EFFECT OF CROSS-REACTING MICROBIAL ANTIGENS AND ANTIBODIES ON THE ALLOGRAFT REJECTION REACTION

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Preliminary sensitization of CBA mice by vaccines of group C Streptococcus and Candida albicans accelerated rejection of skin grafted from C3H mice. Immunization with C. albicans vaccine had a similar action on grafts on CC57BR mice. Antitissue sera against antigens of C3H mice delayed rejection of allografts on CBA and CC57BR mice sensitized by these microbial vaccines. Antistreptococcal and anticandidal sera delayed rejection of allografts on CBA and CC57Br mice, both intact and sensitized with alloantigens.

The existence of antigens related to mammalian tissues in certain microorganisms may lead, in animals sensitized with them, to lesions of autologous tissues and to acceleration of allograft rejection [3, 5, 6]. The ability of an organism, after immunization with these microbial antigens, to accelerate rejection of allografts has been described only for group A Streptococcus and for Staphylococcus [6].

The effect of immunization of animals with group C Streptococcus and with Candida albicans, containing antigens cross reacting with mammalian tissues [2, 7], on the survival times of allogeneic skin grafts was studied. The action of immune sera obtained against these microorganisms and against the donor's tissues also was investigated on the allograft-rejection reaction in intact recipients and recipients previously sensitized with microbial and tissue antigens.

EXPERIMENTAL METHOD

Skin from C3H (H-2^k) female mice was grafted onto female CC57BR (H-2^6) and CBA (H-2^k) mice weighing 16-18 g. Some of the recipient mice were immunized two weeks before the operation by subcutaneous injection of vaccines of group C Streptococcus and C. albicans (10^{10} bacterial cells) mixed with 0.2 ml of incomplete adjuvant. For immunization with the donor's alloantigens, 10^7 spleen cells of C3H mice were injected intraperitoneally into the recipients. Immune sera against vaccines of group C Streptococcus and C. albicans and against the red blood cells and extracts of the skin, liver, kidney, and spleen of C3H mice were obtained in rabbits and CC57BR mice by the usual method [1]. The titer of rabbit antitissue and antimicrobial sera against the injected antigen in the complement fixation test (CFT) was 1:640, while the titer of mouse immune sera was 1:40. The titer of rabbit and mouse antimicrobial sera in the CFT with extract of C3H mouse skin was 1:80 and 1:20, respectively. Before injection into mice the immune sera were adsorbed by lymphocytes of recipient mice. The immune sera were injected intraperitoneally into the recipient mice 3 days after the operation in a volume of 0.3 ml per mouse. The same volume of serum of normal animals was injected into the mice of the control groups. Each experimental and control group consisted of 25 mice.

EXPERIMENTAL RESULTS

Immunization of CBA mice with group C Streptococcus and C. albicans accelerated rejection of the allogeneic skin from C3H mice (the donor and recipient differed with respect to the weak histocompatibility

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TABLE 1. Effect of Antitissue and Antimicrobial Sera on Life Span of Skin Grafts from C3H Mice on CC57BR and CBA Mice Immunized with Microbial Vaccines (M ± m)

Line of recipient mice	Microorganisms used for immunization	Type of serum injected	Immune serum						Normal serum
			against tissues of C3H mice					against vaccine from	
			red cells	skin	liver	kidney	spleen	Streptococcus	C. albicans	
CC57BR	C. albicans	Rabbit P	6,7±0,3 >0,1	7,9±0,4 >0,05	11,8±0,45 <0,001	8,6±0,34 <0,001	14,3±0,3 <0,001	6,6±0,43 >0,1	10,3±0,48 <0,001	6,8±0,3
		Mouse P	6,83±0,5 >0,1	7,0±0,44 >0,1	10,3±0,4 <0,001	6,7±0,35 >0,1	12,0±0,5 <0,001	6,9±0,33 >0,1	7,0±0,44 >0,1	6,85±0,42
	Group C Streptococcus	Rabbit P	10,9±0,6 >0,1	10,4±0,5 >0,1	18,1±0,8 <0,001	10,6±0,4 >0,1	18,4±0,8 <0,001	16,8±0,8 <0,001	10,9±0,6 >0,1	11,0±0,4
		Mouse P	10,6±0,4 >0,1	10,9±0,29 >0,1	10,6±0,45 >0,1	11,0±0,6 >0,1	10,3±0,5 >0,1	10,9±0,57 >0,1	11,2±0,48 >0,1	10,9±0,41
CBA	C. albicans	Rabbit P	10,7±0,4 >0,1	10,0±0,5 >0,1	18,5±0,84 <0,001	10,8±0,5 >0,1	19,0±0,85 <0,001	11,0±0,38 >0,1	16,9±0,87 <0,001	10,86±0,4
		Mouse P	10,9±0,51 >0,1	10,6±0,24 >0,1	11,1±0,43 >0,1	10,9±0,43 >0,1	10,9±0,4 >0,1	10,9±0,44 >0,1	10,9±0,61 >0,1	10,8±0,4

