The effect of tamoxifen on the neonatal development of rat glans penis

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Summary

From the first day of birth to the fifth day, daily subcutaneous 100 µg tamoxifen (Tx) was injected into new-born male rats. The penises that were taken totally were fixated in 10% formaline, and then they were put in paraffin inclusion. The paraffin sections were stained with Hematoxylen-Eosin, Verhoeff and Triple on days 7, 14, 21, 28, 35 and 60. The alterations in the development of glans penis construction were examined. We found that in the glans penis of animals which were given Tx, from the 21st day, the epidermal projections were erased slowly and on the 60th day the epidermal projections and keratinisation completely ceased altogether.

As a result, the development of epidermal projections in rats which were given tamoxifen in the neonatal period were hindered.

Key words: Tamoxifen; Glans penis; Neonatal; Rat.

Introduction

Tamoxifen (Tx), is an antioestrogen which is derived from trifeniletilen and it is not a steroid. It is used mostly in the treatment of breast cancer to support the endocrine treatment of oestrogen receptors [1]. However, some anomalies have been found on the genital organs of animals which are given Tx after birth. In males a delay in spermatogenesis and atrophy of testicles and added glands, while in females lesions like adenosis on cervicovaginal epithelium, pause in development of uterine glands and also dysgenesis of ovaries were determined [2, 3, 4]. Besides, it has been indicated that Tx administration suppresses the ossification of Os pubis and Os ischium in the pelvis [2, 5].

The epidermal projections that cover the glans penis of normal male rats start to thicken and become shaped 10 days after birth. The epidermal projections resemble the filiform papillae of the tongue which are thorny in form. Epithelium which covers the epidermal projections, shows dense keratinisation [6].

The aim of this study was to examine, under a lighted microscope, alterations in development of epidermal projections in the glans penis after birth during the delivery of Tx, which is an antioestrogen agent.

Materials and Methods

We started our study with the selection of male baby rats after birth. From the first to the fifth day, 100 µg Tamoxifen citrate disolved in 0.002 ml serum, was injected subcutaneously in male baby rats every day. Afterwards, on the days shown in Table 1, the penises of the animals were totally extracted under ether anesthesia. During the experiment the baby rats were fed with mother's milk, pellet food and water. The penises of the rats were fixated in 10% formaline. After dehydration and paraffin inclusion, sections were taken from the blocks prepared with sledge microtom, 5 micrometers thick. The paraffin sections were stained with various methods like, Hematoxylen-Eosin (H-E). Masson triple, and Verhoeff [7], Afterwards they were inspected under a lighted microscope and microphotographs were taken. The histopathologic alterations were evaluated.

Table 1.

Control Group (Days of sacrifice)	Saline administration (Subcutaneous)	Indices
21.0	0.02 ml	4
Experimental group (Days of sacrifice)	**Tamoxifen (Tx) - Administration (Subcutaenous)**	**Indices**
7.0	100 µg	4
14.0	100 µg	4
21.0	100 µg	4
28.0	100 µg	4
35.0	100 µg	4
60.0	100 µg	4

Results

Development of prepuce in the skin of rats, in control and TX-administered groups was examined and the following results were obtained:

7-day-old experimental group, given Tx: No anomalies

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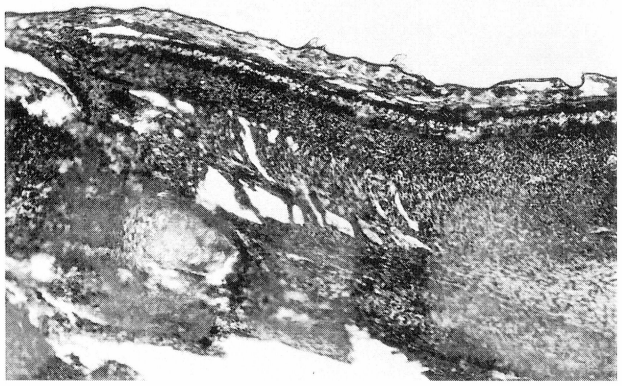

