Exp. Anim. 47(4), 253–256, 1998

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Characteristics of Spontaneous Erythema Appeared in Hairless Rats

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Abstract: *The hairless rat (WBN/Kob-Ht), a dominant mutant rat derived from the Wistar strain, rarely develops spontaneous erythema of a progressive nature on its skin. Erythema was first observed at 8 weeks of age and the incidence at 20 weeks of age was about 4% in both males and females. Histopathologically, erythema was characterised by dermatitis induced by an immunological reaction. Areas of erythema in the skin were decreased by treatment with dexamethasone (1 mg/kg) or ciclosporin (25 or 50 mg/kg). These results suggested that erythema on the hairless rat could be used as an animal model of spontaneous dermatitis.*

Key words: *erythema, immunosuppressant, hairless rat*

The skin is the extensive protective tissue which keeps the internal condition of the body constant. In order to study the function of the skin, many animal models [3, 4, 7] have been developed. The hairless rat (WBN/Kob-*Ht*) is the dominant mutant of the Wistar strain which was established at Ishikawa Institute of Experimental Animals [6]. The hairless rat is a useful animal model for the study of alopesia or hairgrowth. In our center hairless rats are widely used for transdermal experiments for the reason that their skin is more easily treated than that of the normal haired rat [5, 8, 9], but in a few cases spontaneous erythema of a progressive nature has appeared on the skin of the hairless rat [1]. According to a personal communication from the Central Institute for Experimental Animals, no pathogenic bacterium was found in a microbiological survey of the excised erythema, and the erythema was not improved by the application of povidone iodide. The characteristics of the erythema were then studied from other viewpoints.

The hairless rat (WBN/Kob-*Ht*) has been maintained as an inbred SPF animal at the Life Science Research Center of Josai University since 1990. 4–5 rats were kept under controlled conditions (temperature, 23°C; humidity, 50%; lighting, 7:00 a.m.–7:00 p.m.) in a 35 × 40 × 18 cm^3 polycarbonate cage with wood shavings on the floor. They were allowed free access to pelleted rodent chow (CE-2, CLEA Japan Inc., Tokyo, Japan) and sterilized tap water. When erythema appeared on the skin of a hairless rat, it was separated from the

(Received 23 October 1997 / Accepted 1 May 1998)

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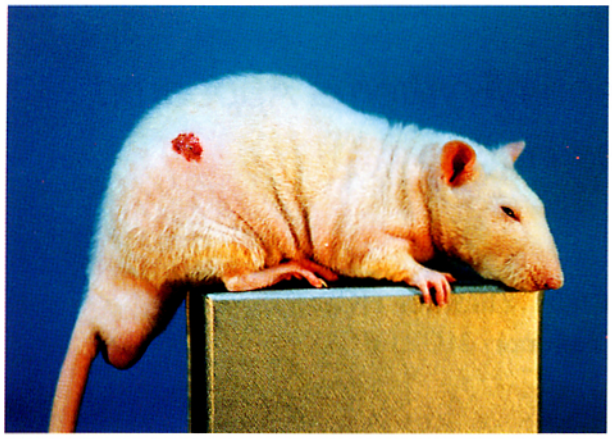

Fig. 1. A Photograph of Typical Erythema on the Male Hairless Rat.

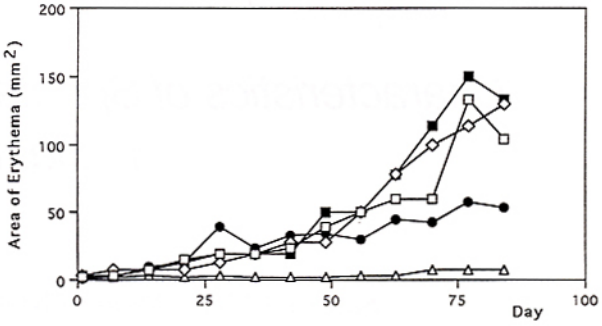

Fig. 2. Development of Erythema Appeared in Individual Female Hairless Rats. Areas (mm^2) of erythema on 5 female hairless rats were plotted as a function of time. Each line represents the change in the area of erythema on an individual rat.