Legend: P) Significance of difference between experiment (injection of immune serum) and control (injection of normal serum).

loci). The survival time of the allografts was reduced to 10.7 ± 0.42 days compared with 18.7 ± 0.63 days in the control (P < 0.001). Acceleration of the rejection of C3H mouse skin grafts (donor and recipient differed with respect to the strong histocompatibility locus) was observed only in the case of sensitization with C. albicans (the survival time of the grafts was 6.8 ± 0.25 days compared with 9.4 ± 0.43 days in the control; P < 0.001).

Injection of rabbit and mouse antimicrobial sera into intact recipients after skin grafting, on the other hand, lengthened the survival time of the graft. After injection of antistreptococcal and anticandidal sera into CBA mice, for instance, the survival time of the allografts was 24.6 ± 1.4 to 25.6 ± 1.5 days compared with 18.6 ± 0.9 days in the control (P < 0.001). Only anticandidal sera were effective as regards prolonging the survival of the graft in CC57BR mice (13.9 ± 0.61 to 15.43 ± 0.8 days in the experimental series compared with 9.5 ± 0.46 days in the control; P < 0.001). Rabbit and mouse antitissue sera against extracts of the spleen, liver, kidney, and skin of C3H mice increased the survival time of the graft in the CBA mice to between 25.6 ± 1.3 and 27.7 ± 1.4 days (P < 0.001) and in CC57BR mice to between 14.3 ± 0.7 and 20.8 ± 1.4 days (P < 0.001).

In CBA mice previously immunized with Streptococcus the survival time of the allografts was increased compared with the control if antistreptococcal rabbit serum was injected after grafting, and in the case of sensitization with C. albicans, the same effect was observed after injection of anticandidal rabbit serum (Table 1). Lengthening of the survival time of the allograft on CC57BR mice immunized with C. albicans took place only after injection of anticandidal rabbit serum. Of the antitissue sera, only antispleen and antikidney rabbit and mouse sera increased the survival time of the allografts on CBA and CC57BR mice immunized with microbial vaccines (Table 1).

The survival time of allografts was lengthened by antimicrobial sera in mice previously sensitized with the donor's alloantigens. The survival time of the allografts on such CBA mice was increased by rabbit antistreptococcal and anticandidal sera to 17.4 ± 0.87 days compared with 11.8 ± 0.67 days in the control (P < 0.001), but the survival time of these grafts on CC57BR mice was lengthened only by anticandidal rabbit and mouse serum, up to 11.5 ± 0.62 days compared with 6.7 ± 0.4 days in the control (P < 0.001). Rabbit and mouse antispleen and antikidney sera had a similar action on the survival time of allografts on CBA and CC57BR mice sensitized with the donor's antigens (the survival times of the grafts were increased to 13.2 ± 0.7 and 18.7 ± 0.9 days, respectively; P < 0.01).

These results show that the shortening of the survival time of allografts observed in CC57BR and CBA mice after immunization with C. albicans and of CBA mice after immunization with Streptococcus may be connected with sensitization of the recipient with microbial antigens related to transplantation antigens of the donor C3H mice. The ability of anticandidal sera to prolong the survival time of allografts on CC57BR and CBA mice and of antistreptococcal serum to do the same on CBA mice, both intact and sensitized with the donor's alloantigens, can probably be explained by the presence of antibodies blocking the donor's transplantation antigens in the antimicrobial sera [4]. The ineffectiveness of antistreptococcal serum as regards prolonging the survival time of allografts on CBA mice sensitized with C. albicans indicates some differences between the antigens of Streptococcus and C. albicans related to the transplantation antigens of C3H mice.

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