Incomplete Testicular Feminization

In 1953, the syndrome of testicular feminization was defined (Morris, 1953). In 1963, the incomplete form of the syndrome was described (Morris and Mahesh, 1963). This distinction is of great clinical importance because while the former patients always become feminized at puberty, the latter may become virilized, and must therefore be treated before the onset of puberty.

Case Report

The patient, now aged 13½ years, was born with ambiguous genitalia and was thought to be a boy. No chemotherapy was given during pregnancy. One of her 4 married aunts is childless but all other female relatives are normal.

At 6 months of age, her phallus was 0.9 cm. She had a single urogenital opening and one palpable gonad. The urethrogram showed a blind vagina (Fig. 1). Skin and polymorphonuclear leucocytes were chromatin negative. Urinary steroids and bone age were normal. Because of the small size of the phallus, the patient was reared as a girl.

Laparotomy at the age of 5½ years showed a blindly-ending vagina with no uterus or tubes. Gonadal histology showed immature testicular tissue with 16% spermatogonia and small groups of Leydig cells close to the basement membranes (Fig. 2).

At 12½ years the patient began to become virilized.

She was 148 cm. tall (50th centile for age). Her phallus was 5 cm. long. She had sparse black pubic hair but no axillary or facial hair. Her voice had not yet deepened. Her chromosomes showed a 46,XY normal male pattern (Mr. L. J. Butler). Her 24-hour urinary 17-ketosteroids were 1.7 mg. and 17-ketogenic steroids were 3.1 mg. No pregnanetriol was found. Her 24-hour urinary testosterone was 13.8 µg. which was higher than expected for a prepubertal male (Dr. J. S. Jenkins). Her plasma testosterone and 5-dihydroxy-testosterone levels were 171 and 100 mg./100 ml. which are about 5 times the levels expected for a girl of 11 years (Mr. B. S. Thomas). Her urinary gonadotrophins (radioimmunoassay) were normal for age.

Bilateral orchidectomy and clitoridectomy were performed at 13½ years. The gonads measured 3×1.7×1.5 and 2.8×1.6×1.4 cm. and macroscopically resembled normal testes. The tubules were small and in 18% there were spermatogonia. Spermatogenesis had proceeded only to the primary spermatocyte stage. The tubular basement membrane was thickened and peritubular fibrosis was seen. Leydig cells and epididymis were normal.

It is proposed to delay oestrogen replacement therapy until about 15 years of age, i.e. when the patient has reached an acceptable adult height.

Discussion

This patient has testicular feminization because she has testes and a vagina and normal male chromosomes. Her testes show no ovarian tissue. She has the incomplete form of the disorder

FIG. 1.—Urethrogram showing the vagina opening into the posterior urethra.

FIG. 2.—Photomicrograph of gonad at the age of 5½ years. Immature seminiferous tubules and persistence of Leydig cells. (van Gieson $\times 100$.)

because she has a clitoris (or small phallus) and fusion of the labioscrotal folds, this indicating that she has some but incomplete tissue response to androgens. Her genitalia have been ambiguous since birth.

She does not have any of the other chromatin-negative disorders causing ambiguity of sex. She is not a true hermaphrodite (no ovarian tissue) and does not have congenital adrenal hyperplasia (because of her repeatedly normal steroid studies). Chromosome studies exclude the XO/XY syndrome. Hypospadiac males do not have a vagina nor such ambiguous genitalia.

The patient's gonads resembled undescended testes histologically and this has been described previously (O'Leary, 1965). In normal children, Leydig cells are present for the first few months of life, then disappear and reappear with the onset of puberty at 9 years or later (Charny, Conston, and Meranze, 1952). Increased numbers of Leydig cells have been found in patients with complete testicular feminization (Morris and Mahesh, 1963; O'Leary, 1965). In our patient, Leydig cells were present at 5½ years. This is abnormal but unexplained.

The clinical and biochemical features of both the complete and incomplete form of the disorder were reviewed recently (Raiti, 1970). Patients with the complete form should not be treated until after puberty, i.e. when growth in stature is complete.

Patients with the incomplete form must be recognized in childhood and must be treated before the age of puberty. Failure to do so will lead to virilization, some features of which (e.g. voice changes) are irreversible.

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