Unilateral Streaked Ovary Syndrome

Slotnick-Goldfarb’s Syndrome

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A case of unilateral streaked ovary (Slotnick-Goldfarb’s syndrome) is reported and documented with hormonal, chromosomal, laparoscopic, and histologic studies. It is postulated that viral oophoritis associated with mumps might explain the coexistence of a streaked ovary of a congenital origin with a hypoplastic ovary, that would be the expression of a factor acting in postnatal life.

Streaked ovary syndromes in phenotypic females with 46/XX karyotypes have been generally classified under the designation of XX gonadal dysgenesis. These patients have primary amenorrhea, lack of secondary sexual development, a normal stature, and a eunuchoid habitus. However, a unilateral streaked ovary associated with a contralateral hypoplastic ovary has been reported in otherwise normal phenotypic females. Some of these patients have associated virilization; others develop secondary amenorrhea after a period of oligohypomenorrhea and seem to be included in the syndrome defined by Slotnick and Goldfarb.

The etiology of this latter entity is not clear. However, it is conceivable that the unilateral streaked ovary results from a congenital unknown factor, whereas the associated hypoplastic ovary is the expression of entirely different factors acting on the only normal ovary in postnatal life. It is noteworthy that among these, the mumps virus can localize in the ovary and completely destroy the follicular apparatus, thus causing fibrosis and ovarian hypoplasia.

Assuming that such a hypothetical viral factor had not been involved, it seems pertinent to question if there may not be a number of women with a unilateral streaked ovary associated with a normal contralateral ovary who are not identifiable just because they are asymptomatic. Only those developing ovarian failure would seek medical care and thus eventually be diagnosed as having gonadal dysgenesis.

The purpose of this presentation is to report 1 patient with Slotnick-Goldfarb’s syndrome in whom a past history of mumps and measles might be related to the etiology of the hypoplastic ovary.

CASE REPORT

This married white female (ICA), 33 years of age, gravida 0, was first seen by us in April 1968 because of primary infertility and longstanding secondary amenorrhea. She had her first and only spontaneous menstrual flow at the age of 15. From then on she developed secondary amenorrhea and complained of hot flashes. Estrogen-progesterin medication administered at irregular intervals sometimes resulted in scanty withdrawal uterine bleeding. There were no other symptoms or complaints.

She was born by a normal vaginal delivery after an uneventful term pregnancy and had good vital signs at birth. Her development was considered to be normal up to adult age. The only diseases she had were mumps and measles in her late childhood. She has only one brother who is fertile. Thearche and pubarche were around age 15.

On physical examination the following data were collected: weight, 73 kg; height, 1.62 m and a span of 1.64 m; arterial blood pressure, 115/85 mmHg. The thyroid gland was not palpable. The breasts were normal size, type 4 (mainly due to adipose tissue, since the mammary gland could hardly be palpated). The patients skin and distribution and growth of the hair system were normal as were the vulva and clitoris. The vagina was normal; maturation index was 0/75/25; the Papaincolau smear was class 1. The cervix was small without any apparent lesions. On pelvic examination a small uterus was palpated with a cervical fundal external height of approximately 5 cm. The adnexa were not palpable.

Pertinent laboratory data included PBI, 3.0 μg/100 ml (total iodine, 4.4 μg/100 ml); BEI, 2.8 μg/100 ml. Routine urinalysis was normal. Total urinary gonadotropins were 15 hMG/units/24 hr; urinary estrogens (in μg/24 hr) estriol, 7.6; estrene, 3.1; 17 β-estradiol, 1.2; the karyotype was 46/XX.

On July 14, 1969, a diagnosis of primary ovarian failure and hypothyroidism was made. A progestosterone withdrawal test (50 mg/day X 3, IM) was negative. The patient was then started on an initial substitutional and continuous medication with thyroid extract (Thyronin, Organon Company) 50 mg/day, triiodothyronine (20 μg) and thyroxine (180 μg) (Diotroxin, Gliaxo, equivalent to 2 tablets), and enthynylestradiol, 10 μg daily (Lynoral, Organon).

* Humegon, Organon Company, OSS, Holland

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Company). After 4 months the patient discontinued the medications because of tachycardia and tremors. On December 21, 1969, she had a scanty "menstrual" bleeding. The basal body temperature (BBT) charts were hypothermic and monophasic. Two months later she resumed the medication with thyroid extract, 75 mg/day. On August 8, 1970, she was doing well, with no hot flashes but still amenorrheic; the uterus was still small and the cervix had a little mucus. Cyclic estrogen therapy was then instituted with 150 µg/day ethinylestradiol (Lynoral) for periods of 3 weeks with a pause of 1 week. She had regular withdrawal bleedings and felt well. A sequential oral contraceptive was then prescribed as adequate substitutional therapy.

