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Histological Changes of the Scrotal Testis in Unilateral Cryptorchidism*

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A clinical case of acquired unilateral cryptorchidism after herniotomy was described. Extensive degenerative changes were histologically observed not only in the cryptorchid testis but also in the scrotal one, and were regarded as underlying processes of sterility in the case of unilateral cryptorchidism.

In experimental unilateral cryptorchidism in dogs, histologically demonstrable spermatogenesis was suppressed in both cryptorchid and scrotal testes. Oxygen consumption and respiratory quotient of the organs were enhanced, while the activity of succinic dehydrogenase was lowered. These histological and biochemical findings were more or less normalized after reposition of the cryptorchid testis into the scrotum.

It was concluded that suppressed spermatogenesis in the contralateral scrotal testis in unilateral cryptorchidism was induced in some way by the degenerative changes in the cryptorchid testis.

It is well known that sterility is frequently observed in cases of cryptorchidism. MacCollum[1] stated that only 21 out of 69 patients with unilateral undescended testicles had children, and spermatozoon counts studied on 54 of these 69 cases revealed subnormal values, except in 3 cases with high counts, 50 per cent of the subnormal counts being below 50,000,000 per cubic centimeter.

The degenerative changes which occur in the cryptorchid testis have been noted by many workers and are believed to be a cause of male sterility in bilateral cryptorchidism. But the cause of sterility which occurs in a large number of unilateral cryptorchid men remains still unknown.

We accidentally experienced a case of 23-year-old male with acquired unilateral cryptorchid testis which had been brought about by herniotomy at eleven years of age. No history was confirmed on abnormal position of the testis before the operation, nor was any past history of serious diseases, injury or operation. Urinary excretion of 17-KS, 17-OHCS and estrogen was within the

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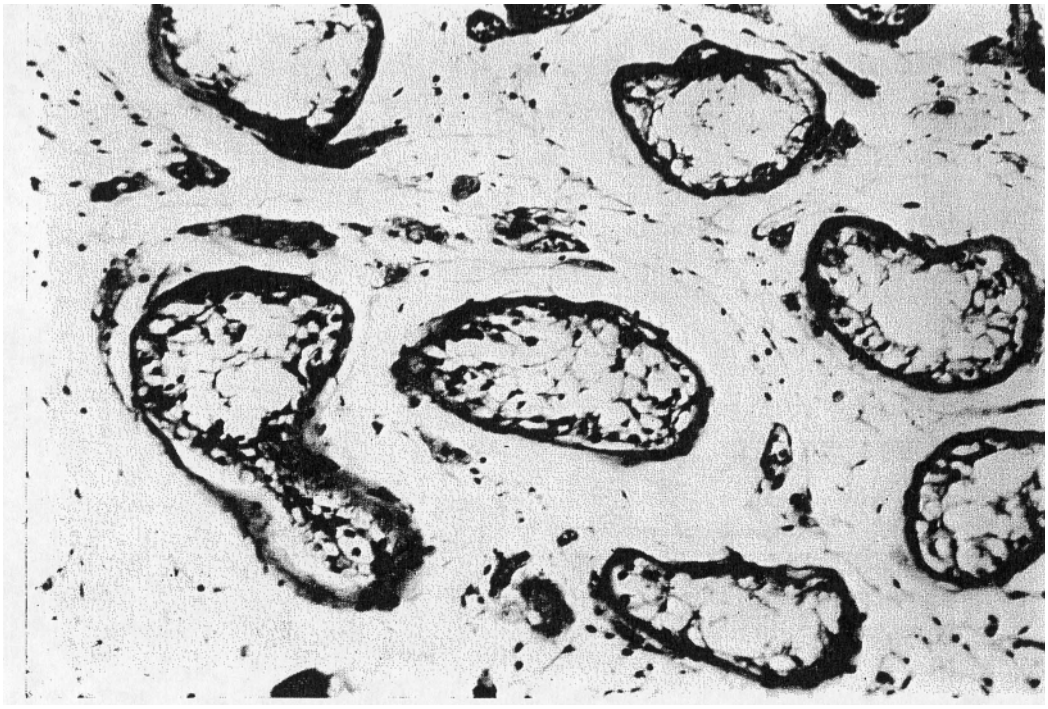

Fig. 1. Biopsy specimen of cryptorchid testis from a 23-year-old man with unilateral cryptorchidism. Note absence of germinal epithelium and relatively intact appearance of Leydig cells. H-E stain, ×100.

