Age Difference in the Prostate Hypertrophy Induced by the Removal of the Seminal Vesicle in Rats

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Synopsis

The removal of the seminal vesicle in 4-week-old, 6-week-old or 1.2-year-old rats resulted in a significant increase in the weight of the lateral prostate 6 weeks later examined. The weight change was mainly due to a marked distension of alveoli but showing close resemblance to structures of the control animals with secretory activity. RNA/DNA ratio in the unit tissue increased. Constricted alveoli and epithelial hyperplasia in many alveoli were demonstrated after removal of the seminal vesicle only in the lateral prostate of aged rats, though a less marked change in the weight was shown. The degree of the hypertrophy of the prostate was largely dependent on the age of rats. The greatest increase in the weight of both lateral and ventral prostatic lobes was observed when the seminal vesicle was removed at 4 weeks of age. More than one hundred per cent, 94% and 48% increase in the weight of the lateral prostate over the control values were shown in immature, young adult and aged rats respectively. The weight of the ventral prostate also increased after removal of the seminal vesicle but to a lesser extent as compared to that seen in the lateral prostate. No response of the ventral prostate to the ablation of the seminal vesicle was found in aged rats. Factors which might be involved in the cause of the prostate hypertrophy in absence of the seminal vesicle were discussed.

The seminal vesicle and prostate, responding to the same hormonal stimuli, differ in their response to exogenous androgen (Hooker, 1942; Dorfman, 1950; Fujii and Villee, 1969) or to estrogen (Korenchevsky and Dennison, 1935; Fuji and Villee, 1968) and in the degree of retarded development after castration (Price, 1936; Hooker, 1942; Fujii and Villee, 1968 and 1969). More striking difference in both organs is in the frequency with which they give rise of tumors in man. Although biochemical or structural changes of the prostate and seminal vesicle have been extensively studied in relation to the mechanism of action of androgens, functional significance of the individual organ in reproduction has not definitely been established so far.

The present study was undertaken as a preliminary study to further investigations on the physiological role of the seminal vesicle or prostate in reproduction. The influence of age on the behavior of the prostate and other male accessory sex organs after removal of the seminal vesicle was studied in rats.

Materials and Methods

Male albino rats, Wistar strain aged 4 weeks, 6 weeks and 1.2 years were used in this experiment. They were maintained on a standard laboratory chow (Oriental Yeast Co., Tokyo) and tap water ad lib. and kept in an air conditioned room (temperature: 22±2°C, humidity: 55±5%) throughout the experimental period. Their body weight was 50 to 60 g, 200 to 250 g and 400 to 500 g respectively. They were divided into two groups; sham-operated group and seminal-vesiculectomized one. By the anterior approach the bilateral seminal vesicles were freed from the coagulating glands and main vessels supplying the seminal vesicle, and dissected out at the site of entrance of its ducts into the urethra under ether anesthesia without making any special ligation in immature animals and with a ligation on the secretory tract of the seminal vesicle.
in adult or aged rats (1.2-year-old rats were referred to aged animal in this experiment).

One and half a month after the operation animals were sacrificed by decapitation and the ventral and lateral prostatic lobes, coagulating gland, preputial gland, testis, kidney, adrenal and pituitary gland were dissected free from surrounding connective tissues and adipose tissues, and then weighed. All the secretory fluid was expressed from the seminal vesicle and the tissues were rinsed in 0.9% cold-saline before weighing. One lobe of the ventral and lateral prostates or coagulating gland was fixed in 10% formalin. Formalin-fixed tissues were serially sectioned and stained with either hematoxyline and eosin or Masson's staining solution. The other lobe of the tissues was determined for DNA and RNA contents according to Schneider's modification of the Schmidt-Thannhauser procedure (1946). RNA amount was determined by orcinol reaction (Schneider, 1957), DNA by Burton's diphenylamine reaction (1956). Yeast RNA and calf thymus DNA (Daiich Pure Chemicals Co., Tokyo) were served as standards.

In an additional experiment, the ventral prostates of immature and young adult rats were removed by abdominal incision. Changes in the weights of other accessory sex organs, testis, kidney, adrenal and pituitary gland were also analyzed. DNA and RNA determinations and histological examination of the tissues were carried out in the same manner described above for comparative purpose.

