REACTION OF THYMECTOMIZED RATS TO SKIN HOMOGRAFTS

A. V. Abuladze

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The immune response of 65-70% of noninbred albino rats thymectomized at birth to skin homografts is weakened. Only the epidermis and subepidermal zone of the dermis are detached 12-15 days after transplantation, after which the hair follicles are slowly eliminated. In 30-35% of rats, as in the controls, rejection of the homograft takes place on the 8th-10th day.

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Reactions of thymectomized animals to skin homografts have been investigated in recent years. On the basis of results of skin grafting on thymectomized mice, Miller [12-14] concluded that they are tolerant to homografts. Successful interlinear skin grafting after thymectomy was carried out by Biege [7]. Other workers have demonstrated delay in rejection of skin homografts by thymectomized animals [6, 11] or no effect of thymectomy on homograft rejection [15]. Many workers associate the rejection reaction with lymphocyte function [3, 8, 9, 10]. Lymphocytes are also known to stimulate repair processes in tissues [4, 5]. These lymphocyte responses largely determine the result of transplantation.

In the present investigation tissue responses to skin homografting on thymectomized rats were studied. Disturbance of postnatal differentiation of the skin in such animals has previously been demonstrated [2].

EXPERIMENTAL METHOD

Circular full-thickness pieces of dorsal skin, 0.6 cm in diameter, were grafted on 5-day noninbred albino rats belonging to the same litter and thymectomized at birth. Including the control, 82 young rats were used, in 42 of which areas of skin containing the homograft were investigated (3, 7, 14, and 21 days after transplantation), while in the remainder the times of rejection were recorded. The skin was fixed in Zenker's fluid, and paraffin sections (6μ) were stained with Regaud's iron-hematoxylin, azure-eosin, azo carmine with counterstaining by Mallory's method, and by Van Gieson's method.

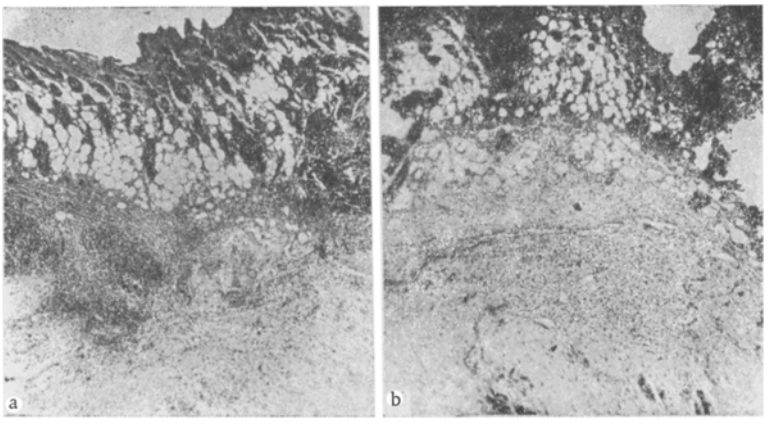

Fig. 1. Skin graft 3 days after transplantation. a) Control; b) thymectomy, 40 ×.

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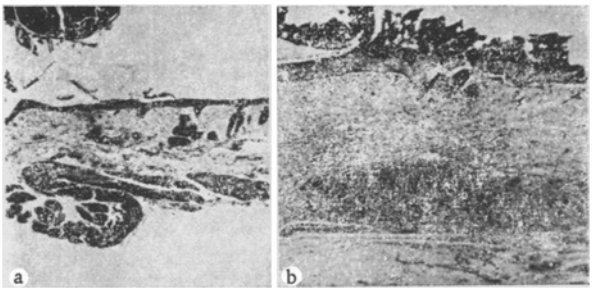

Fig. 2. Regeneration 2 weeks after transplantation.
a) Control; b) thymectomy, 40×.

EXPERIMENTAL RESULTS

Rejection of the homograft by intact animals took place on the 8th-9th day after transplantation. Only the epidermis and subepidermal zone of the dermis were detached from most (60-70%) thymectomized rats on the 12th-15th day, after which the epidermal derivatives were slowly eliminated; rejection of the homograft by the remaining rats took place on the 8th-10th day. Histological analysis of an area of skin containing the homograft revealed some differences between the tissue reactions of the thymectomized animals. On the 3rd day after transplantation, dilated blood vessels with abundant leukocyte infiltration were observed in the rats of the control group in areas of skin bordering on the graft (Fig. 1a). The leukocyte barrier appeared to separate the graft from the underlying tissues. Tongues of regenerating epidermis spread out from the thickened marginal areas of the recipient's epidermis beneath the leukocyte barrier toward the center of the wound; under them, on the connective-tissue bed on the recipient, rich in cells, lay fragments of the subcutaneous muscle of the graft, so that consequently the deep parts of the graft had not been rejected.

As a rule in the thymectomized rats 3 days after transplantation the number of infiltrating leukocytes was less numerous and they consisted mainly of neutrophils (the number of lymphocytes in the blood showed a sharp decrease). The border between the tissues of the graft and recipient was less distinct than in the control (Fig. 1b). The recipient's connective-tissue bed contained fewer cells.

In most cases the skin defect had epithelized in the rats of the control group after 7 days. On the surface of the epidermis, areas of rejected graft still remained. The regenerating dermis (granulation tissue) was rich in cells, especially lymphocytes, some of them penetrating into the epidermis. Fibrous structures of the dermis lay parallel to the skin surface and capillaries had grown as far as the border with the epidermis. In the deep layers fragments of subcutaneous muscle of the graft still remained, invaded by young connective tissue and surrounded by lymphocytes.

In the thymectomized rats at this period the skin defect was partly or completely covered by regenerating epidermis growing between detached areas of the graft (the epidermis and subepidermal zone of the dermis) and by its remaining layers attached to the floor of the wound. The epidermis grew deep into the dermis of the graft, covering the degenerating hair follicles.

After two weeks the regenerating skin in the control rats consisted of an epidermis of 10-12 rows of cells and a wide dermis, not containing hair (Fig. 2a). Regeneration of the subcutaneous muscle was taking place.

In the thymectomized rats the regenerating epidermis covered the dermis of the graft, which contained few cells (Fig. 2b); bands of epidermis sank into the depths of the dermis, so that the boundary between them followed an irregular course.

After 3 weeks the regenerating skin in the control rats differed from the intact skin in the thickness of its epidermis and dermis and by the absence of hair roots. The subcutaneous muscle, especially at the boundary with the regenerating skin, was hypertrophied. In thymectomized animals the site of the graft was sharply distinguished from the surrounding skin. The epidermis, irregular in thickness, formed deep ingrowths into the dermis of the graft.

One of the causes of the disturbances of immunogenesis and regeneration described above may perhaps be a deficiency of lymphocytes in the wound exudate and blood [1] of the thymectomized animals caused by absence of the thymus, a highly important lymphopoietic organ in early ontogenesis.

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