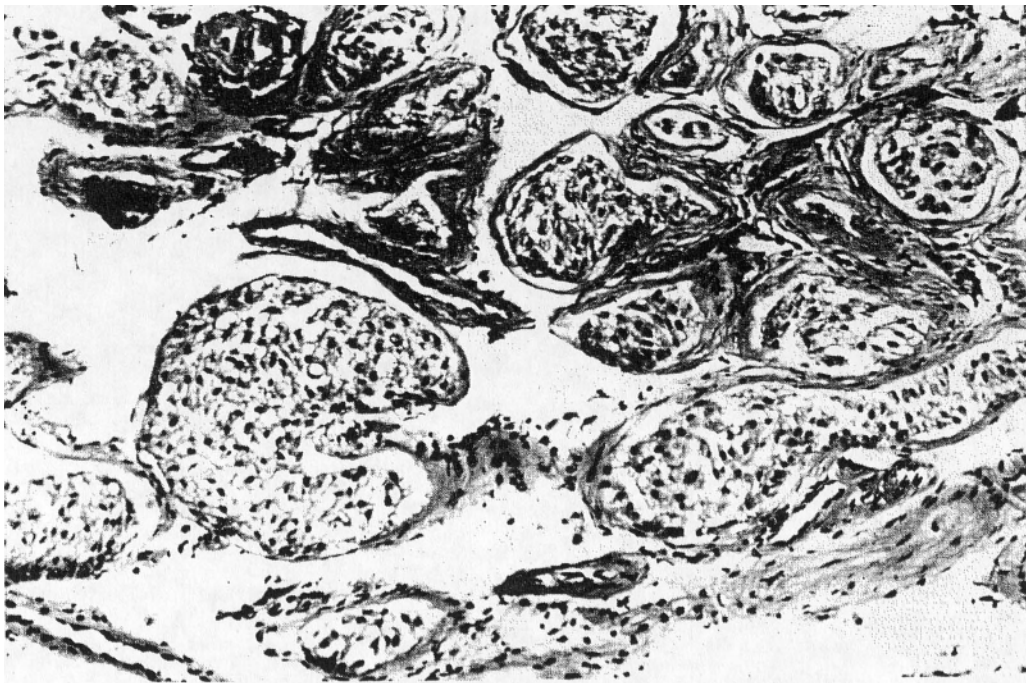

Fig. 2. Biopsy specimen of contralateral scrotal testis from a 23-year-old man with unilateral cryptorchidism. Note remarkable decrease of spermatogenetic cells, thickening of basement membrane and intact appearance of the interstitial cells. H-E stain, ×100.

normal range. But the total urinary gonadotropin was over the normal range. When left-sided orchidopexy was performed, testicular biopsies on both sides were done.

Microscopic findings of the testicular biopsies were as shown in Figs. 1 and 2. A remarkable change was recognized in the seminiferous tubules of contralateral scrotal testis as well as of acquired-cryptorchid testis.

We have been of the opinion that such a degenerative change in contralateral scrotal testis as well as undescended testis is a cause of sterility in unilateral cryptorchidism. However, only a few experimental studies have yet been attempted to elucidate this problem. Therefore, we have made an effort in the present study to clarify histological and biochemical changes in the contralateral scrotal testis in unilateral cryptorchidism.

Materials and Methods

Mature male dogs were used. The right testis of these animals was operatively elevated up to the iliacal level. Biopsies of both testes were performed before the operation as controls (Fig. 3). Particular care was taken that the efferent ducts were not obstructed and the testicular arteries were not injured at the operation.

The operated animals were divided into the following two groups.

