GONADOBLASTOMA OCCURRING IN A PATIENT WITH FAMILIAL GONADAL DYSGENESIS

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Recent morphologic and histogenetic studies provide a basis for the classification of testicular and ovarian tumors of germinal, mesenchymal, and sex cord origin. That gonadal tumors in the male and female are identical and homologous is attributed to totipotentiality of the cellular components that contribute to the formation of the gonad. Seminoma, embryonal carcinoma, teratoma, and choriocarcinoma represent examples of germinal derivatives, whereas tumors of Leydig and theca cells and those of granulosa and Sertoli cells represent, respectively, mesenchymal and sex cord derivatives. Testicular tumors of multiple cell type usually arise from the germinal epithelium. Participation of sex cord and mesenchymal elements in the same tumor is more generally found in the ovary. The presence of all 3 embryologic forerunners in 1 tumor, which is least frequently found in the ovary, was first reported by Scully in 1953 under the name gonadoblastoma. This paper deals with the histologic and endocrine aspects of a case of gonadoblastoma and with a review of cases in the literature in which the morphologic or clinical findings, or both, were similar.

CASE HISTORY

The patient, a 22-year-old white woman (H.F.H., Case No. 797542), was first examined for a complaint of total absence of menstruation. Growth and development during childhood had been regarded as entirely normal. Body hair growth accompanied by some slight growth of the breasts occurred at the age of approximately 12 years, but full female secondary sex development did not follow. Strength and energy were normal, and there was no tendency to obesity. In the teens the patient developed moderate facial hypertrichosis, which was successfully treated by electrolysis. Administration of thyroid was not accompanied by any observed benefit. A period of estrogen therapy had produced a moderate vaginal discharge but no menses.

The past medical history was otherwise unremarkable. There was no history of mumps or pelvic inflammatory disease. The patient was of average stature for her family. Several siblings and half-siblings were apparently normal, with the exception of 1 younger sister who also experienced primary amenorrhea. Investigation of the gonadal status of this sister, reported to us by Drs. Sternberg and Gaskill of New Orleans, revealed rudimentary gonads and hypoplastic uterus. She presented none of the congenital anomalies characteristic of Turner’s syndrome, but the buccal smear for sex chromatin was negative.

When first examined, the patient was 65 inches tall and weighed 137 lb. Body proportions were normal, but an obvious absence of characteristic female subcutaneous fat gave the patient a lean angular appearance. There was little hypertrichosis, inasmuch as excessive facial hair had been removed. The voice was feminine. Breasts were small and flat. Gynecologic examination revealed a prominent 4-cm. clitoris and a very small but palpable uterus and cervix. No adnexal mass or gonads were delineated by physical examination, and the remaining findings were normal.

As the vaginal smear contained only cells from the basal layer no signs of stimulation by estrogen were revealed. No sex chromatin bodies were seen. Examination of leukocytes revealed no chromatin “drumsticks” in 1000

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cells counted and thus confirmed the sex chromatin-negative vaginal smear. Urinary gonadotropin titer exceeded 128 mouse uterine units, and urinary 17-ketosteroids were 13.5 and 14.4 mg. per 24 hr. Seventeen-hydroxysteroids were 12.5 and 14.9 mg. per 24 hr. (Porter-Silber chromagen with normal values for the method of 8 to 20 mg. per 24 hr.) There was a normal steroid response to administration of ACTH.

Exploratory laparotomy revealed a small uterus with normal fallopian tubes. The right gonad was rudimentary, being represented by a white band of tissue, and the left one appeared as a smooth mass, 2 by 4 cm., with a thick white capsule and cortical varicosities. Biopsy of the mass was interpreted as dysgerminoma, and the left fallopian tube and gonad were removed.

Recovery was uneventful. Institution of therapy with stilbestrol, 2 mg. daily in 3-week cycles, was followed by regular vaginal bleeding and by softening and rounding of the body contours with breast development and a further decrease in facial hair growth. Urinary 17-ketosteroids were 8 mg. per 24 hr. In the subsequent 6 years the patient has married and remains in good health, with no evidence of recurrence or metastasis of the tumor.