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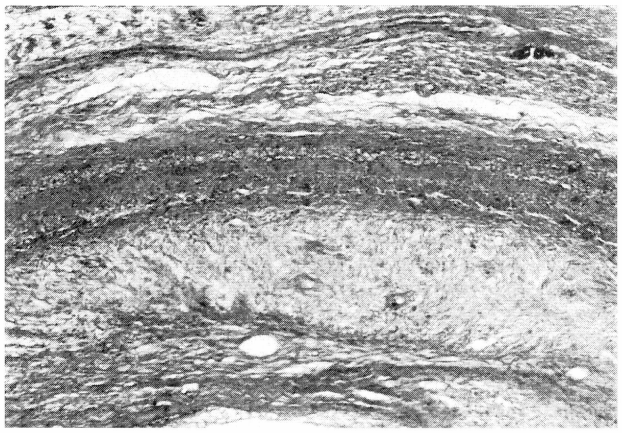

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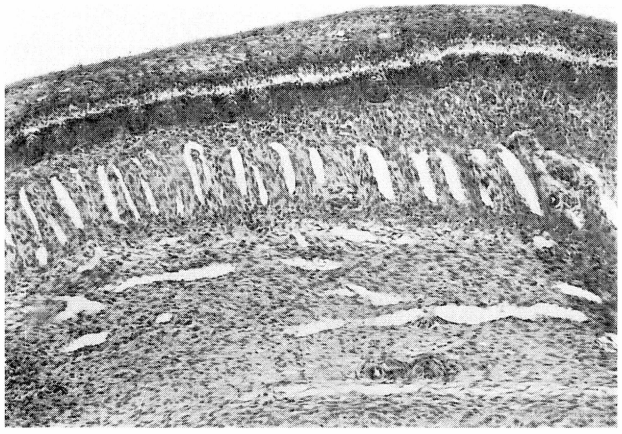

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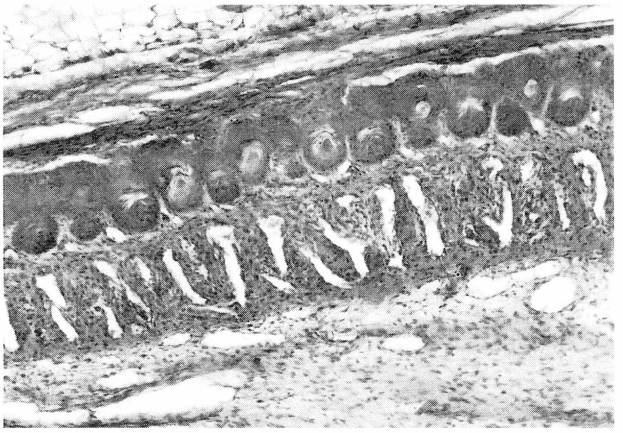

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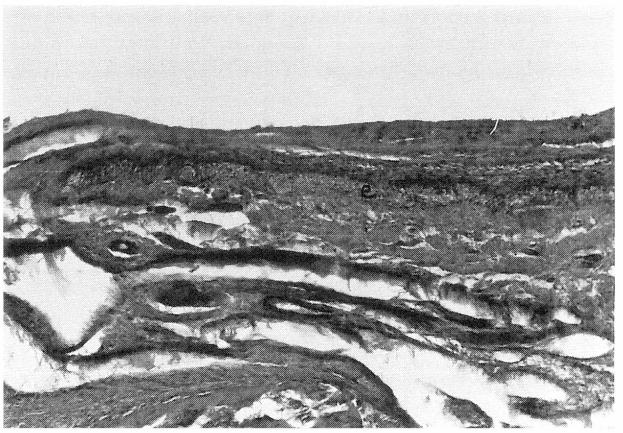

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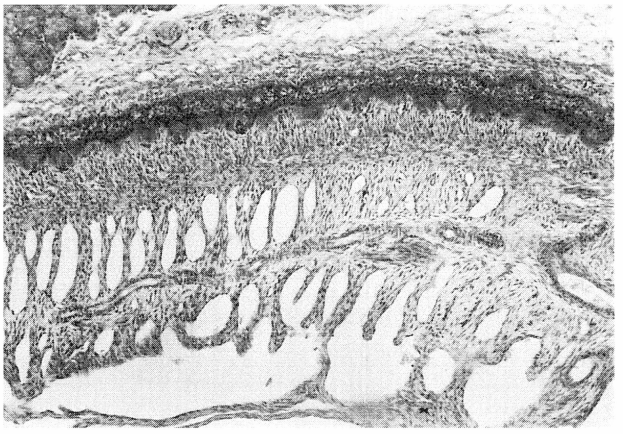