Group 1. Animals belonging to this group were killed by bleeding three

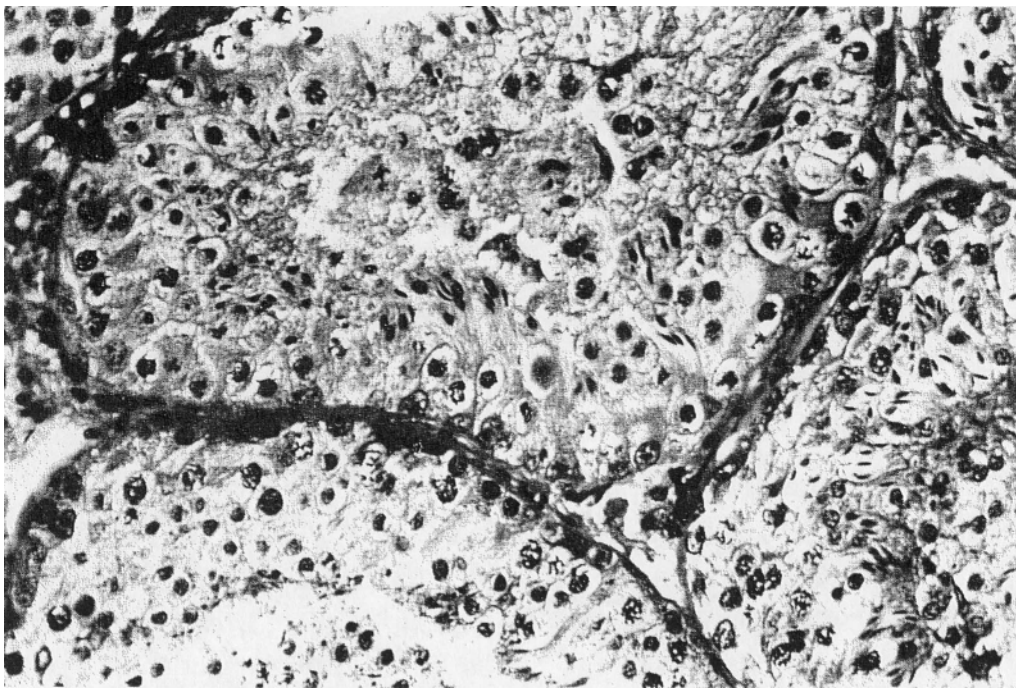

Fig. 3 Biopsy specimen from the testis of a normal dog. Many mature sperms are seen in the tubules. H-E stain, ×250.

weeks to three months after the operation.

Group 2. Reposition of the elevated testis into the scrotum was performed three weeks after the operation. Testicular biopsies were also done at the reposition of the testis. The animals of this group were killed three months after the reposition of the testis.

The testicular tissue was excised and quickly divided into several pieces. A portion of the testicular tissue or the specimens of testicular biopsies were fixed in Bouin's fixative and embedded in paraffin. The paraffin sections were stained with hematoxylin-eosin, Mallory's, elastica-Masson's, periodic acid-Schiff (PAS) techniques and so on. A portion of the testicular tissue, about 100–150 mg, was placed immediately into a chilled Warburg's vessel containing Krebs isotonic phosphate buffer of pH 7.4. The Warburg's vessels containing the testicular tissue were attached to a Warburg's manometer. The water bath was maintained at 38°C. The rate of shaking was set at 90 per minutes. A 20-minute equilibration period was allowed and then the tissue respiration in endogenous state, the succin hydrogenase activity and the lactic dehydrogenase activity (the gas phase being air) were determined at 10-minute intervals for 1 hour.

These values were expressed as microliter per hour per 100 mg of dry tissue weight. The value of O_2 consumption and CO_2 production of testicular tissue were measured without substrate as described by Usami.[2] Measurements of the succinic and the lactic dehydrogenase activities were made according to the method described by Suzuki[3] and Yamamura and Kusunose.[4]

Results

1) Histological observations

a) Group 1

Three weeks after the operation, the germinal cells were remarkably reduced and the Sertoli cells were prominent in the unilateral cryptorchid testis. The basement membrane was slightly thickened in some seminiferous tubules. There was an increase in relative numbers of fibroblast-like cells and young Leydig cells (Fig. 4).

In the contralateral scrotal testis, many immature spermatogonia were present, but mature or normally appearing sperms were seen only in a few tubules. There was an increase in relative numbers of fibroblast-like cells, but the change in Leydig cells was not significant (Fig. 5).

Three months after the operation, the testis on the operated side was smaller than the one on the opposite side. Spermatogenesis had completely ceased. The germinal cells were almost lost and the Sertoli cells were prominent (Fig. 6).