**PATHOLOGY**

The left gonad, which measured 3.6 by 2.4 by 1.2 cm., was cystic with intervening, moderately firm, tan, calcified areas (Fig. 1). The fallopian tube was not remarkable. The microscopic appearance of the gonad varied. The greater portion was cellular and divided by fibrous septums into irregular masses consisting of 2 distinct cell types with little pleomorphism. One type was loosely arranged large cells with moderate, lightly eosinophilic cytoplasm and single large vesicular nuclei that often contained prominent nucleoli and resembled cells of the germnoma. These were arranged in masses of varying size separated by fibrous stroma containing scattered single and small groups of lymphocytes (Figs. 2 and 3). Mitoses were infrequent, averaging 4 per 50 high power fields. The cells of the second type, which were smaller, with little visible cytoplasm and delicate nuclear chromatin and nucleoli, were loosely arranged in large masses separated by thick bands of hyalized fibrous tissue or lined cysts of varying size (Figs. 4 and 5). Mitoses were not found in 50 high power fields. At the periphery of the masses, the cells were often arranged radially with the long axis perpendicular to the central portion of the mass (Fig. 4). Within the aggregates the cells were arranged circumferentially around an eosinophilic, amorphous, laminated material, which sometimes contained irregular small calcium particles, or about a single large cell of the first type, being separated from it by a clear space. The former arrangement of cells resembles the Call-Exner bodies of granulosa cell tumors and occasional structures found in Sertoli cell tumors, whereas the latter simulates the primordial follicles of ovarian cortex (Fig. 6).

Associated with the above but not inextricably mixed was a lesser quantity of loosely arranged fibrillar tissue. The accompanying cells were uniform, elongated, oval, and polygonal, with round and oval uniform nuclei and a finely granular eosinophilic cytoplasm that infrequently contained fine brown pigment granules and small vacuoles. These resembled theca, luteinized theca, or Leydig cells (Figs. 7 and 8). The latter were present as single or small groups of cells blending with the loose theca tissue. A discrete large nodule of Leydig cells was found at the periphery of 1 section. Their nuclei were uniform, round, and centrally placed in an abundant eosinophilic cytoplasm that occasionally contained finely dispersed or clumped brown pigment granules (Figs. 9 and 10). No Reinke crystals were found.

At the periphery of this complexity of cells was a moderately vascular, compact, poorly fibrillar tissue containing many interlacing, elongated cells with little detectable cytoplasm. This tissue had the appearance of ovarian cortex. No primordial follicles were found. The surface was covered by a single layer of cuboidal germinal epithelium (Fig. 11).

The periodic acid-Schiff stain demonstrated a diastase-digestible polysaccharide in the cytoplasm of both germinal and granulosa-like cells. This stain was also posi-
Fig. 1. Solid and cystic cut surface of the enlarged left ovary and adherent fallopian tube. X 2.

tive in the eosinophilic tissue associated with the second cell type and in the pigment granules of cells of the Leydig nodule and the polygonal cells within the theca tissue, but here the reaction was unaltered by diastase. Sudan Black B and Flaming Red stains applied to paraffin sections colored the granules of the Leydig cells black and very pale pink, respectively. The Alcian Blue stain was negative.

The epithelium of the fallopian tube was typical but lacked cilia. The mucosal folds were delicate and the muscular wall thin.

DISCUSSION

There is no doubt that all 3 basic cell types are present in gonadoblastoma, but characterization of the tissue as ovarian or testicular is not always possible. The germinal cells are common to both seminoma and dysgerminoma, and the identity of the Leydig and ovarian hilus cell is generally accepted. Classification of the small dark cells of the reported tumor as granulosa or Sertoli cells is particularly difficult, but the problem is not unexpected in view of the inability to distinguish the 2 normal gonads at early developmental stages. The presence of apparently mature ovarian stroma at the periphery of the tumor favors its classification as an ovarian neoplasm, but the rudimentary right gonad and the negative sex chromatin study are evidence for tumor growth in a dysgenetic gonad.

