Formation of Lymphoid Nodules in the Thymus in Allograft Immunity

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Summary. The formation of lymphoid nodules was observed in the thymus of mice that had received lymph node allografts in diffusion chambers. No lymphoid nodules were seen in the thymus of control non-treated mice or those bearing empty diffusion chambers. A preliminary allografting experiment of another type also showed similar lymphoid nodule formation in the thymus of albino rats. This fact suggests that the prolonged retention of the allograft in the body of experimental animals may induce thymic follicle formation.

INTRODUCTION

There have been a number of reports suggesting that the development of lymphoid nodules in the thymus is caused by "specific" antigenic stimulation (Marshall and White, 1961 ; Svet-Moldavsky and Raffkina, 1963 ; Awaya, 1963 ; Sherman, Adner and Dameshek, 1964 ; Kotani, Manabe, Seiki, Yamashita and Horii, 1966) and by autoimmunization (Castleman and Norris, 1949 ; Mackay and De Gail, 1963 ; Burnet and Holmes, 1964). These observations suggested a search for the formation of lymphoid nodules in the thymus following allogeneic tissue grafting. While studying allograft immunity, we have observed that occasional mice bearing lymph node allografts in diffusion chambers develop a lymphoid nodule-like structure in their thymuses. The present report is a description of this subject and an interpretation of its significance.

MATERIALS AND METHODS

Mice used as donors and recipients were 2-month-old mice of randomly bred ddT and ddY strains and of inbred strains Cb, Strong A, Db and C_{57}BL. Pieces of the mesenteric lymph nodes obtained from male and female donor mice were placed in the diffusion chambers, then were implanted into the peritoneal cavities of the allogeneic host mice of the comparable sex. The host mice were killed at

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intervals of 15, 30 and 60 days following implantation, when the chamber and the host thymolymphatic tissues were removed and examined microscopically. The chambers employed were a modification of that of Algire, Weaver and Prehn, 1954; Prehn, Weaver and Algire, 1954. The construction of the chamber and histologic examination of their contents were described in detail elsewhere (Awaya, 1964). In the present report the histologic changes in host thymus are chiefly described.

As control, the thymus of the non-treated intact and the empty chamber bearing mice of the same age and sex was presented for histological observations.

RESULTS AND DISCUSSION

Of 138 host mice bearing the lymph node allografts in diffusion chambers, 12 developed structural characteristics in their thymuses which made them resemble very closely lymphoid nodules or follicles (Table 1). These 12 host mice were confined for the most part to ddT strain mice and consisted of 7 with HA type chamber (pore size 0.45 μ) and 5 with AA type chamber (pore size 0.8 μ); 3 of these were killed on the 15 th day, 7 on the 30 th day and 2 on the 60 th day following implantaion (Table 2). In these animals lymph node allografts in the chambers were destroyed in varying degrees.

This structure is a sharply circumscribed, round or oval lymphoid nodule having as a major cellular component reticulum cells and small lymphocytes (Figs. 1 to 4). This is much the same as the ordinary secondary nodule, except for the absence of mitotic activity therein and the lack of a dark zone consisting of small lymphocytes. The lymphoid nodule rarely contained plasma cells. All of the nodules appeared in the medullary portions and were not seen elsewhere. The majority of them were defined almost completely from surrounding tissue by a thin fibrillar capsule or a lining of flattened cells (Figs. 1 to 4). These lymphoid nodules were often seen in the immediate vicinity of small blood vessels (the arterioles, venules or capillaries).

Lymphoid nodules were not seen in the thymus of any control mice (Table 1).

In addition, a preliminary experiment performed in our department showed that similar thymic follicles were observed in some occasional albino rats of Donryu strain grafted subcutaneously with canine teeth obtained from rats of Wistar strain. These structures were identical in form and appearance in host mice examined in the present study.

These facts suggest that the prolonged retention of an allograft in the body of experimental animals may induce thymic follicle formation. The use of diffusion chambers as the site of allografting seems to facilitate the production of such conditions.

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Table 1. Number of mice developing lymphoid nodules in their thymuses in the present study.

	Strain of mice	Number of mice	Number of mice with thymic follicles
Control (mice bearing an empty diffusion chamber)	ddT	60	0
	Strong A	12	0
	$C_{57}BL$	12	0
	Cb	9	0
	Db	9	0
Mice bearing the allograft in diffusion chamber	ddT	61	11
	Strong A	38	1
	$C_{57}BL$	23	0
	Cb	9	0
	Db	7	0

Table 2. Details of 12 mice that developed the lymphoid nodules in their thymuses following transplantation of lymph node in diffusion chamber.

