Elevated Levels of Endometrial Lactate Dehydrogenase in Hyperplasia and Carcinoma of Human Endometrium

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SUMMARY

Total lactate dehydrogenase levels and M-type subunits of this enzyme were greatly increased, compared with normal values, in hyperplastic endometrium. The levels of lactate dehydrogenase in 43 cases of hyperplastic endometrium were similar to those in 3 cases of carcinoma of the endometrium. The findings suggest that a biochemical relationship exists between hyperplasia and carcinoma of endometrium.

INTRODUCTION

There is now considerable evidence to suggest that carcinoma of the endometrium may develop in some patients with endometrial hyperplasia as a result of prolonged endogenous estrogen stimulation without the cyclic intervention of progesterone (1, 5, 7). The purpose of the present study was to compare the level of LDH in normal endometrium with the level in hyperplastic endometrium and carcinoma of endometrium. Previous studies from this laboratory (2, 9) involving a large group of women have established normal values for a number of enzymes of carbohydrate metabolism in endometrium. These studies have also shown that interesting alterations occur in the isoenzymic composition of human endometrium following the change from proliferative to secretory phase. For instance, in normal endometrium during the proliferative phase the percentage of LDH-M subunits was 11%. This increased to 32% during the secretory phase. In some human cancer tissues there is usually an increase in total LDH levels compared with the tissue of origin and a concomitant increase in the percentage of LDH-M subunits (8).

SUBJECTS AND METHODS

Endometrial biopsies were taken from 43 patients (age range, 18 to 40 years) who were under investigation for menstrual abnormalities. Curettage was performed under general anesthesia. A sample of the biopsy was examined histologically, and the remainder was extracted for enzyme analysis as before (9). Patients with hyperplasia of the endometrium were subdivided on the basis of histology into hyperplastic nonsecretory endometrium and cystic hyperplasia of endometrium. LDH activity was also measured in endometrium from 3 diagnosed cases of carcinoma of the endometrium.

Total LDH activity and the amounts of isoenzymic subunits were measured as described before (2, 9). Electrophoresis of endometrial extracts for LDH isoenzymes was also described previously (2, 9). Enzyme activity is expressed in IU/g, wet weight, of tissue; this method of expressing enzyme activity was found previously to compare favorably with other methods (9).

RESULTS AND DISCUSSION

The levels of LDH were very high in endometrium from all cases of endometrial hyperplasia; the mean level was over 4-fold greater than values previously cited (9) for control biopsies in the proliferative phase (Table 1). The levels of LDH were higher still in the 3 cases of carcinoma of endometrium examined to date (Table 1). The percentage of LDH-M subunits was calculated as before and confirmed by examining the intensity of the various isoenzymes after starch-gel electrophoresis (2). Because relatively large endometrial biopsies are required for these latter studies, only 3 results are presented in Table 1. The values for LDH-M

<table>
<thead>
<tr>
<th>Patients</th>
<th>No. of patients</th>
<th>Range of values</th>
<th>Mean ± S.D.</th>
<th>% M-type LDH subunits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (9)</td>
<td>99</td>
<td>27-59</td>
<td>44 ± 7.4</td>
<td>11</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplastic</td>
<td>34</td>
<td>130-249</td>
<td>166 ± 18.6</td>
<td></td>
</tr>
<tr>
<td>Nonsecretory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic Hyperplasia</td>
<td>9*</td>
<td>275-470</td>
<td>331 ± 31.8</td>
<td></td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case A</td>
<td>504</td>
<td></td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>Case B</td>
<td>219</td>
<td></td>
<td></td>
<td>72</td>
</tr>
<tr>
<td>Case C</td>
<td>344</td>
<td></td>
<td></td>
<td>70</td>
</tr>
</tbody>
</table>

* Of these women, 6 have had a hysterectomy since this study began.
subunits in the hyperplastic endometrium (Table 1) were 5- to 6-fold higher than normal (9); likewise, in 3 cases of carcinoma of endometrium very high levels of LDH-M subunits were encountered (Table 1). Relatively high LDH values and the predominance of LDH-M subunits are characteristics of many tumors (3).

It is of interest in the light of our results that estrogens preferentially induce the synthesis of M-type subunits of LDH in the rat uterus (4). Although no such information is available about the human uterus, the present findings suggest that the similarities in LDH patterns between hyperplasia and carcinoma of the endometrium might be the result of prolonged endogenous stimulation by estrogens.

Regarding the possible diagnostic implications of this study, efforts are now being made to measure total LDH and the percentage of M-type subunits in plasma from patients with hyperplasia or carcinoma of endometrium. Elevated plasma LDH levels occur in many different types of cancer (6).

ACKNOWLEDGMENTS

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