$, into recipient mice regularly led to suppression of the immune response. In all experiments a high degree of suppression of formation of antibody-forming cells (AFC) was observed in the recipients. In the control of the immune response (without transfer of donors' splenocytes) the number of AFC on the 5th day after immunization with SRBC in a dose of $2 \cdot 10^8$ was 57,825-76,050 per spleen; in the case of injection of splenocytes from mice with induced suppressive activity, it was 15-17 times less. In groups in which the donors were treated with pertussis serum 24 h after injection of $5 \cdot 10^9$ SRBC, a suppression effect was observed on transfer of the splenocytes. The AFC level in the recipients 5 days after immunization with $2 \cdot 10^8$ SRBC was not below the AFC level in the control mice, receiving SRBC alone in the same dose. Complete abolition of suppression also was observed on treatment of the donors with total purified pertussis antibodies, isolated on the immunosorbent with ultrasonically treated pertussis antigen.

Pure antibodies to dialyzate pertussis antigen also were investigated. This dialyzate antigen is distinguished by strong immunogenic activity combined with almost complete areactogenicity when injected into animals. Treatment of the donors with antibodies to pertussis dialyzate also reduced the intensity of suppression during syngeneic transfer, but it was not completely abolished. The level of AFC in the recipients remained significantly lower than in the control mice (Table 1).

The specificity of the observed phenomenon and its association with pertussis antibodies were confirmed in experiments using a different antibacterial serum, namely staphylococcal antitoxic serum. Injection of this serum into the donors at the same times did not prevent the formation of cells suppressing humoral responses in recipients in them (Table 1).

Changing the time of injection of the serum pertussis preparations into donors of the splenocytes to the 13th day after immunization with SRBC led to reduction of the suppression abolition effect. Splenocytes obtained from these donors essentially preserved the ability to suppress AFC formation by the recipients (Table 1). These data are evidence that pertussis antibodies act predominantly on precursor cells and not on mature suppressors of humoral immunity.

The use of antipertussis immunoglobulins, isolated in the pure form, in the experiments confirmed the connection of the antilymphocytic action observed with antibody production in response to injection of pertussis antigens. As a result of these experiments a quantitatively different immunomodulating effect of the antipertussis antibodies was discovered: antibodies to a whole-cell pertussis vaccine had a marked action on the formation of suppressor T cells in the host, whereas this effect in the case of antibodies to protective dialyzate antigen was very weak. It must be assumed that the areactogenicity of the dialyzate antigen of Bordetella pertussis cells and, in particular, the absence of any marked automimmune disturbances in the postvaccinal period [5], are the result of the restricted ability of the antibodies induced by it to influence maturation of suppressor T cells, which play a role in the maintenance of immune homeostasis.

LITERATURE CITED

1. G. A. Belokrylov, V. G. Morozov, and V. Kh. Khavinson, Immunologiya, No. 6, 63 (1982).
2. M. M. Zotina, Postvaccinal Allergic Reactions and Allergens [in Russian], Moscow (1974), pp. 67-69.
3. I. M. Lyampert, Immunologiya, No. 3, 11 (1983).
4. E. P. Moskalenko, S. I. Il'ina, L. N. Chernavskaya, and M. P. Shamne, Zh. Mikrobiol., No. 3, 100 (1975).
5. E. P. Moskalenko, S. I. Il'ina, V. K. Podgorodnichenko, and A. M. Poverennyi, Byull. Éksp. Biol. Med., No. 8, 95 (1978).
6. L. A. Osterman, Chromatography of Proteins and Nucleic Acids [in Russian], Moscow (1985).
7. V. M. Pisarev and L. A. Pevnitskii, Byull. Éksp. Biol. Med., No. 5, 571 (1977).