Occurrence in a single tumor of all 3 of the basic cell types that enter into the formation of the gonad in the single tumor is rare and sets the rare gonadoblastoma apart from other ovarian and testicular neoplasms. Survey of the literature has revealed 3 cases reported as gonadoblastoma (Table 1) and 3 others that have been reviewed by Morris and Scully, of which has been reported. There are a number of other reported tumors that, although not histologically identical to gonadoblastoma, have some similar morpho-
logic features or associated endocrine abnormality, or both, that make them worthy of review. All of these have been basically dysgerminomas, a tumor generally regarded as being composed of neuter cells incapable of hormone production, and may be conveniently divided into 2 groups. One contains follicular structures resembling granulosa cells in addition to dysgerminoma, but without evidence of hormonal activity (Table 2), and the other is reported as a unicellular dysgerminoma with associated clinical endocrine abnormality, either in the form of masculinization or precocious puberty (Tables 3 and 4).

Dysgerminoma, unlike its counterpart the seminoma of the testicle, is generally found in “pure” form, but it has been associated with choriocarcinoma, teratoma, and granulosa cell elements. The latter has been reported 9 times unassociated with endocrine abnormality (Table 2). Schiller’s and Föderl’s cases were reported from the same institution and probably represent the same patients.

Endocrine abnormalities are not an uncommon occurrence with dysgerminoma, and associated virilization, with or without demonstrable hormonal abnormality, has been reported (Table 3). One of these tumors was “impure” and was interpreted as containing Leydig, follicular, and questionable theca tissue. We were permitted to review a representative section of the tumor and believe it is a gonadoblastoma containing mostly dysgerminoma, with a lesser quantity of theca-Leydig tissue and only rare small aggregates resembling granulosa and Sertoli cells.

The hormonal basis of the clinical endocrine abnormality associated with reported unicellular dysgerminoma is not clear, inasmuch as these cells are thought to be hormonally inactive. In order to induce sexual precocity, the tumor must either produce estrogen or secrete sufficient chorionic gonadotropin to stimulate the normal immature ovary. The lack of precocity even in those tumors containing recognized granulosa cell tissue makes unlikely the possibility of secretion of estrogen by an apparently unicellular dysgerminoma. On the other hand, increased titers of urinary gonadotropin, even with positive Ascheim-Zondek pregnancy tests, have been reported in dysgerminoma cases. Although these high levels of chorionic gonadotropin have been observed with apparently unicellular tumors, the known occurrence of choriocarcinoma in conjunction with dysgerminoma suggests that small foci of the former tumor may have been missed in random sections of a large growth. Inasmuch as choriocarcinomas 1 mm. in diameter have been reported to produce metastases with endocrine effects, it would be difficult to find such a focus in a large tumor by any method other than serial or subserial sections. Masculinization can be explained only by the excessive secretion of androgenic steroids. Chorionic gonadotropin is not virilizing in women. Accepting the hypothesis that the neutral dysgerminoma cell

![Fig. 2. Nodular cell masses similar to those of germinoma of the ovary and testis. Hema-toxylin and eosin. X 150.](https://academic.oup.com/ajcp/article-abstract/38/6/615/1763082)
FIG. 3 (upper left). Magnified area from Figure 2. Hematoxylin and eosin. X 730.

FIG. 4 (upper right). Areas resembling granulosa or Sertoli cells. Hematoxylin and eosin. X 150.

FIG. 5 (lower left). Cells lining one of the noncalcified small cysts resembling a Graafian follicle. Hematoxylin and eosin. X 730.

FIG. 6 (lower right). Higher magnification of a portion of Figure 4, showing an area with structures resembling Call-Exner bodies (A) and primary oocytes (B). Hematoxylin and eosin. X 730.
Fig. 7 (upper left). An area of thecomatous-appearing tissue with an admixture of elongated and polyhedral cells. The latter resemble Leydig cells. Hematoxylin and eosin. X 150.
Fig. 8 (upper right). Higher magnification of a portion of Figure 7. Hematoxylin and eosin. X 390.
Fig. 9 (lower left). Nodule of Leydig cells with adjacent calcification. Hematoxylin and eosin. X 150.
Fig. 10 (lower right). Higher magnification of a portion of Figure 9. Hematoxylin and eosin. X 730.
is not capable of secreting androgen, the presence of either theca or Leydig elements, or both, cells known to produce gonadal androgen, must be postulated. The gonadoblastoma with its virilizing effects is a classic example of such a combination of tissues.