Results

Organ Weights

Six weeks after the removal of the seminal vesicle at the immature age or young adult age in rats, the weights of the lateral and ventral prostatic lobes increased (Fig. 1). The increase in the weight of the lateral lobe was much greater than that of the ventral prostate. A relatively little increase in the weight of the lateral lobe and no change in the weight of the ventral lobe were demonstrated in aged animals whose seminal vesicle was removed when they were 1.2 years old. The dorsal prostate did not show any significant changes in all groups. The removal of the seminal vesicle in immature and young adult rats produced a decrease in the weight of the coagulating gland whereas an increase was
Table 1. Effects of the removal of the seminal vesicle or ventral prostate on the weights of the kidney, adrenal, testis, preputial gland and pituitary in immature, young adult and aged rats

<table>
<thead>
<tr>
<th>Age at the surgery</th>
<th>Treatment</th>
<th>No. of rats</th>
<th>Body wt. (g)</th>
<th>Kidney</th>
<th>Adrenal</th>
<th>Testis</th>
<th>Preputial gland</th>
<th>Pituitary</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-week-old</td>
<td>C</td>
<td>7</td>
<td>250±19a</td>
<td>861±38</td>
<td>17.8±1.5</td>
<td>1115±69</td>
<td>55.2±1.9</td>
<td>2.73±0.14</td>
</tr>
<tr>
<td></td>
<td>SVx</td>
<td>7</td>
<td>290±5</td>
<td>828±19</td>
<td>15.6±1.1</td>
<td>994±60*</td>
<td>55.8±3.3</td>
<td>2.96±0.15</td>
</tr>
<tr>
<td></td>
<td>Prx</td>
<td>6</td>
<td>264±13</td>
<td>851±32</td>
<td>17.8±1.0</td>
<td>1090±44</td>
<td>54.6±4.4</td>
<td>2.95±0.21</td>
</tr>
<tr>
<td>6-week-old</td>
<td>C</td>
<td>4</td>
<td>365±22</td>
<td>835±47</td>
<td>20.6±3.5</td>
<td>814±92</td>
<td>50.5±12.4</td>
<td>2.85±0.14</td>
</tr>
<tr>
<td></td>
<td>SVx</td>
<td>5</td>
<td>390±12</td>
<td>848±39</td>
<td>17.0±0.8</td>
<td>753±80</td>
<td>34.7±4.0</td>
<td>3.14±0.08</td>
</tr>
<tr>
<td></td>
<td>Prx</td>
<td>5</td>
<td>383±14</td>
<td>783±29</td>
<td>18.3±1.2</td>
<td>788±50</td>
<td>44.6±2.3</td>
<td>2.69±0.31</td>
</tr>
<tr>
<td>1.2-year-old</td>
<td>C</td>
<td>5</td>
<td>441±30</td>
<td>8.2±0.5</td>
<td>797±35</td>
<td></td>
<td></td>
<td>2.98±0.14</td>
</tr>
<tr>
<td></td>
<td>SVx</td>
<td>5</td>
<td>470±23</td>
<td>8.7±0.8</td>
<td>747±41</td>
<td></td>
<td></td>
<td>2.93±0.07</td>
</tr>
</tbody>
</table>

Animals were killed 6 weeks after the surgery. Organ weights were expressed as mg/100 g body weight. a, Mean ± standard error; C, Sham-operated control rats; SVx, Rats whose seminal vesicle was removed; Prx, Rats whose ventral prostate was removed; *, P<0.05 vs. controls.

noted in aged rats (Fig. 1). No considerable changes in the weights of the adrenal, pituitary, kidney and preputial gland were observed (Table 1). The weight of the testis decreased when the seminal vesicle was removed at 4 weeks of age.

The removal of the ventral prostate in immature rats resulted in an increase in the weight of the lateral prostate 6 weeks later. However, the weight changes in the lateral prostate were less marked as compared to those of animals in which the seminal vesicle was removed at the same age (Fig. 2). No response of the seminal vesicle to the ablation of the ventral prostate was shown in young adult rats.