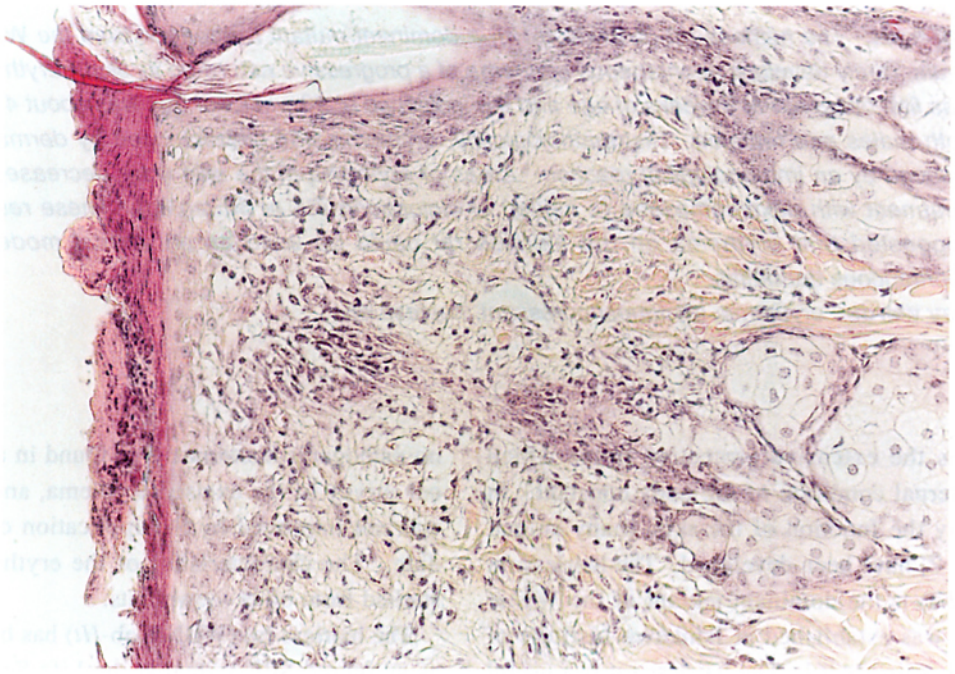

Fig. 3. A Light Micrograph of the Section of Erythema. Spongiosis, acanthosis and parakeratosis are evident. (× 200)

others and transferred to a conventional room.

The erythema usually appeared after about 8 weeks of age, and its incidence was about 4% in both male and female rats at 20 weeks of age. Figure 1 shows the macroscopic features of a rat with typical erythema on its skin. Erythema usually appeared on the dorsal skin, and gradually became widespread and of a progressive nature, but the rate of development was different in each rat (Fig. 2). A few rats scratched or licked their skin lesions.

For the light microscopic study, skin including the erythema was fixed in 10% formalin, and paraffin sections were stained with hematoxylin and eosin. A photomicrograph of erythema on dorsal skin is shown in Fig. 3. Parakeratosis in the horny layer and spongiosis in the prickle cell layer were observed. Because

