THE ANDROGEN TREATMENT OF FEMALES
WITH INCURABLE GENITAL CANCER

By

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The use of hormonal therapy in the management of advanced prostatic and mammary cancers is now well established. But clinical trials to influence advanced genital cancer in the female are much more recent. The cause seems to be, that a relation between sex hormones and cancer of the female genital organs is not yet clear, especially concerning the most frequent genital cancer – the cervix cancer. But if we regard that sooner or later about 60 per cent of all women with cervix cancer will come into a stage of incurability, it is clear, that even those cases not curable by established methods of surgery and irradiation have been considered for hormonal therapy. In most cases androgenic hormones have been administered. Many reports of therapeutical investigations have appeared in the literature. Often only a small number of cases have been investigated, but most authors agree that nearly half of all patients treated with sufficient doses, show favourable results, especially concerning their well-being.

In order to get an own opinion about the value of androgenic administration in females with incurable genital cancer, we treated 191 women in incurable stage from about 1950 to 1955. The ages of these patients ranged from 30 to 70 years. The amount of hormone received by 63 patients was on account of different reasons less than 500 mg. In no one of these cases a favourable effect was observed, which could be attributed to hormonal administration. Therefore the remainder of this report will not deal with these cases.

128 women received androgen doses from 600 to 4000 mg. In most cases 2000 mg. were administered. Most frequently we used testosterone-propionate in oily solution or in crystal-suspension. During the last time we used chiefly testosterone-oenanthate, and especially in young women also methyl-androstenediol. According to organs involved, these 128 cases have been tabulated under consideration of previously therapeutical measures (Table 1).
Table 1.
Distribution of Genital Cancer According to Organ Involved and Previous Therapy in our Study Group (1950-1955).

<table>
<thead>
<tr>
<th>Previous Therapy</th>
<th>Number of Cases</th>
<th>Cervix</th>
<th>Endometrium</th>
<th>Ovary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Incurable</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Primary Incurable and Palliative Treatment</td>
<td>4</td>
<td>2</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Primary Progressed after Intensive Treatment</td>
<td>46</td>
<td>39</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Recidivation after Intensive Treatment</td>
<td>71</td>
<td>64</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>128</td>
<td>108</td>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>

108 patients showed cervix cancers. Three of them had primary incurable cancer, for which no further therapy had been administered. 2 patients had primary incurable cancer with palliative irradiation. 39 were treated intensively, but showed no reaction. And 64 had recidivations after previously intensive treatment. 6 patients had endometrial cancers, one of them was primary incurable, 2 were treated intensively and primary progressed, and 3 showed recidivations after previously intensive treatment. 14 patients had ovarian carcinomas. 3 of them were primary incurable with palliative treatment, 5 remained advanced, and 4 showed recidivations after intensive treatment.

The next table demonstrates our clinical observations of the reaction of our patients by hormonal treatment (Table 2).

Table 2
Results of Androgen Treatment in Incurable Genital Cancer.

<table>
<thead>
<tr>
<th>Clinical Observations</th>
<th>Number of Cases</th>
<th>Cervix</th>
<th>Endometrium</th>
<th>Ovary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Influenced</td>
<td>43</td>
<td>35</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Subj. Improved</td>
<td>57</td>
<td>48</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td>Subj. a. Obj. Improved</td>
<td>28</td>
<td>25</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>128</td>
<td>108</td>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>
43 patients showed no favourable response to hormonal therapy: 35 with cervix cancer, 3 with endometrial cancer, and 5 with ovarian cancer. In 85 females a favourable effect was to be seen. 57 patients showed only a subjective improvement, whereas in 28 patients as well a subjective as an objective improvement could be noted.

48 of the subjective improved patients had cervix cancers and 9 ovarian cancers. Of the subjective and objective improved patients 25 had cervix cancers and 3 endometrial cancers. From this result is to be seen, that the organ localisation with regard to the favourable influence by testosterone administration, seems to be without any importance. But the small number of cases with endometrial and ovarian cancer must here be taken into consideration.

In patients only subjective improved, the favourable effect of treatment consisted of an improvement of well-being, condition, decrease of troubles, especially pains, which was objectively to be seen in a diminution of opiate consumption. In most of the objective improved patients, an increase or keeping of weight was observed, likewise an increase of serum protein levels, and a considerable diminution of opiate consumption. 10 of these females recovered so much, that they were able to do easy work at home. A favourable response to hormonal administration was attained in a majority of cases from 800 to 1000 mg., and lasted from a few months to several years. But then, in spite of continuous hormonal therapy, a rapid decay and quick exitus occurred. The extraordinary good feeling stood mostly in a striking contrast to the physical state. It is difficult to decide, whether this improvement is really caused by hormonal treatment, because we also know patients with untreated incurable genital cancer, who survived for a long time without any therapy.

28 patients showed osseous metastases. In 8 of these patients the bony process seemed to remain stationary by testosterone treatment. In some cases recalcification could be seen by X-ray examination. In 17 females pulmonary metastases were observed, which were not influenced by this therapy. An influence on the growth of cancer could be noted neither in positive, nor in negative sense.

In 16 patients we observed virilism, especially hirsutism and depending of voice. In 4 patients these signs occurred by a hormonal dose from 1500 to 2000 mg., in 10 patients from 2000 to 3000 mg., and in 2 patients from 3000 to 4000 mg. It is remarkable, that we could note these side-effects only in favourable influenced females. Only in one case a hypercalcemia was to be seen already after a testosterone dose of 1000 mg. In the other females the serum calcium levels were found within normal limits.

Several investigators have published schemes for the dosage of androgenic hormones. On account of our observations we think it important to administer a sufficient dose for a sufficient time and to continue therapy also, when a
favourable effect can be noted. Depots preparates are especially suitable for this.

There are different opinions about the mechanism of action of this hormonal therapy. In our opinion the favourable effect of androgenic treatment in females with incurable genital cancer can be attributed to extragenital effects of androgens, especially of the protein anabolic action. It has still to be clarified, whether in this connection antigonadotrophic and antiestrogenic effects are of any importance. If there is an importance, we think it will be rather in endometrial and ovarian cancers, than in cervix cancers.

Finally we should like to state that the administration of androgenic hormones in females with incurable genital cancer is probably not of the same value as in females with mammary cancer. Nevertheless from our observation is to be seen, that also in females with incurable genital cancer a favourable effect may be attained by this therapy. Therefore the androgen treatment can be considered as an enrichment of the limited therapeutical methods, that are available in this stage of cancerous disease.

REFERENCES

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Nowakowski, H.: In: »Stoffwechselwirkungen der Steroidhormone«, Springer-Verlag