**DNA and RNA Contents**

RNA content per unit tissue of the lateral and ventral prostatic lobes increased in rats whose seminal vesicle was removed at the age of 4 weeks. In addition, a significant decrease in DNA concentration per unit tissue of the lateral prostate resulted subsequently in a pronounced increase in RNA/DNA ratio (Table 2). In spite of the increase in the weight of the lateral prostate after the removal of the seminal vesicle in aged rats, no significant

Table 2. Effects of the removal of the seminal vesicle or ventral prostate at various ages in rats on the contents of DNA and RNA in the lateral or ventral prostatic lobe

<table>
<thead>
<tr>
<th>Age at the surgery</th>
<th>Treatment</th>
<th>No. of rats</th>
<th>Lateral prostate Wt.</th>
<th>DNA (µg/mg)</th>
<th>RNA (µg/mg)</th>
<th>RNA/DNA ratio</th>
<th>Ventral prostate Wt.</th>
<th>DNA (µg/mg)</th>
<th>RNA (µg/mg)</th>
<th>RNA/DNA ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-week-old</td>
<td>C</td>
<td>7</td>
<td>28.1±5.9a</td>
<td>245±26</td>
<td>726±55</td>
<td>3.03±0.36</td>
<td>73.7±5.6</td>
<td>580±66</td>
<td>749±99</td>
<td>1.31±0.07</td>
</tr>
<tr>
<td></td>
<td>SVx</td>
<td>7</td>
<td>63.5±4.5</td>
<td>186±15*</td>
<td>800±56</td>
<td>4.48±0.50*</td>
<td>111.0±6.1</td>
<td>528±21</td>
<td>847±55</td>
<td>1.61±0.11</td>
</tr>
<tr>
<td></td>
<td>Prx</td>
<td>6</td>
<td>57.5±5.1</td>
<td>166±11*</td>
<td>578±46</td>
<td>3.65±0.26</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2-year-old</td>
<td>C</td>
<td>5</td>
<td>39.2±6.1</td>
<td>356±26</td>
<td>501±33</td>
<td>1.41±0.02</td>
<td>120.3±7.3</td>
<td>274±24</td>
<td>418±47</td>
<td>1.51±0.08</td>
</tr>
<tr>
<td></td>
<td>SVx</td>
<td>5</td>
<td>58.0±10.6</td>
<td>313±21</td>
<td>458±30</td>
<td>1.55±0.02</td>
<td>115.5±10.8</td>
<td>327±10</td>
<td>354±36</td>
<td>1.08±0.10**</td>
</tr>
</tbody>
</table>

DNA and RNA contents were expressed as µg/100 mg wet tissue, organ weight as mg/100 g body weight. a, Mean ± standard error; C, Sham-operated control rats; SVx, Rats whose seminal vesicle was removed; Prx, Rats whose ventral prostate was removed; *, P<0.05 vs. controls; **, P<0.01.
changes in DNA and RNA contents per unit tissue were shown, i.e., the levels of DNA and RNA in the tissue increased proportionally to the increase of the organ weight. An increase in DNA concentration and a slight decline in RNA concentration with a consequent decrease in RNA/DNA ratio were shown in the ventral prostate of aged rats.

Histological Findings

The lateral and ventral prostates of rats whose seminal vesicle was removed when they were 4 weeks old, had greater acinous distensión with secretory activity Fig. 3–6). The lateral prostate in aged rats whose seminal vesicle was removed when they were 1.2 years of age, had slightly complicated structures as compared to those of control rats. Epithelial hyperplasia and constricted alveoli were shown (Figs. 7, 8). Histological structure of the seminal vesicle of the rats whose ventral prostate was removed at 4 weeks of age did not differ from that of the control animals.

Discussion

The removal of the seminal vesicle of immature or adult rats resulted in a striking increase in the weight of the lateral prostate.
Fig. 3. The ventral prostate of a rat given the sham-operation at 4 weeks of age and examined 6 weeks later. Hematoxyline-eosin. ×35.

Fig. 4. The ventral prostate of a rat 6 weeks after the removal of the seminal vesicle at the age of 4 weeks showing the marked distension of alveoli. ×35.

Fig. 5. The lateral prostate of a rat given the sham-operation at 4 weeks of age and examined 6 weeks later. ×35.

Fig. 6. The lateral prostate of a rat 6 weeks after the removal of the seminal vesicle at the age of 4 weeks showing the distended alveoli but close resemblance to Fig. 5. ×35.