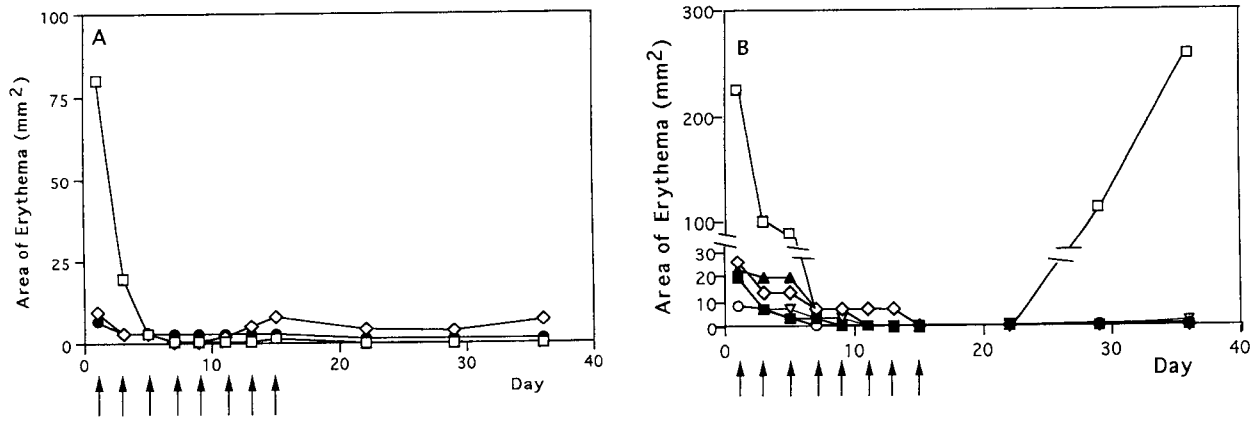

Fig. 4. Effect of Dexamethasone on Area of Erythema. Dexamethasone (1 mg/kg) was subcutaneously injected into hairless rats with erythema on the days indicated by arrows for two weeks. The area of erythema was measured during and after dexamethasone treatment. Each line represents the change in the areas of erythema on 3 individual male (A) and 6 female rats (B). One acute recurrence was seen in (B).

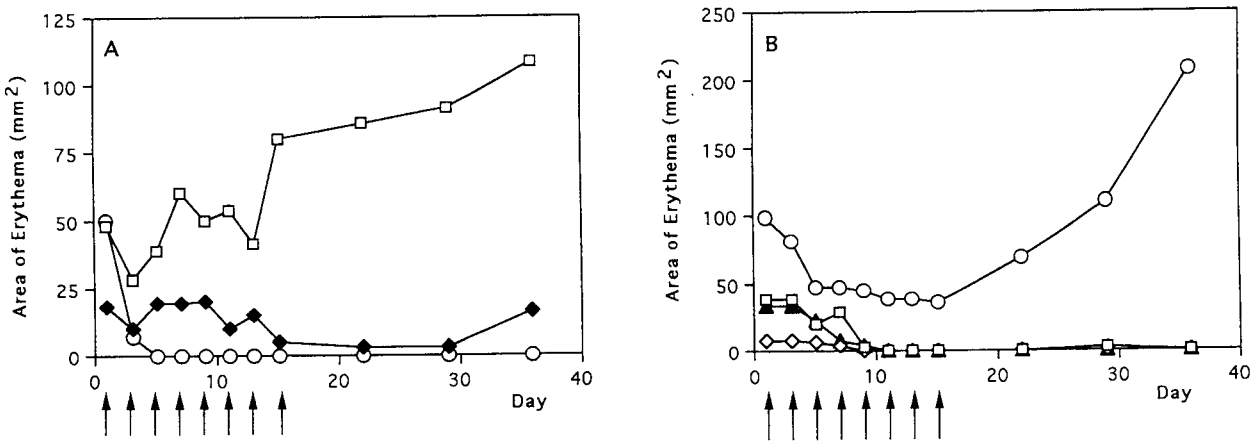

Fig. 5. Effect of Ciclosporin on Area of Erythema. Ciclosporin (50 mg/kg) was subcutaneously injected on the days indicated by arrows for 2 weeks. The area of erythema was measured during and after ciclosporin treatment. Each line represents the change in the area of erythema on 3 individual male (A) and 4 female rats (B). Intractable and recurrent cases were seen in (A) and (B), respectively.

lymphocytic infiltration in the dermis and acanthosis in the epidermis were also seen, the erythema was characterized as dermatitis.

Itagaki reported that many more S-100 immunoreactive cells or Langerhance cells were detected in the epidermis of the dorsal skin of a hairless rat than in normal Wistar rats [2]. These findings suggested that erythema in the hairless rat was characterized by dermatitis induced by an immunological reaction, but it was supposed that the lesion might be modified by scratching or licking.