In October 1972, after having stopped all medication for 3 months she was reinvestigated. Total urinary gonadotropins were 18 hMG units/24 hr; urinary estrogens (in µg/24 hr): estriol, 5.4; estrone, 2.3; 17β-estradiol, 2.0; PB1 was 7.3 µg/100 ml; total iodine, 7.8 µg/100 ml; urinary testosterone, 10.5 µg/24 hr.

The sequential oral contraceptive was again prescribed, and thereafter the patient bled every month. In April 1973, after a pause of 2 months, the patient was again reevaluated; total urinary estrogens were 1.2 µg/24 hr; thyroxin (adjusted) was 9.12 µg/100 ml of blood.

A hysterosalpingogram was then done and showed bilateral tubal patency. The patient's husband was studied and was considered subfertile in view of a sperm count of 11,000,000/ml with an ejaculate of 2.5 ml.

Because this patient was very anxious to become pregnant, it was decided to give her a trial of hMG stimulation therapy although it was anticipated that the chances of success were practically none if the bioassays of urinary gonadotropins were correct. The radioimmunoassays for FSH and LH were not yet set for our laboratory. However, blood was collected and the plasma frozen for evaluation at a later date.

The first course of stimulation with hMG (Humegon) was started in October 1973 with daily monitoring of total urinary estrogens. The initial dose was 75 hMG units/day; this was increased by two-thirds after 5 days if there was no response, and thereafter by two-thirds of the previous daily dose every 5 days if no change was observed in the excretion of total urinary estrogens.
Thus, in the first course of treatment a total of 4615 units of hMG were given over 26 days. The daily excretion of total urinary estrogens remained always below 5 μg/24 hr (Figure 1).

A second course of treatment was started in March 1974. The initial daily dose was 225 hMG units. The increase in injected hMG followed the same pattern as in the first treatment. A total of 6300 IU hMG was administered over 18 days. The excretion of total urinary estrogens again was always below 5 μg/24 hr (Figure 2). The BBT was always low and monophasic. There was no enlargement of the gonads. The cervix remained closed and showed no mucus. Two weeks after discontinuing the treatment, blood was again collected for plasma FSH and LH radioimmunoassay.

Plasma FSH taken prior to the first course of hMG stimulation was later found to be 45.6 mIU/ml. Two weeks after the last course, plasma FSH was 48 mIU/ml, and LH was 9.2 mIU/ml. A laparoscopy was then performed and biopsies taken from both ovaries. A unilateral streaked ovary with a contralateral hyperplastic ovary was found (Figure 3). The histologic examination showed marked fibrosis and a complete absence of graafian follicles in both ovaries (Figures 4 and 5). An attempt was made to do a chromosome study with fragments from both ovaries, but the cultures failed to grow. A stimulation of the pituitary with 100 μg of synthetic FSH-LHRH* showed a positive response of FSH with a peak of 73 minutes. LH could not be assayed due to an accidental loss of the samples (Figure 6).

**DISCUSSION**

The fact that this 46/XX patient with Slonick-Goldfarb's syndrome developed normally through puberty is strongly suggestive that up to the onset of her secondary amenorrhea the hyperplastic ovary was at least partially active in secreting estrogens. If this had not been the case, one would expect to see in this patient an eunuchoid habitus and a lack of secondary sexual development.

* Synthetic FSH-LHRH and kits for the radioimmunoassay of FSH and LH, Istituto Farmacologico Serono, Rome, Italy.
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Another alternative source of estrogens could have been the adrenal, which in puberty increases its steroid secretion (adrenarche). Although these corticosteroids may indeed play a role in secondary sexual development, they are not involved in the onset of spontaneous menstrual bleeding. Even assuming that gonadotropins might stimulate adrenal function (an assumption which has never been demonstrated), the lack of response to a massive treatment with hMG does not support such a view.

Therefore, it seems more appropriate to postulate that in this case the hypoplastic source of estrogens might have been the result of a silent viral oophoritis which partially destroyed a normal ovary. The functional potential of this ovary would be limited, thus resulting in a premature failure. Other factors of premature ovarian failure could also be involved in this case.10

The work of Jones et al 17 indicating that the ovaries of some patients with amenorrhea and hypergonadotropism may sometimes respond to hMG suggested our trial of stimulation at a time when the ovarian biopsy which showed that there was a lack of follicular apparatus had not yet been studied.

In view of the fact that this patient had a normal karyotype, it was decided not to perform a bilateral oophorectomy as a prophylactic measure against gonadal tumor development.

The patient is now on substitutional therapy with a sequential oral contraceptive.

REFERENCES

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