Fig. 7. The lateral prostate of an aged control rat. Hematoxyline-eosin. ×7.5.

Fig. 8. The lateral prostate of an aged rat 6 weeks after the removal of the seminal vesicle showing the epithelial hyperplasia. ×7.5.
The weight of the ventral prostate increased also in both groups but to a lesser extent as compared to that seen in the lateral prostate. Histological findings indicate that the increase in the weights of both lobes of the prostate was mainly due to hypertrophy of the secretory epithelial cells. Distended acini were shown. Appearance of the prostate hypertrophy in the present experiment was significantly dependent on the age of animals. The degree of the hypertrophy decreased concomitantly with the increasing age of rats. Over one hundred per cent increase in the weight of the lateral prostate was demonstrated when the seminal vesicle of rats was removed at 4 weeks of age. An increase in the weight of the ventral prostate was also marked when the seminal vesicle was removed in the immature period of life. The prostatic lobes in aged rats, over 1-year-old, showed a lower response to the removal of the seminal vesicle; forty eight per cent increase in the weight of the lateral prostate and no increase in the weight of the ventral prostate were observed.

Age difference in the responsiveness of the lateral and ventral prostates to removal of the seminal vesicle could be caused from different sensitivity of these organs to circulating androgens rather than from the different level of circulating androgens. If the level of circulating androgens is largely implied in the cause of the hypertrophy of these tissues after ablation of the seminal vesicle, the prostate of young adult rats will show a more marked enlargement than those of immature animals. The highest threshold of the accessory sex organs to testosterone was found around 6 weeks of age in male rats castrated at birth (Hooker, 1942). Price and Ortiz (1944) have also reported that the highest sensitivity to the 6 daily injections of androgen is demonstrated at the age of 14 days to 18 days for the prostate, and at the age of 26 days for the seminal vesicle. Exposure to circulating androgens for a certain period of time around sexual maturation, in absence of the seminal vesicle, may play an important role in presenting the higher degree of the hypertrophy of the prostate. In the premature period, the cells of accessory sex organs with the lowest threshold setting will be the most exposed to the resultant excessive hormone stimulus in spite of the low level of circulating androgens. Adrenal androgen in premature animals may also be a contributory factor to such response of the prostate to the ablation of the seminal vesicle. Burrill and Greene (1939) or Howard (1941) have suggested that the prostate of immature rats during a certain phase in the development is under the influence of adrenal androgen.

In general, it has been suggested that the aging process may be reflected in the decreased ability of the prostate or seminal vesicle to respond to circulating androgens. In the present experiment, an apparent loss of ability of the prostate to respond in weight change to the lack of the seminal vesicle in aged rats but an increase in irregular hyperplasia of epithelial cells could be a reflection of change in physiological function of the prostate in their aged phase. One year and two months old rats at the beginning of the experiment were referred to aged rats in the present experiment. A decrease in 5α-reductase activity in the ventral prostate of more than one year old rats was clearly demonstrated (Shimazaki, et al., 1969). A consistent reduction in response of both lateral and ventral prostates according to the growth of rats and a differential response of each prostatic lobe to ablation of the seminal vesicle must await further elucidation. Furthermore, a greater response of the ventral prostate to the removal of the seminal vesicle than the response of the seminal vesicle to the removal of the ventral prostate must also be analyzed in further experiments in relation to the functional characteristics of both organs in rats. Tveter (1969) demonstrated that the pattern of the uptake and distribution of labeled testosterone into all the part of the prostatic lobes were essentially the same in rats, though the ventral prostate had a greater capacity to take up and
retain androgen than the dorsal lobe and coagulating gland.

The weight changes of the lateral or ventral prostate were associated with a definite increase in the RNA content and a decrease in the DNA content in the tissue, suggesting a benign hypertrophy of the prostate. Histological structures also indicated benign hypertrophy of the organ. Spontaneous hypertrophy of the prostate is a rare occurrence in the rodent. This leads to a difficulty to use small laboratory animals for the study on etiology of hypertrophy of the prostate. It is of interest that the histological structures of the lateral prostate in aged rats showed hyperplasia of the secretory epithelium and many constricted alveoli 6 weeks after removal of the seminal vesicle, though the weight change was less than that seen in immature or young adult animals and no significant change in RNA/DNA ratio in the unit tissue was noted.

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References