We have had the opportunity of reviewing a single section of 2 of the reported dysgerminomas that have been associated with endocrine abnormality, 1 with a positive Ascheim-Zondek test, amenorrhea, and deep voice, and the other with virilization. Although a tissue explanation for the endocrine changes is not apparent in the sections, there are features suggesting that both tumors are more complex than dysgerminoma and that the hormone-secreting tissue had not been discovered. Although the first tumor was composed of germinal type cells, a tubular arrangement of Sertoli cells was the predominant tissue in the section examined. Compact mesenchymal tissue was also present. The second tumor, also composed chiefly of germinal cells, contained a small focus of granulosa-Sertoli cells surrounding individual germinal elements.

The cases reported by Hain and by Talas and associates further illustrate the need for persistence in searching for tissue elements to explain endocrine abnormalities, as well as the importance of hormone assays in the study of gonadal tumors. In the former, dysgerminoma had been diagnosed in a patient with precocious puberty and a positive Ascheim-Zondek test, but subsequent sectioning of the tumor uncovered a small focus of choriocarcinoma. The amenorrhea, hirsutism, and positive Friedman test associated with the tumor reported by Talas and associates were partially accounted for by the chorionepithelioma accompanying the dysgerminoma. The virilizing signs were attributed to increased tumor 17-ketosteroids. The authors believed that their failure to demonstrate Leydig elements to explain the elevated hormone values might be accounted for by inadequate sampling.

Hormonal abnormalities associated with gonadal neoplasms indicate the need for careful search for endocrinologically active tissue within the tumor. In an attempt to explain masculinization associated with dysgerminoma, Ber postulated hormone production of varied types by the tumor, which, although reported as a dysgerminoma, was of more complex nature in the opinion of a number of consulting pathologists. Plate, on the other hand, suggested that adrenal hyperactivity was the cause of the masculinization in his unusual case of dysgerminoma. Although removal of the tumor was followed by reduction of the elevated urinary 17-ketosteroids, the signs of masculinization were not abated. Assay of the tumor failed to reveal 17-ketosteroids. Subsequently the 17-ketosteroids returned to high levels but could be greatly reduced by adrenal-suppressing prednisolone therapy. Through the courtesy of Dr. Plate we have reviewed multiple sections of the tumor and of the opposite rudimentary gonad. The major
<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex Chromatin</th>
<th>Voice</th>
<th>Clitoris</th>
<th>Uterus</th>
<th>Ovaries</th>
<th>Menses</th>
<th>Breast</th>
<th>Fallopian Tubes</th>
<th>Hormone†</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Scully34</td>
<td>19</td>
<td>Negative muscle of appendix</td>
<td>Legs, arms, chest</td>
<td>Enlarged</td>
<td>Small</td>
<td>Left, no gonad; right, tumor</td>
<td>Primary amenorrhea</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Postoperative: no regression of virilization; rise in gonadotropins and hot flashes; alive 6½ yr. without recurrence</td>
</tr>
<tr>
<td>Scully34</td>
<td>8</td>
<td>Negative muscle of fallopian tube</td>
<td>Pubic hair</td>
<td>—</td>
<td>Enlarged</td>
<td>Right, tumor; left, not identified; tumor in cul-de-sac also</td>
<td>None</td>
<td>Underdeveloped</td>
<td>Left, not identified</td>
<td>Negative estrin and prolan in urine 24 hr. postoperatively</td>
<td>Increase in clitoris and pubic hair postoperatively; died within 18 mo. of rheumatic heart disease; no autopsy.</td>
</tr>
<tr>
<td>Teter46</td>
<td>19</td>
<td>Normal hair</td>
<td>—</td>
<td>Penile</td>
<td>Infantile</td>
<td>Right, tumor; left, ovary with seminiferous tubules</td>
<td>Infantile</td>
<td>Infantile</td>
<td>—</td>
<td>5 to 7.3 mg. 17-ks./day. &gt;100 and &lt;200 I.U. gonadotropin</td>
<td>Vagina infantile</td>
</tr>
</tbody>
</table>