To confirm whether erythema was induced by an immunological disorder or not, we tried to inject immunosuppressants into the hairless rat with erythema. Dexamethasone (Sigma Chemical Co., MO., USA), at a dose of 1 mg/kg in olive oil or ciclosporin (Sandimmun; Sandoz, Switzerland), at a dose of 50 mg/kg was subcutaneously injected every other day for 2 weeks. Changes in the area (mm^2) of the erythema were measured during and after the treatment for 5 weeks, and results are individually shown in Figs. 4 and 5. The area of the erythema was apparently decreased by the injection of dexamethasone or ciclosporin. In rats with only a little erythema, it was

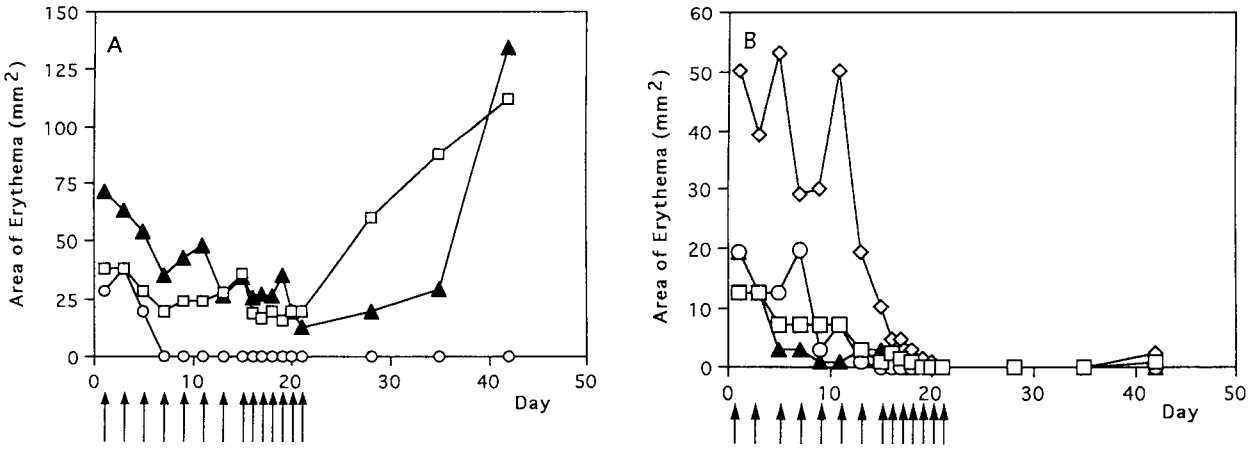

Fig. 6. Effect of Ciclosporin on Area of Erythema. Ciclosporin (25 mg/kg) was subcutaneously injected on the days indicated by arrows for 3 weeks. The area of the erythema was measured during and after ciclosporin treatment. Each line represents the change in the area of erythema on 3 individual male (A) and 4 female rats (B). Intractable and recurrent cases were seen in (A).

completely eliminated by injecting the chemical for a shorter period, and the rate of recurrence was low. When the rats had extensive erythema, it was difficult to cure it completely, and it sometimes rapidly recurred after the termination of treatment with the chemical.

Since ciclosporin was less effective than dexamethasone, we changed the injection schedule. The rats with erythema were subcutaneously injected every other day for 2 weeks and then every day for a week with ciclosporin at a dose of 25 mg/kg. The results are shown in Fig. 6. The areas of erythema were reduced by daily injection of ciclosporin more than by injection every other day, even though the dose was half of that in the former case.

Treatment with immunosuppressants, dexamethasone or ciclosporin reduced or cured the spontaneous erythema which occurred in hairless rats. These results indicated that erythema was a kind of inflammation. Furthermore, after the termination of the treatment, in a few cases, new erythema appeared or small areas of erythema developed rapidly. In this way erythema was characterized in terms of intractability and recurrence. Although the hairless rat was derived from the Wistar rat, the appearance of such spontaneous erythema in the Wistar rat was previously not known. Erythema in hairless rats may be caused by a gene mutation, but the possibility that it is contact dermatitis still remains, because hairlessness allows the skin to contact the surroundings. The pathogenesis of erythema in the hairless rat is obscure, and we have not yet analyzed the blood components. Nevertheless, these facts indicated that erythema on the skin of hairless rat could be used as an animal model of spontaneous dermatitis.

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