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Enhanced Production of Lymphocyte Alloimmune Antibodies After Plasmapheresis

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Plasmapheresis is used to remove from the body toxic substance which entered the organism with food [3] or drug overdose [12], endogenously forming pathological macroglobulins [6], pathological clone cells or fragments thereof [7], to remove cholesterol in hypercholesteroemia [8], immune complexes [9,10], and antiD antibodies [11], and in other similar clinical situations. However, the range of clinical applications of apheresis is not confined to the above cases. There are grounds for proposing that plasmapheresis be used to stimulate immune antibody production. Previous experiments with mice and rats have demonstrated that regeneration of some organs, namely, the liver and kidneys, after resection is associated with increased production of immune antibodies [1-3]. The present work was aimed at the investigation of lymphotoxic alloimmune antibody production under the action of plasmapheresis.

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MATERIALS AND METHODS

Plasmapheresis sessions were administered to hematological patients with, mainly, aplastic anemia, myelodisplastic syndrome, and some other diseases; the patients were sensitized to HLA by repeated transfusions of blood and its components (platelets). Removal of antiHLA antibodies directly before the next transfusion of blood components to prevent nonhemolytic posttransfusion reactions was an indication for apheresis, Plasmapheresis sessions were carried out using K-26D, PC-6 refrigerator with plasticized hemacon 500/300 sacs with gluguicir 1000 and imported sacs with citrate solution ACDA-600. The volume of plasma removed was 1/4 and 1/2 of the total circulating plasma volume. It was replaced with quick-frozen plasma, normal saline, and albumin. The patients were administered 5 to 10 sessions with intervals of 4 to 7 days.

The lymphocytotoxic test was the basic method for antibody assessment [5,13]. Each patient's sample was examined with lymphocytes of several donors. Lymphocytes were isolated from fibrin-free

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or heparin-treated blood by centrifugation in a Ficoll-Verografin gradient [5,13]. Plasma samples of 17 patients were examined before and after apheresis. Changes in antibody activity were assessed by the plasma reaction titers.

RESULTS

When 700 to 2000 ml of plasma were removed during a single apheresis session, all the patients showed regular changes in their antibody titers, consisting in a noticeable reduction of plasma after each apheresis session. It is important to note that a 5-7-day-long period of recovery of lymphocytotoxic antibodies was observed after each session. Moreover, the immunological activity of the plasma surpassed the initial level. Such an increase of lymphocytotoxic antibody level was observed starting from dilutions 1:2 and 1:4 and up to dilutions 1:16-1:32 and even higher. This immunostimulating effect of apheresis was observed in ten patients and was particularly marked after the first two or three sessions. It must be noted that for studies of the effect of repeated apheresis sessions on antibody levels we selected patients who had received any transfusions of platelets or other components in the course of plasmapheresis treatment and one month before it. As a rule, antibody levels increased 1-1.5 weeks after the first apheresis session (Fig. 1). A rise of antibody levels (in patients Pi-in and Ko-aya) then gave way to a reduction (Table 1), sometimes at periods long after the plasmapheresis course (patient Po-va). In some cases a successive reduction of antibody levels was seen (patients Ve-va, Is-va), particularly so when

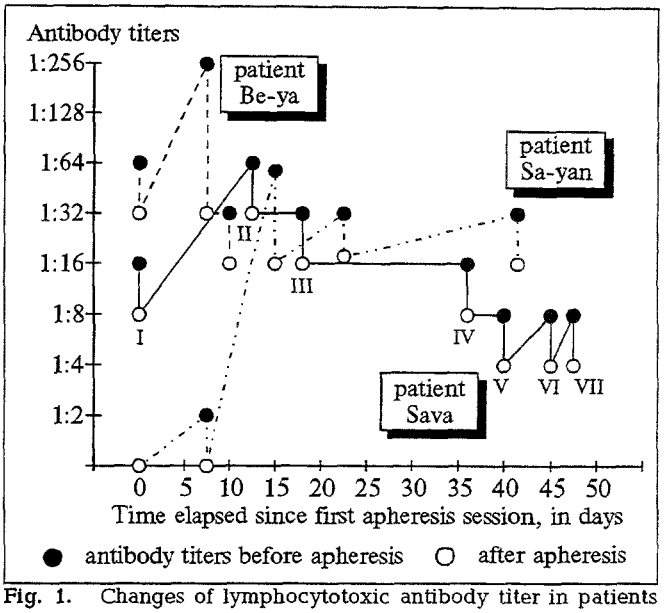

Fig. 1. Changes of lymphocytotoxic antibody titer in patients undergoing apheresis.