* Dashes in the various columns indicate that the information was not included in the articles.
† ks., ketosteroids; F.S.H., follicle-stimulating hormone; M.U., mouse units; I.U., international units.
‡ Same case discussed by Mallory.14
TABLE 2  
DYSGERMINOMA WITH FOLLICULAR STRUCTURES*

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex Chromatin</th>
<th>Hirsutism</th>
<th>Voice</th>
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<th>Uterus</th>
<th>Ovaries</th>
<th>Menses</th>
<th>Breast</th>
<th>Fallopian Tubes</th>
<th>Hormone</th>
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<tr>
<td>Babes</td>
<td>13</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Very small</td>
<td>Bilateral tumor</td>
<td>None</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Metastases in lymph nodes</td>
</tr>
<tr>
<td>Föderl (Case 2)</td>
<td>13½</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Bilateral tumor</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Right tumor had follicles</td>
</tr>
<tr>
<td>Föderl (Case 9)</td>
<td>51</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Metastases had no follicles</td>
</tr>
<tr>
<td>Forster (Case 7)</td>
<td>25</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Left, normal; right, tumor</td>
<td>Infrequent</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Menses regular after removal of tumor</td>
</tr>
<tr>
<td>Klaften</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Granulosa elements predominated</td>
</tr>
<tr>
<td>Reifferscheid</td>
<td>21</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Small</td>
<td>Right, small</td>
<td>None</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sailer (Case 5)</td>
<td>21</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Normal</td>
<td>Left, normal; right, tumor</td>
<td>Normal</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Schiller (Case 7)</td>
<td>14</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Normal</td>
<td>—</td>
<td>None</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Schiller</td>
<td>51</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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* Dashes in the various columns indicate that the information was not included in the articles.
<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex Chromatin</th>
<th>Hirsutism</th>
<th>Voice</th>
<th>Clitoris</th>
<th>Uterus</th>
<th>Ovaries</th>
<th>Menses</th>
<th>Breast</th>
<th>Fallopian Tubes</th>
<th>Hormone†</th>
<th>Comment</th>
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</thead>
</table>
| Ber⁴  | 25  | —             | Positive  | Low   | Enlarged | Small  | Right, small; left, tumor | None   | Small  | —               | Preoperative: F.S.H., 1066 M.U./l. urine; L.H., 833 M.U./l. urine; <167 M.U. estrogen/l. urine; 67 M.U. androgen/l. urine  
Postoperative: F.S.H., 555 to 833 M.U./l. urine; L.H., <333 M.U./l. urine; <167 M.U. estrogen/l. urine; <20 M.U. androgen/l. urine extract; <10,000 M.U. gonadotropins/kg. tumor; <100 M.U. gonadotropins/kg. tumor extract; positive Ascheim-Zondek test | Well 18 mo. postoperatively |
<p>| Blocksa² | 21  | —             | Positive  | Low   | Enlarged | Small  | Bilateral tumors | —      | Moderately developed | Small  | —               | Reared as a male |
| Gough⁸ | 15½ | —             | Positive  | Deep  | Very large | Small  | Right, rudimentary; left, tumor | None   | Small  | Small          | —               | Decrease in virilization after removal of tumor; “no hair growth on face, never shaves. Less mannish in outlook, but not married at age 49” |</p>
<table>
<thead>
<tr>
<th>Plate</th>
<th>22, 24</th>
<th>Seegar</th>
<th>Teter</th>
<th>Tietze</th>
<th>Usizima</th>
<th>23 to 28 mg. 17-ks./24 hr.; 0.72 mg. 11 oxytocoids/24 hr.; estrogen, 25 U./24 hr.; negative 17-ks. in tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 12</td>
<td>27</td>
<td>Negative (skin)</td>
<td>Positive</td>
<td>Deep</td>
<td>Enlarged</td>
<td>Normal</td>
</tr>
<tr>
<td>30</td>
<td>Heavy beard</td>
<td>Deep</td>
<td>Enlarged</td>
<td>Infantile</td>
<td>Present</td>
<td>—</td>
</tr>
<tr>
<td>Case 8</td>
<td>26</td>
<td>Negative</td>
<td>Normal</td>
<td>—</td>
<td>Penile</td>
<td>Fetal</td>
</tr>
<tr>
<td>10</td>
<td>—</td>
<td>—</td>
<td>Somewhat enlarged</td>
<td>Small</td>
<td>Left, tumor; right, —</td>
<td>None</td>
</tr>
<tr>
<td>48, 49</td>
<td>Positive</td>
<td>Deep</td>
<td>Somewhat enlarged</td>
<td>Small</td>
<td>Right, tumor; left, normal</td>
<td>None</td>
</tr>
</tbody>
</table>