In contralateral scrotal testis, degeneration of the tubules was more distinctly noticeable and the germinal cells were reduced remarkably. Thickening

of the basement membrane and changes in the interstitial tissue were not so remarkable (Fig. 7.).

b) Group 2

Three weeks after the operation, the histological changes were similar to those seen in Group 1. The amount of germinal cells on the operated side had considerably decreased and only the Sertoli cells were recognized in some seminiferous tubules. Thickening of the basement membrane and an increase in numbers of fibroblast-like cells in the interstitial tissue were recognized (Fig. 8).

In the contralateral scrotal testis, spermatogenesis was found to be depressed or stopped completely in many tubules. But an increase of the Leydig cells was not recognized (Fig. 9).

Three months after reposition of the cryptorchid testis into the scrotum, there were regeneration and restoration of structures in the tubules on the operated side. The basement membrane reduced its thickness. But mature sperms in the tubules were not yet present and the increase of fibroblast-like cells in the interstitial tissue were still recognized (Fig. 10).

The contralateral scrotal testis resumed spermatogenesis of which rate was, however, far below normal. There was no remarkable change in the interstitial tissue (Fig. 11).

2) Biochemical observations

The results of biochemical investigations are summarized in Table 1.

Three weeks after the operation, the cryptorchid testis in unilateral cryptorchidism demonstrated a significant increase in both Q_{O_2} (O_2 consumption) and Q_{CO_2} (CO_2 production), especially in Q_{CO_2}. Moreover, the value of R.Q. (respiratory quotient) showed a very marked increase. While SDH (succinic dehydrogenase) and LDH (lactic dehydrogenase) activities were strikingly

TABLE 1. *The change of the biochemical activity (μl/100 mg dry wt./hr.)*

Biochemical activities measured	Duration after operation	R.Q.	Q_{O_2}	Q_{CO_2}	SDH	LDH	SDH/LDH
Untreated controls		0.55	173.5	94.4	566.3	461.6	1.22
Cryptorchid testis	3 wk.	2.29	222.3	510.8	55.0	14.8	3.71
Contralateral scrotal testis		1.27	185.2	235.7	82.6	17.5	4.71
Contralateral scrotal testis	3 mo.	1.00	111.4	111.4	216.3	275.1	0.78

suppressed. SDH/LDH (the ratio of SDH and LDH) showed a significant increase.

In the contralateral scrotal testis, there was a striking increase in Q_{O_2}, Q_{CO_2} and R.Q. The SDH and LDH activities were distinctly lower than normal, but the ratio SDH/LDH showed an increase.

Three months after the operation, the values of Q_{O_2} of the contralateral scrotal testis decreased and Q_{CO_2} increased slightly. R.Q. showed a marked increase. The SDH and LDH activities were still decreased, but these values gradually returned to the normal level. The ratio SDH/LDH was lower than normal.

Discussion

In general, removal of, or damage to, one of a pair of glandular organs results in compensatory hypertrophy or hyperplasia in the other or intact gland. The question of compensatory change in the testes has frequently been discussed.

Benoit,[5] Bloch[6] and several other authors believed that compensatory hypertrophy did not occur after unilateral orchidectomy in adult animals. On the other hand, Trélant and Peyrot[7] and Korenchevsky[8] reported that in experimental unilateral cryptorchidism in animals the scrotal testes were frequently larger and slightly heavier than those of controls. Clegg[9] stated that experimental unilateral cryptorchidism in the rat is accompanied by compensatory changes including hypertrophy, but without hyperplasia of germ cells or hyperplasia and hypertrophy of Leydig cells in the scrotal testis. He also said that these changes were due to increased secretion of both follicle stimulating hormone and interstitial cell stimulating hormone by adenohypophysis. Clinically, Bunge and Bradbury[10] reported two cases of 4- and 6-year-old boys with unilateral cryptorchidism who had apparent compensatory hypertrophy unaccompanied by hyperplasia of the interstitial cells. Shida[11] emphasized that almost all the cases with unilateral or bilateral undescended testes had an inherent congenital defect, and more or less distinct congenital morphological and functional disorders in the contralateral scrotal testis were also recognized even in unilateral cryptorchidism. While Mancini *et al.*[12] stated that there was reason to assume that the germinal epithelial cells of cryptorchid testis were already damaged at early stages of development and were relatively unresponsive at puberty to endogenous gonadotropin stimulation. They also said that no obvious differences were observed between the contralateral and the normal scrotal testis with regard to cytological and cytochemical characteristics. In our present investigations, clinical and experimental, compensatory changes in the contralateral scrotal testis could not be found. On the contrary, remarkable degenerative changes in the contralateral scrotal testis of the unilateral

cryptorchidism were recognized and this might not be a result of congenital defect.

