Concentration of Radiolabeled Cholesterol In a Feminizing Adenoma of the Testis

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Quantitative tissue studies demonstrated increased 19-\([{^{131}}I]\)iodocholesterol concentration in a feminizing adenoma of the testis. The potential application of iodocholesterol and its isomers in the detection of steroid-secreting neoplasms of the testis and ovary is suggested.


The recognition that the adrenal cortex concentrates radiolabeled cholesterol to a greater extent than other tissues has led to the development of a method for adrenal imaging (1,2). Subsequently radioiodocholesterol imaging has proven useful in the diagnosis of both neoplastic and non-neoplastic disorders of the adrenals (3–5). Since the steroid-synthesizing cells of the testis and ovary share with the adrenal cortex the ability to take up cholesterol from the plasma, radioiodocholesterol imaging might also help to demonstrate functioning gonadal tumors.

In this report we describe a young man with feminization in whom tissue studies following the administration of 19-\([{^{131}}I]\)iodocholesterol demonstrated increased radioactivity in a steroid-secreting tumor of the testis.

CASE REPORT

The patient, a 28-year-old man, was referred to our clinic for evaluation of gynecomastia of 3½ years duration. Both breasts had been slowly increasing in size over this period, with tenderness during the last 6 mo. There was no nipple discharge and he denied any change in libido or potency. There had been transient breast enlargement during puberty but no other significant history.

Pertinent findings on physical examination included normal vital signs, bilateral gynecomastia (right breast diameter 17 cm; left 19 cm) with prominent areolae. The right testis was smaller than normal (6) (3.2 cm by 2 cm); the left testis was normal in size (3.8 cm by 2 cm) with a firm, nontender, 1-cm nodule in the lower pole. Routine laboratory studies were normal. Plasma estradiol, testosterone, luteinizing hormone, and follicle-stimulating hormone levels were measured by radioimmunassays (Table 1). Catheter sampling of the spermatic veins was attempted but failed.

At surgery the left spermatic vein was cannulated and a sample obtained for measurement of estradiol and testosterone (Table 1). A mass was readily palpable in the left testis and an orchietomy was performed. On section, a well-encapsulated 1 × 1-cm tumor was seen. Microscopy showed the tumor to consist of interstitial cells. One week after surgery, the peripheral hormone concentrations were normal, and recovery was uneventful.

Special studies. Preoperatively the patient was given 2.32 mCi of 19-\([{^{131}}I]\)iodocholesterol* and scintiphotos were made with a conventional gamma camera, using a 20% window to cover the 364-keV peak. The testes were imaged at 8 and at 10 days (pinhole collimator), and at 10 days the anterior abdomen and posterior adrenal area were also imaged (medium-energy, parallel-hole collimator).

Testicular activity was seen well at 8 days (Fig. 1), with uptake on the left a little denser than on the right. There was, however, no definite focal accumulation ascribable to the palpable mass. The penile activity is perhaps due to the large blood pool of this organ. The 10-day image showed no definite concentration in the testes. Images of the anterior abdomen and the adrenal region at 10 days failed to show identifiable tracer concentration. (Before the iodocholesterol, patient had been taking dexamethasone, 2 mg/day, to suppress the normal adrenal activity).

Samples from the left testis and its adenoma, which were excised 14 days after tracer injection, were assayed in a standard well counter with NaI(Tl) crystal and single-channel analyzer: 0.15 g of tumor and 0.46 g of normal tissue were counted. Water was added to each sample to bring the total volume to 1 ml and minimize absorption differences. The normal testis contained 7.74 × 10⁶ % dose/g of tissue; the adenoma 24 × 10⁶ % dose/g.