* Dashes in the various columns indicate that the information was not included in the articles.
† M.U., mouse units; F.S.H., follicle-stimulating hormone; L.H., luteinizing hormone; ks., ketosteroid.
TABLE 4

**DYSGERMINOMA WITH PRECOCIOUS PUBERTY**

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex Chromatin</th>
<th>Hirsutism</th>
<th>Voice</th>
<th>Clitoris</th>
<th>Uterus</th>
<th>Ovaries</th>
<th>Menses</th>
<th>Breast</th>
<th>Fallopian Tubes</th>
<th>Hormone†</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hain¹⁰, ¹³</td>
<td>8</td>
<td>—</td>
<td>Pubic and axillary</td>
<td>—</td>
<td>—</td>
<td>Adult</td>
<td>Right, normal; left, tumor</td>
<td>Yes</td>
<td>Developed</td>
<td>—</td>
<td>17-ks., 8.4 mg./24 hr.; positive Ascheim-Zondek test Postoperative: excessive follicle-stimulating hormone in urine</td>
<td></td>
</tr>
<tr>
<td>Rendu and Pouaet²⁷</td>
<td>6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Normal</td>
<td>Right, normal; left, tumor</td>
<td>Yes</td>
<td>Enlarged during menstruation</td>
<td>Normal</td>
<td>—</td>
<td>&quot;Signs and symptoms of precocious puberty disappeared after tumor was removed. Menarche 5 yr. postoperative (age 13) with regular menses. Well, without recurrence or metastases 14 yr. later. Choriocarcinoma discovered subsequent to report.&quot;¹² Considered left gonad an ovo-testis.</td>
</tr>
</tbody>
</table>

* Dashes in the various columns indicate that the information was not included in the articles.

† ks., ketosteroids.
portion of the tumor was dysgerminoma, but there was a peripheral rim of loose theca-Leydig tissue that, we believe, could have contributed to the virilization. The opposite gonad was primarily a mass of interweaving spindle cells, in the midst of which was a small group of Leydig cells. A small group of tubules in 1 area resembled rete testis or ovarii. The absence of granulosa-Sertoli elements precludes classification of the tumor as gonadoblastoma. We believe it should be regarded as a combined germinal-mesenchymal gonadal tumor, although it could be termed a germinoma arising in a dysgenetic male gonad of which the Leydig cells are a remnant.

Gonadal tumors have been reported to arise frequently in the dysgenetic gonad. Apparently the failure of normal differentiation and maturation of germinal tissue is related to the genesis of germinomas, and Meyer claimed that dysgerminoma most frequently developed in hermaphroditic subjects, although subsequent reports encompassing more than 400 cases have not confirmed the frequency of this relation. Spielman and Motyloff have again reported dysgerminoma occurring in a male hermaphrodite whose sister also presented the features of gonadal dysgenesis. Other well established instances of germinomas associated with dysgenetic gonads are the cases of Teter and Tarlowski and Plate (Table 3). Both patients had negative sex chromatin with a rudimentary gonad on the side opposite the germinoma. Theca-Leydig remnants of the dysgenetic gonad rather than the dysgerminoma may account for the virilizing signs in these instances.