Host		Donor	Days after allografting	Type of diffusion chamber	Condition of lymph node allograft
Animal No. and sex	Strain				
HAL 18, ♂	ddT	ddY*	15	HA, pore size 0.45μ	living
HAL 63, ♀	ddT	ddY*	15	HA, pore size 0.45μ	living
HAL 35, ♂	ddT	ddY*	30	HA, pore size 0.45μ	living
HAL 48, ♂	ddT	ddY*	30	HA, pore size 0.45μ	living
HAL 65, ♀	ddT	ddY*	30	HA, pore size 0.45μ	living
HAL 66, ♀	ddT	ddY*	30	HA, pore size 0.45μ	living
HAL115, ♀	Strong A	Db	30	HA, pore size 0.45μ	living
AAL 14, ♀	ddT	ddY*	15	AA, pore size 0.8μ	dead
AAL 12, ♀	ddT	ddY*	30	AA, pore size 0.8μ	dead
AAL 17, ♂	ddT	ddY*	30	AA, pore size 0.8μ	dead
AAL 10, ♂	ddT	ddY*	60	AA, pore size 0.8μ	dead
AAL 21, ♀	ddT	ddY*	60	AA, pore size 0.8μ	dead

*Donor *ddY* strain mice are considered to be allogeneic to the host *ddT* mice, because all of the skin grafts from the donors were rejected by the host mice.

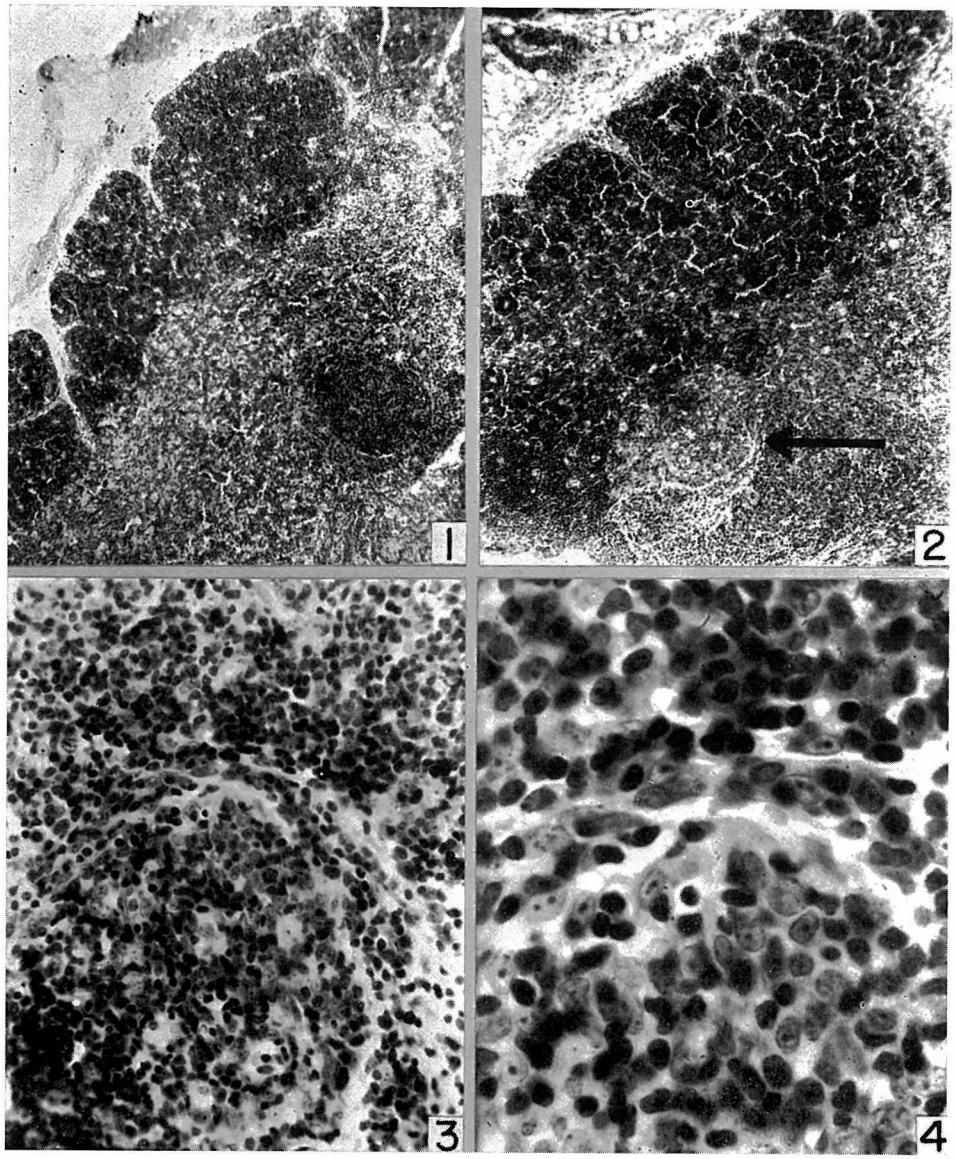

Fig. 1. A lymphoid nodule seen in the medullary portion of thymus of a ddT strain mouse bearing allogeneic lymph nodes in a diffusion chamber for 15 days. The nodule is surrounded by a thin layer of fibrillar capsule. Animal No. AAL 14. × 100.

Fig. 2. A lymphoid nodule seen in the corticomedullary portion of thymus in a ddT mouse bearing allogeneic lymph nodes in diffusion chamber for 30 days. The nodule is surrounded by a thin layer of fibrillar capsule. Animal No. HAL 48. × 100.

Fig. 3. Medium power view of the lymphoid nodule in Fig. 2. × 400.

Fig. 4. High power view of the lymphoid nodule in Fig. 2. The nodule is surrounded by a lining of flattened cells and consists of small and medium-sized lymphocytes and reticulum cells. × 1000.

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