Figure 1. — The longitudinal section of a 7-day-old rat penis, given Tx: Normal development of epidermis (Masson triple, original enlargement x 41).
Figure 2. — 14-day-old experimental group given TX. A reduction in legth of epidermal projections (Verhoeff, original enlargement x 16).
Figure 3. — 21-day-old experimental group given Tx. Diminishing of epidermal projections in glans penis and prepuce (H-E, original enlargement x 41).

Figure 4. — Longitudinals ection of 21-day control group of rats. Well developed epidermal projections and keratinisation in glans penis and prepuce (H-E, original enlargement x 41).
Figure 5. — 28-day-old experimental group given Tx. Atrophy of epithelium of glans penis and prepuce, epithel and also diminishment of keratinisation of epidermal projections (Verhoeff, original enlargement x 41).
Figure 6. — 35-day-old experimental group given Tx. No definition of epidermis layers was seen (H-E, original enlargement x 41).

were found on development of epidermis in this group of rats (Fig. 1).

14-day-old experimental group given Tx: a reduction in density and length of epidermal projections was seen in this group of rats (Fig. 2).

21-day-old control group: well-developed epidermal projections and keratinisation appeared in the glans penis (Fig. 3).

21-day-old experimental group given Tx: epidermal projections were not seen in the gland penis or in epidermis of prepuce (Fig. 4).

28-day-old experimental group given Tx: atrophy of

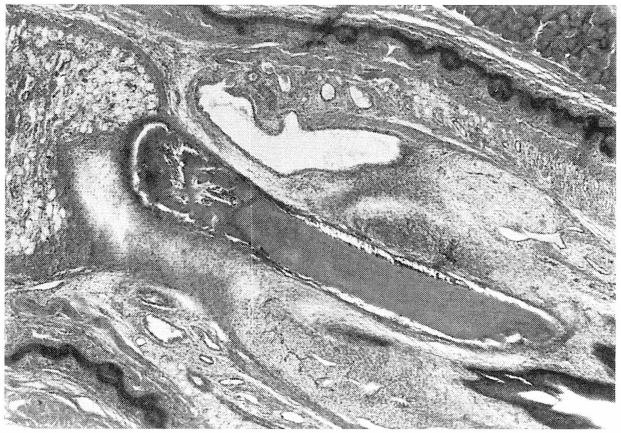

Figure 7. — Longitudinal section of a 60-day-old rat penis, given Tx: End of atrophy and keratinisation in epidermis altogether (H-E, original enlargement x 41).

epithelium of the glans penis and prepuce, and also diminishment of keratinisation of epidermal projections (Fig. 5).

35-day-old experimental group given Tx: No definition of epidermis layers was seen (Fig. 6).

60-day-old experimental group given Tx: Although keratinisation on atrophic epidermis ceased altogether in some places epidermal projections were seen (Fig. 7).

Discussion

Epidermal projections in glans penis skin were forming both in controls and in the Tx injected 5-10 day-old experimental animal groups. But the density of these projections diminished in the 10-60 day-old rat groups, given Tx, relative to the control group of rats. Identically, there are studies that indicate that the epidermis of prepuce and glans penis separate on the 10th day in controls [6, 8].

In our study no distinguishable difference was seen in epidermal projections between the controls and Tx administered 7-14 day-old rat groups.

We have determined that from the 21st day in experimental animals that were given Tx, epidermal projections were getting erased slowly, and in the 60-day-old rat group given Tx the epidermis was atrophic and keratinisation had ceased altogether. As has been reported in previous studies [8, 9], we also observed in our study that the epidermis of prepuce and glans penis do not separate from each other.

Conclusion

The development of epidermal projections in the glans penis skin of rats undergo an interval when given Tx right after birth.

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