The gonadoblastoma reported here arose in 1 of 2 similar siblings. Scully reported chromatin negativity in tissues obtained from his 2 cases, although the preparations were probably not ideal for this study. The tumor reported by Usizima, however, which we have reviewed and classified as gonadoblastoma, apparently arose from a normal ovary. The virilization of this patient abated after excision of the tumor, and that menstruation ensued provides substantial evidence of a normal remaining ovary. It can not be stated that dysgenesis of the gonad is a prerequisite for the growth of gonadoblastoma.

Virilization has characterized all patients with gonadoblastoma. The clinical lack of estrogen has not been validated by hormone assay; although the elevated gonadotropin titer in the present case (if not chorionic gonadotropin) is consistent with failure to secrete estrogen. The virilism is believed to be caused by secretion of androgen by the tumor and abates with its removal. Present evidence indicates that 17-ketosteroids are not significantly elevated, as is common in cases of the virilizing adrenal tumor.

The clinical features of the present case suggested male pseudohermaphrodism. The physical habitus was that of a mildly virilized female with primary amenorrhea. Sex chromatin was negative. Deficiency of estrogen was confirmed by demonstration of atrophic vaginal epithelium, and the elevated urinary gonadotropin is interpreted as reflecting the failure of the mechanism for estrogen feedback. The possibility that the tumor produced gonadotropin, however, can not be excluded, inasmuch as the urine assay was not repeated postoperatively and exact characterization of the gonadotropin was not performed. Clinical evidence of androgenic influences were undeniable but not conspicuous. The 17-ketosteroids were in the normal range, and the 5-mg. decrease in 17-ketosteroids after removal of the tumor does not necessarily reflect the removal of the growth. The patient was receiving estrogen at the time, a therapy capable of reducing urinary 17-ketosteroid levels in virilized women. The feminization that occurred with postoperative estrogen therapy and that was not obtained prior to removal of the tumor is substantial clinical evidence that the tumor was secreting androgen. The patient's sister was not virilized but presented the problem of primary amenorrhea, hypoestrinism, and sex chromatin negativity. There was no tumor arising from her rudimentary gonads. The case under consideration is believed to represent the same genetic defects, but to have developed the virilizing gonadoblastoma at puberty.

SUMMARY

This paper pertains to the clinical and pathologic findings associated with a complex masculinizing tumor that featured cellular elements related to germinal, sex
cord, and mesenchymal derivatives and arose in a patient with dysgenetic gonads. The pertinent literature was reviewed, and tumors of similar morphology and dysgerminomas with endocrine abnormality are tabulated. The endocrine manifestations of gonadoblastoma and apparent functional dysgerminomas are discussed.

Although the number of recognized gonadoblastomas is small, evaluation of some of the functional dysgerminomas indicates that more careful scrutiny of the morphology of the tumor and its correlation with endocrine abnormalities may lead to recognition of a greater number of ovarian tumors featuring varying combinations of germinal, sex cord, and mesenchymal derivatives.

SUMMARY IN INTERLINGUA

Iste communication presenta le constataiones clinic e pathologic associate con un complexe tumor masculinisante que exhibiva elementos cellular relationate con derivatos germinal, mesenchymal, e de funiculo de sexo e que se disveloppava in un patiente con gonades dysgenetic. Le pertinente litteratura es revistate, e tumores de simile morphologia e dysgerminomas con anormalitate endocrin es tabulate. Le manifestationes endocrin de gonadoblastoma e apparente dysgerminomas functional es discutite.

Ben que le numero del recognoscite gonadoblastomas es micre, le evalutation de certes del dysgerminomas functional indica que un plus meticulose scrutinio del morphologia del tumor e su correlation con anormalitates endocrin va possibilemente resultar in le recognition de un plus grande numero de tumores ovarian con varie combinationes de derivatos germinal, mesenchymal, e de funiculo de sexo.

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