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Clinical mixed gonadal dysgenesis without Y chromosome

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GONADAL DYSGENESIS most commonly presents with a 45,X karyotype (Turner's syndrome). The characteristic clinical features include short stature, low-set hairline and ears, pigmented nevi, short fourth metacarpal, cubitus valgus, coarctation of the aorta, hypertension, renal anomalies, and lack of secondary sexual characteristics.

The next most common type of gonadal dysgenesis is

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the chromatin-positive mosaic (Turner variant), which usually has the karyotype 45,X/46,XX. The phenotype can range from normal to that of Turner's syndrome depending on the percentage of 45,X cells.

Less commonly the karyotype may be a mosaic with a 45,X cell line and a Y chromosome-bearing line, usually 45,X/46,XY. These individuals present with varying degrees of testicular differentiation and consequently present with varying degrees of male and female internal and external genital development depending in part on the percentage of Y-bearing cells.

In a small percentage of patients with the Turner syndrome or the variant, phallic enlargement or some degree of masculinization may be present.¹ However, testicular differentiation will not be present. We will report what we believe is the first case of clinical gonadal dysgenesis with a mosaic 45,X/46,XX karyotype and a differentiated testis.

W. D. was born with a normal vagina and developed an enlarged clitoris at 6 months of age that was amputated at age 2 years. Because of suspected intersex problems an intra-abdominal left gonadal biopsy was performed at age 4 years. This histologically revealed seminiferous tubules and epididymis. Pubarche began at age 12 years. At age 13½ years there was voice deepening and an increase of hair on the upper lip. At age 15 the patient underwent exploratory laparotomy for gonadectomy at Philadelphia General Hospital. The larche had not occurred as yet. The vagina had a normal depth of 6 cm. A small cervix and small arcuate uterus were present. An ectopically placed right Fallopian tube was removed. A streak gonad was visualized in the right pelvis and was surgically removed. Histology showed tubular structures and epididymis. On the left side, a 1.5 by 1 by 0.5 cm., smooth and glistening gonad was removed. Pathologic examination revealed male testicular tissue.

At age 17 years the patient was only 56 inches tall. Karyotype revealed mosaicism with seven of 19 cells being 46,XX and 12 of 19 cells being 45,X. However, she had no other somatic features of Turner's syndrome other than short stature. Intravenous pyelogram showed crossed, fused ectopic kidneys. Physical examination was normal with the exception of a Grade 2 crescendo-decrescendo murmur in the aortic area.

Laboratory studies prior to gonadectomy revealed a serum testosterone level of 220 µg per 100 ml. (normal up to 60). Follicle-stimulating hormone was 47 mI.U. per milliliter, luteinizing hormone was 31 mI.U. per milliliter, serum estrogen was 70, and progesterone was 0.8. 17-Ketosteroids were 12.4 mg. per 24 hour period, while hydroxycorticosteroids were 2.4 mg. every 24 hours with urinary creatinine at 964 ng. per 24 hour period. Bone age was commensurate with chronologic age.

At age 17 years further chromosome evaluation was under-

taken. Karyotyping of skin revealed the same 46,XX/45,X pattern. Banding failed to reveal any evidence of a Y chromosome. Her blood was also negative for H-Y antigen.

The patient has a teenage brother and a teenage sister and both have normal sexual development.

Individuals with 45,X/46,XX mosaicism, which is the most common type of chromatin-positive gonadal dysgenesis, usually have fewer of the somatic abnormalities characteristic of the Turner syndrome. The most common abnormality in this Turner syndrome variant is short stature as seen in the patient presented. The renal abnormalities seen in this case also are common. In persons with this mosaicism one or both gonads can be streak, hypoplastic, or normal gonads. In this case the left gonad was definitely identifiable as a testicle while the right gonad showed no gametic tissue.

Because of decreased negative feedback from dysgenetic gonads there may be relatively increased gonadotropins prenatally causing excessive stimulation of the hilar-mesonephric cells with resultant increased androgens. This may result in phallic hypertrophy or other masculinization in patients with Turner syndrome or the chromatin-positive variant. However, to our knowledge there has never been a report of a subject with 45,X/46,XX mosaicism with testicular differentiation, as in this report. Phenotypically, for this patient a diagnosis of mixed gonadal dysgenesis and a 45,X/46,XY karyotype would be most consistent. However both chromosome banding and H-Y antigen studies failed to demonstrate the presence of a Y chromosome.²

The testis in this patient apparently functioned to a degree to cause phallic enlargement, and voice change and hirsutism at puberty. The testis apparently did not secrete müllerian inhibitory factor since bilateral Fallopian tubes were present as well as the upper half of the vagina, the cervix, and the uterus.

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