DISCUSSION

Testicular neoplasms are among the more common tumors in men between 20-40 years of age. (7,8) Most are of germinal-cell origin, do not secrete steroids, and would not be expected to concentrate radiocholesterol. However, about 1.2% of them are interstitial-cell tumors, which may secrete testosterone, estrogen, or both (9). Although usually palpable, occasionally the tumor is difficult to detect. In women, functioning tumors account for 15-20% of all solid ovarian neoplasms and are less readily palpable (10). Currently available procedures for detection of testicular and ovarian neoplasms are limited. The plasma hormone levels in samples obtained by selective venous catheterization are informative in testicular neoplasia (9), but hospitalization and an experienced venographer are necessary. Venography is helpful in confirming the presence and site of adrenal adenomas but is not applicable to gonadal neoplasms. Thus a noninvasive imaging method for the detection of gonadal tumors would be useful.

The steroid hormones are formed only in the gonads and the

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TABLE 1. PLASMA ESTRADIOL, TESTOSTERONE, LUTEINIZING HORMONE AND FOLLICLE STIMULATING HORMONE IN PERIPHERAL AND SPERMATIC VENOUS BLOOD

<table>
<thead>
<tr>
<th></th>
<th>Estradiol (pg/ml)</th>
<th>Testosterone (µg/100 ml)</th>
<th>Luteinizing hormone (mIU/ml)</th>
<th>Follicle-stimulating hormone (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral vein</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal male range</td>
<td>13-59</td>
<td>0.28-1.44</td>
<td>4-24</td>
<td>50-450</td>
</tr>
<tr>
<td>Patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-op</td>
<td>226</td>
<td>1.0</td>
<td>9.2</td>
<td>&lt;25</td>
</tr>
<tr>
<td>Post-op</td>
<td>44</td>
<td>1.43</td>
<td>23.8</td>
<td>306</td>
</tr>
<tr>
<td>Left spermatic vein</td>
<td>7750*</td>
<td>27.7*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
* Obtained at surgery

adrenal cortex, with cholesterol as the principal precursor. Adrenocortical and gonadal cells can synthesize cholesterol directly or absorb it from the plasma (11,12). Iodocholesterol and endogenous cholesterol appear to be metabolized similarly by the steroid-secreting cells (1).

Data are limited regarding the uptake of iodocholesterol by human gonads (13,14). Distribution studies in animals indicate that it is concentrated by both ovary and testis, although less than by the adrenal glands, whose cholesterol content and daily steroid production are normally much greater than those of either gonad. Steroid-secreting gonadal neoplasms may perhaps have an enhanced uptake of cholesterol from the plasma. In the patient reported here, the adrenal uptake of 1-131 cholesterol was suppressed by the administration of dexamethasone. Thus, through reduced competition, might have enhanced the concentration of radiocholesterol by the testicular tumor, though this is speculative.

Our patient's tumor was not seen in the 8- and 10-day images, and these intervals may not have been optimum. Background problems should be less constraining in testicular than in adrenal imaging, so perhaps our scintigrams should have been made earlier. The 3:1 tumor-to-normal ratio that we found for the excised specimens suggests perhaps only 1:2:1 for the S/N ratio in a clinical scintigram, owing to background. Moreover, the fragments that we received for counting were so small that a sampling error cannot be ruled out. We need not be surprised, therefore, that the tumor was not visualized.

An isomer of iodocholesterol, 6-iodomethylcholesterol, has been shown to have significantly higher adrenal uptake than iodocholesterol itself (15), with an improvement of up to fiftyfold in rats (16). Possibly the testicular adenoma in our patient would have been visualized had iodomethylcholesterol been used.

The potential application of 19-[131I]-iodocholestrol and its isomers in the visualization of steroid-secreting neoplasms of the testis and ovary warrants further study.

FIG. 1. Pinhole scintiphoto of testes 8 days after injection of 1-131 iodocholesterol. There is slightly more generalized activity in left testis, but no focal accumulation in region of adenoma.

FOOTNOTE

* Searle Laboratories.

REFERENCES


THE JOURNAL OF NUCLEAR MEDICINE

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