repeated intensive apheresis sessions were administered. Antibody levels remained unchanged in only two patients (Su-na, Mi-va).

Hence, plasmapheresis treatment is often associated with stimulation of patient antiHLA antibodies. This phenomenon is observed when large volumes are removed during the first sessions of apheresis.

Some authors report individual cases of increased antibody production during apheresis treatment, a phenomenon which has been termed "the rebound syndrome". This syndrome of increased antibody production may be particularly significant in apheresis treatment of patients with autoimmune diseases caused by humoral immunity factors, be-

TABLE 1. Effect of Plasmapheresis on Alloimmune Lumphocytotoxic Antibody Production

Patient	Diagnisis	Mean volume of plasma removed in 1 apheresis, ml	Number of apheresis sessions	Number of sessions per week	Number of sessions after which antibody level changed	Antibody titers	
						before apheresis	after apheresis
Ve–va	AA	930.0	4	1	3	1:8	1:2
Ush–va	AA	1010.0	5	1	2	1:2	1:32
Sa–va	MDS	1100.0	5	1	3	whole	1:64
Ezh–va	AA	1000.0	10	2	4	1:4	1:16
Ga–ze	AA	900.0	7	1	2	1:8	1:64
Po–ov	RA	1100.0	6	2		1:16	1:32*
Ko–ya	NDS	780.0	7	2	5	1:280	1:256**
Sa–yan	CRI	2000.0	7	0.5	2	1:8	1:32
Be–ya	CRI3	1500.0	3	1	1	1:64	1:256
Ne–ga	AML	2100.0	7	2	3	1:4	1:32
Dzh–ma	AA	1000.0	6	3	4	1:16	1:32
Is–va	MDS	870.0	4	2	1	1:32	1:4

Note. AA: aplastic anemia, MDS: myelodysplastic syndrome, RA: refractory anemia, CRI: chronic renal insufficiency, AML: acute myeloleukemia; asrerisk: 10 months after treatment antibody titers reduced to 1:2; two asterisks: antibody titer reduced to 1:32 after the 7th session.

cause of exacerbation of the disease may be expected in such cases. Apheresis stimulation of immune antibody production seems to be largely due to the cyclic pattern of changes occuring during such treatment, namely, a drop of the antibody level resulting from a removal of immunoglobulins along with the plasma, followed by antibody hyperproduction due to reparative regeneration of removed plasma proteins. These data suggest that brief courses of apheresis may stimulate to the greatest degree production of existing immune antibodies.

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Monoclonal Antibody ICO-166 Against CD45RA Antigen

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Antigens belonging to the CD45 family of common leukocyte antigens exist in four isoforms that have molecular weights of 170 to 220 kD and are expressed in a cell-specific manner. Antigens of this family are subdivided into two main clusters. Anti-CD45 monoclonal antibodies (mAb) recognize epitopes shared by all molecules of the family, whereas anti-CD45R mAb recognize limited epitopes present only on the higher-molecular-weight species that are predominantly expressed on B lymphocytes and on a T-cell subset [3,5,7]. During the Fourth Workshop on Human White Cell Differentiation Antigens, held in Vienna in 1989, CD45R antigens were assayed on transfectant cells using a panel of anti-CD45R mAb, which led to the separation of these antigens into CD45RA, CD45RO, and CD45B [7]. CD45RA is an isoform of the 220-kD common leukocyte antigen.

Since no Russian-manufactured mAb to CD45RA antigen exist, the purpose of this study was the

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