Mancini *et al.*[12] reported that the majority of cryptorchid testes showed a decrease in the content of glycogen and lipids, and exhibited perinuclear basophilia of the various types of spermatogonial cells, as well as diminished cytoplasmic enzyme activity, but no obvious differences among the cryptorchid, contralateral and normal organs were observed with regard to cytological and cytochemical characteristics of the Leydig cells and stromal connective tissue.

Q_{O_2} of the testicular tissue rises, as shown on the cryptorchid testis by Tepperman *et al.*[13] They suggested that the altered ratio of germinal epithelium to the Leidig cells was reponsible for the changes in Q_{O_2}.

In the present experiments, Q_{O_2} and Q_{CO_2} of the tissues of both cryptorchid and contralateral scrotal testes increased three weeks after the operation, but in the contralateral scrotal testis these values gradually returned to the normal level three months after the operation. Both SDH and LDH activities of the contralateral scrotal testis as well as the cryptorchid testis were remarkably decreased three weeks after the operation. But these values recovered gradually.

The degenerative changes which occur in the testis in experimental cryptorchidism have been demonstrated by many workers and it is generally accepted that, if the condition is maintained for a sufficiently long time, the great majority of germ cells are lost, and that reposition of the organ into the scrotum does not result in a recovery of the normal spermatogenesis. However, Clegg[9] found that in adult rats with experimental bilateral cryptorchidism limited regenerative changes occurred during the 4th and 5th weeks of operation. Nelson[14] stated that experimental cryptorchidism maintained for 28 days in rats was followed by recovery of spermatogenesis in 40 to 100 days after reposition of the testes into the scrotum. In our investigation, experimental cryptorchidism maintained for 3 weeks in dogs was followed by recovery of spermatogenesis in 3 months after reposition of the testis into the scrotum. Furthermore, it was interesting that recovery of spermatogenesis in contralateral scrotal testis was observed after reposition of the undescended testis to the scrotum.

As mentioned above, some workers recognized compensatory changes in the scrotal testis of experimental unilateral cryptorchidism. On the contrary, in our clinical and experimental investigations, degenerative changes rather than compensatory hyperplasia of the germinal cells in the contralateral scrotal testis of unilateral cryptorchidism were recognized. We suppose such degenerative changes in the contralateral scrotal testis as well as in the undescended testis might be a cause of sterility in unilateral cryptorchidism. We believe that these degenerative changes of contralateral scrotal testis are induced by the degeneration of cryptorchid testis, because the degenerative changes of contralateral scrotal testis recover after reposition of the cryptorchid testis into the scrotum.

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Legends

Fig. 4. Biopsy specimen of the cryptorchid testis from a dog three weeks after the operation. Note absence of germinal epithelium and increasing fibroblast-like cells in the nterstitial tissue. H-E stain, × 100.

Fig. 5. Biopsy specimen of the contralateral scrotal testis from the same case as shown in Fig. 4. Note reduction of mature or normally appearing sperma. H-E stain, ×100.

Fig. 6. Section of the crytorchid testis from the same dog as shown in Fig. 4 sacrificed three months after operation. Note the germinal epithelium composed almost of Sertoli cells and slightly increasing Leydig cells. PAS stain, × 100.

Fig. 7. Section of the contralateral scrotal testis from the same dog as shown in Fig. 4 sacrificed three months after the operation. Note absence of germinal epithelium and relatively intact appearance of the interstitial tissue. PAS stain, × 100.

Fig. 8. Biopsy specimen of the cryptorchid testis from a dog three weeks after the operation. Note absence of germinal epithelium and thickening of basement membrane. H-E stain, × 100.

Fig. 9. Biopsy specimen of the contralateral scrotal testis from the same dog as shown in Fig. 8. Note depression or cessation of spermatogenesis in some tubules. H-E stain, × 100.

Fig. 10. Section of the cryptorchid testis from the same dog as shown in Fig. 8 three months after reposition. Note regeneration and restoration of structures in tubules. H-E stain, × 100.

Fig. 11. Section of the contralateral scrotal testis from the same dog as shown in Fig. 8 three months after reposition. Spermatogenesis is resumed, but its rate is below normal. H-E stain, × 100.